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SIMPLE SYNTHETIC METHOD FOR 1,2,3,3a,8,8a-HEXAHYDRO-PYRROLO[2,3-*b*]INDOLES HAVING A HALOGEN OR AN OXYGEN FUNCTIONAL GROUP AT THE 3a-POSITION[1,#]

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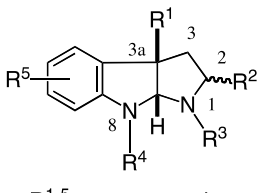
Abstract – 1-Methoxy-*N*b-methoxycarbonyltryptamine derivatives are successfully converted by either halogenating reagents or iodine/morpholine to 1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indoles having a halogen or an oxygen functional group at the 3a-position. Synthesis of the corresponding methyl 1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole-2-carboxylates is also reported.

INTRODUCTION

We have thus far created our own lead compounds such as potent root growth promoters,[3] anti-osteoporosis agents,[4] α_2-blockers,[5] and inhibitors of platelet aggregation.[6] In our continuing research for finding new biologically active compounds, we noticed 1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indoles having a functional group at the 3a-position, a group of compounds having general formula of **1** (Figure



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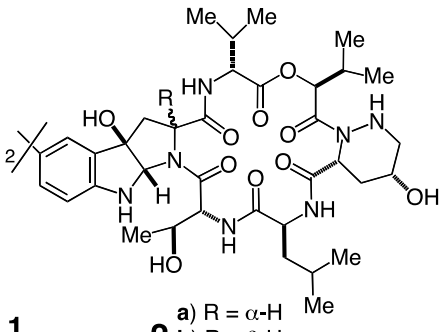
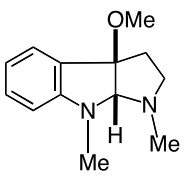


2 **a**) R = α-H **b**) R = β-H



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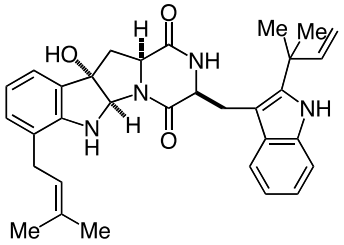

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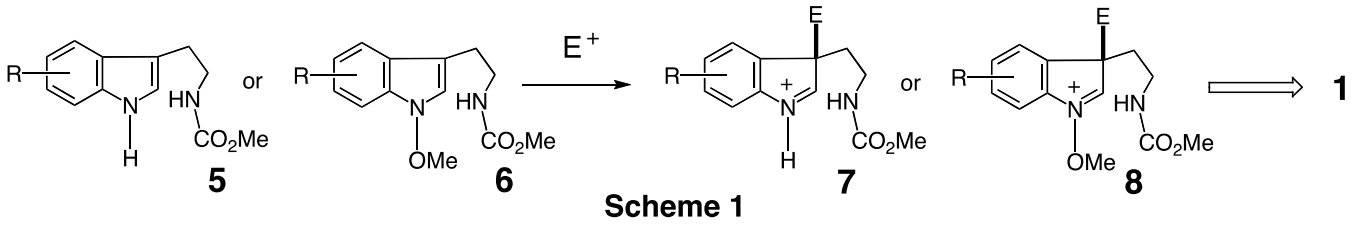
Figure 1

Dedicated to the 75th birthday of Prof. Dr. Lutz F. Tietze

1), as a promising candidate. Himastatin[7] (**2a**), *iso*-himastatin[7] (**2b**), FP1[8] (**3**), and (+)-okaramine J[9] (**4**) are typical examples belonging to 1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole alkaloids with an oxygen functional group at the 3a-position. We considered that electrophilic addition reaction of an appropriate tryptamine derivative (**5** or **6**), has a chance to achieve our goal (Scheme 1). Especially 1-methoxytryptamine derivatives would be suitable substrates because comparing the reaction intermedi-



Scheme 1

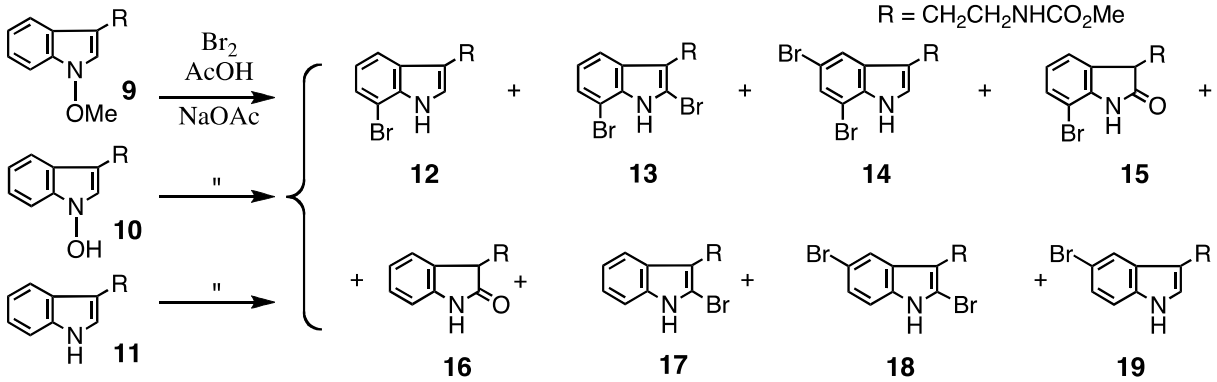
ates (**7** or **8**), **8** is expected to be more stable than **7** due to the presence of oxygen atom at the 1-position, culminating into the formation of **1**. Based on the working hypothesis, we intensively examined halogenation of *N*b-substituted tryptamine, 1-hydroxy-, and 1-methoxytryptamine derivatives. This report is a full paper for the previous communications[10, 11] with new results.

RESULTS AND DISCUSSION

I. Reactions of 1-methoxy- (9), 1-hydroxy-*N*b-methoxycarbonyltryptamine (10), and *N*b-methoxycarbonyltryptamine (11) with halogenating reagents

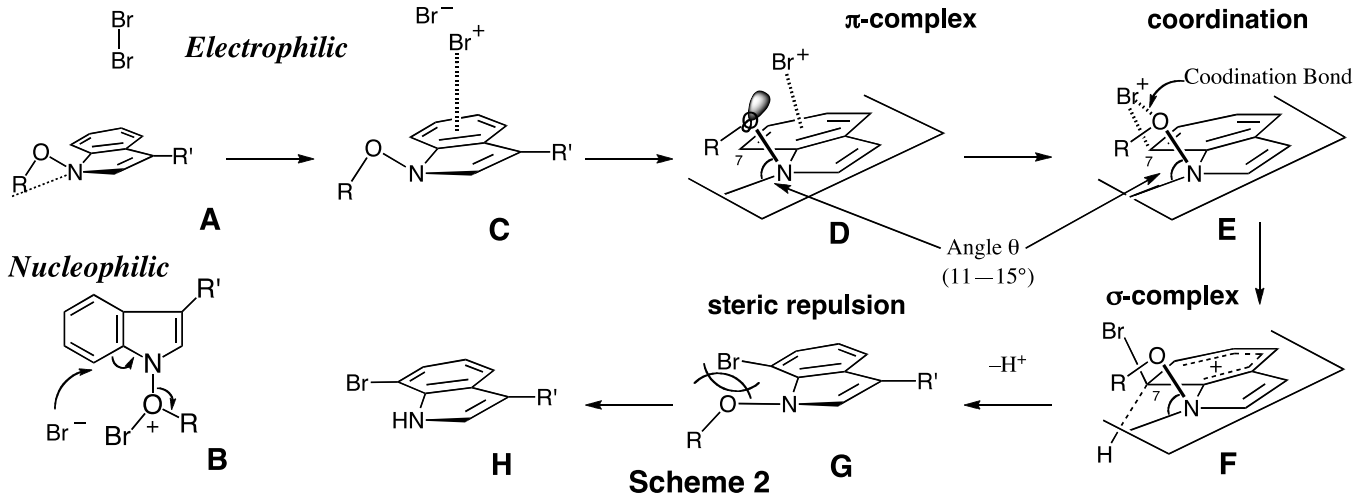
Since we have created 1-hydroxyindole chemistry,[12] we can supply any type of 1-hydroxyindole

Table 1. Bromination of *N*b-methoxycarbonyltryptamines (**9**, **10**, and **11**)



Entry	Starting Material	Bromine (mol eq.)	Yield (%) of 12	13	14	15	16	17	18	19	Total Yield (%)	7-Bromination (total)
1	**9**	0.7	23	9	0	1	9	8	7	0	57	33
2	**9**	1.2	0	22	12	3	5	0	10	0	52	37
3	**9**	3.0	0	0	0	0	0	0	0	0	0	0
4	**10**	1.2	0	11	10	0	0	0	8	0	29	21
5	**11**	1.2	0	0	3	0	44	0	4	3	54	3

derivatives. Therefore we selected 1-hydroxy-*N*b-methoxycarbonyltryptamine derivatives.[13] Bromination of **9,** N(1)–OMe tryptamine, proceeded in a quite different way from that of the corresponding N(1)–H tryptamine (**11**). Among various results, typical examples are shown in Table 1. Thus, bromination of **9** with Br_2/NaOAc/AcOH afforded many products such as 7-bromo- (**12**), 2,7-dibromo- (**13**), 5,7-dibromotryptamines (**14**), 7-bromo-2-oxy- (**15**), 2-oxy- (**16**), 2-bromo- (**17**), and 2,5-dibromotryptamines (**18**) depending on the bromination conditions (Entries 1–2). When an excess amount of bromine was used, the reaction was dirty and isolable product was none (Entry 3). 1-Hydroxy-*N*b-methoxycarbonyltryptamine (**10**) showed almost the same results as **9** though the total product yield is lower (Entry 4). On the other hand, under similar reaction conditions, **11** afforded **14**, **16**, **18**, and 5-bromo-*N*b-methoxycarbonyltryptamine (**19**) (Entry 5). The general trend of bromination of indole derivatives prefers 5-position. In contrast to **11**, **9** was found to prefer bromination at the 7-position to 5-position comparing the total yield of 7-brominated compounds with those of 5-position. These results demonstrate the 1-methoxy or 1-hydroxy group promotes selective bromination at the 7-position. The phenomenon could be explained by the following either electrophilic (**A**) or nucleophilic mechanisms (**B**), as illustrated in Scheme 2. In the former mechanism, bromine initially approaches the indole ring and forms a π-complex (**D**) through **C**. Then a coordination bond develops between the bromonium ion and the lone pair of 1-methoxy oxygen (**E**) that is deviated from the indole molecular plane with an angle θ (11-15°) as shown in our previous literature.[14] As a result, the bromonium ion is attracted close to the 7-position and forms a σ-complex (**F**) at the 7-position, which collapses to **H** through **G**. In the latter mechanism, a nucleophilic substitution reaction takes place through transition state (**B**), where the bromide ion attacks the nearby 7-position with the concomitant liberation of the oxonium group from the 1-position.

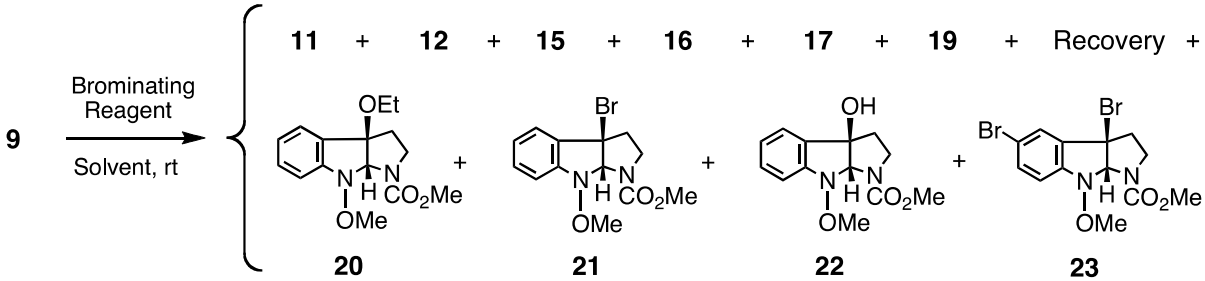


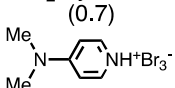
Scheme 2

Utilizing **9** as a substrate, further trials of bromination were carried out and the desired results were

obtained as summarized in Table 2. When Br_2 in pyridine was used in $CHCl_3$, 3a-ethoxy-1,2,3,3a,8,8a-hexahydro-8-methoxy-1-methoxycarbonylpyrrolo[2,3-*b*]indole (**20**) was obtained for the first time although the yield was 9% (Entry 1). EtOH was contained as a stabilizer for $CHCl_3$ and incorporated into the product. In the same solvent system, 4-dimethylaminopyridinium tribromide produced **20**, 3a-bromo-1,2,3,3a,8,8a-hexahydro-8-methoxy-1-methoxycarbonylpyrrolo[2,3-*b*]indole (**21**), and 1,2,3,3a,8,8a-hexahydro-3a-hydroxy-8-methoxy-1-methoxycarbonylpyrrolo[2,3-*b*]indole (**22**) together with other products (Entry 2). Bromine in $CHCl_3$ generated 3a,5-dibromo-1,2,3,3a,8,8a-hexahydro-8-methoxy-1-methoxycarbonylpyrrolo[2,3-*b*]indole (**23**) in addition to other products (Entry

Table 2. Bromination of 1-methoxy-*N*b-methoxycarbonyltryptamine (**9**)



Entry	Reagent (mol eq.)	Solvent	Reaction Time (min)	Yield (%) of 11	12	15	16	17	19	20	21	22	23	Recovery
1	Br_2/Pyridine (0.7)	$CHCl_3$*1	60	0	0	0	0	0	0	9	0	0	0	22
2	 (0.7)	〃	20	0	15	6	0	2	2	7	8	10	0	2
3	Br_2/$CHCl_3$*2 (0.7)	$CHCl_3$*2	20	5	25	0	9	5	4	0	0	0	0.4	5
4	Br_2/EtOH (0.7)	EtOH	20	0	0	0	0	0	0	13	24	0	0	43
5	NBS (0.9)	〃	60	0	0	0	0	0	0	39	8	0	0	9

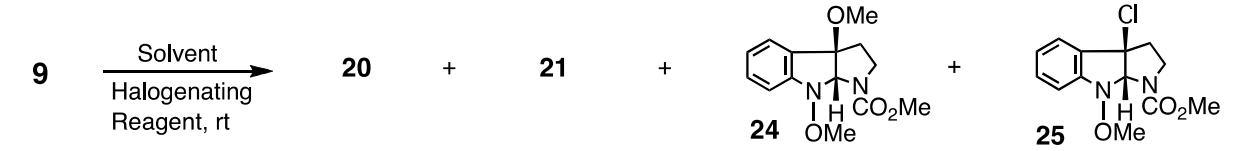
*1: EtOH in $CHCl_3$ was not excluded. *2: EtOH in $CHCl_3$ was excluded by washing with H_2O.

3). Based on these findings further trials were carried out in EtOH utilizing either Br_2 or NBS (Entries 4 and 5). As a result the yields of pyrrolo[2,3-*b*]indoles (**20** and **21**) were improved.

After various trials using NBS, NIS, and NCS, we found that the use of 0.9 mol eq. of brominating reagent to the substrate is the most suitable. As can be seen from the Table 3, NBS in MeOH produced 3a,8-dimethoxy-1,2,3,3a,8,8a-hexahydro-1-methoxycarbonylpyrrolo[2,3-*b*]indole (**24**) in 59% yield (Entry 1). When EtOH was employed, **20** was obtained in 39% yield (Entry 2). NIS in MeOH provided **24** in 58% yield (Entry 3). NCS in MeOH yielded 3a-chloro-8-methoxy-1,2,3,3a,8,8a-hexahydro-1-methoxycarbonylpyrrolo[2,3-*b*]indole (**25**) in good yields (Entries 4 and 5).

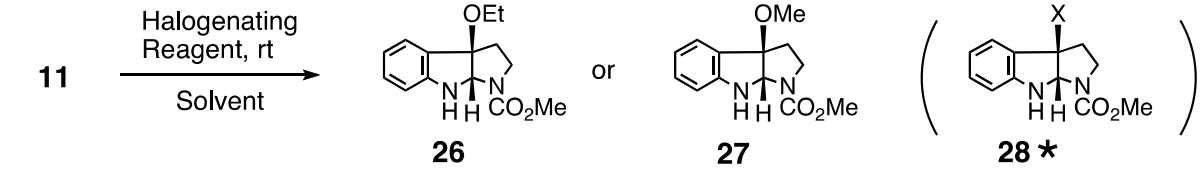
Considering these results we changed reaction solvent to MeCN to block the incorporation of alcohol to the products. Consequently, we found a new method for producing 8-methoxy-1,2,3,3a,8,8a-hexahydro-1-methoxycarbonylpyrrolo[2,3-*b*]indoles having a halogen at the 3a position. Thus, NCS and NBS in MeCN produced **25** and **21** in 87 and 85% yields, respectively (Entries 6 and 7).

Table 3. Halogenation of 1-methoxy-*N*b-methoxycarbonyltryptamine (**9**)



Entry	Halogenating Reagent (mol eq.)	Solvent	Reaction Time (h)	Yield (%) of 20	21	24	25	Recovery	Total Yield (%)
1	NBS (0.9)	MeOH	1	0	12	59	0	3	74
2	" (0.9)	EtOH	1	39	8	0	0	9	56
3	NIS (0.9)	MeOH	1	0	0	58	0	33	91
4	NCS (0.9)	"	2	0	0	2	53	22	77
5	" (1.0)	"	2	0	0	4	64	7	75
6	" (0.9)	MeCN	0.5	0	0	0	87	0	87
7	NBS (0.9)	"	0.5	0	85	0	0	0	85

Table 4. Halogenation of *N*b-methoxycarbonyltryptamine (**11**)



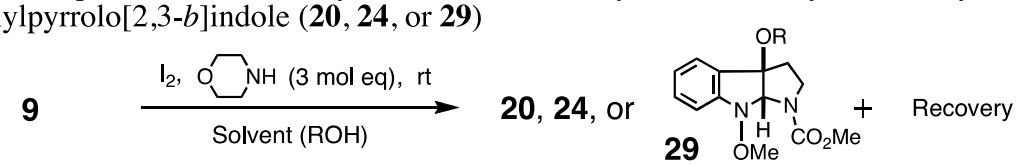
Entry	Halogenating Reagent (mol eq.)	Solvent	Reaction Time (h)	Yield (%) of 26	27	Recovery	Total Yield (%)
1	NBS (0.9)	EtOH	1	4	0	25	29
2	NCS (0.9)	"	1	15	0	64	79
3	"	MeOH	2	0	33	29	62
4	NIS (0.9)	"	1	0	40	36	76
5	NCS (1.1)	"	4	0	49	20	69
6	NBS (0.9)	MeCN	1	0	0	0	Tar and Many Spots
7	NCS (0.9)	"	1	0	0	31	Many Products

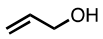
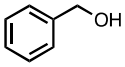
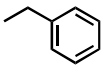
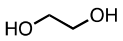
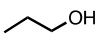
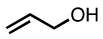
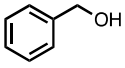
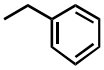
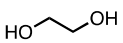
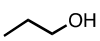
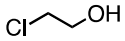
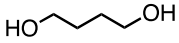
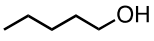
* Formation of **28**, where X = Br or X = Cl, was not observed at all.

Under similar reaction conditions, **11** (N(1)–H tryptamine) could also produce 1,2,3,3a,8,8a-hexahydro-1-methoxycarbonylpyrrolo[2,3-*b*]indoles as shown in Table 4. When NBS or NCS was employed in EtOH, 3a-ethoxy-1,2,3,3a,8,8a-hexahydro-1-methoxycarbonylpyrrolo[2,3-*b*]indole

(**26**) was obtained in 4 or 15% yields, respectively (Entries 1 and 2). Utilizing MeOH instead of EtOH, 1,2,3,3a,8,8a-hexahydro-3a-methoxy-1-methoxycarbonylpyrrolo[2,3-*b*]indole (**27**) was obtained in good yields (Entries 3–5). However the yields of **26** and **27** were inferior to those of the corresponding 8-methoxy products (**20** and **24**) obtained from **9** (N(1)–OMe tryptamine). It should be noted that when MeCN was employed as a solvent, **11** did not produce the expected 3a-halogenated compound (**28**) at all (Entries 6 and 7) in contrast to **9** giving the corresponding **21** and **25** in excellent yields.

Table 5. Preparation of 3a-alkoxy-1,2,3,3a,8,8a-hexahydro-8-methoxy-1-methoxycarbonylpyrrolo[2,3-*b*]indole (**20**, **24**, or **29**)



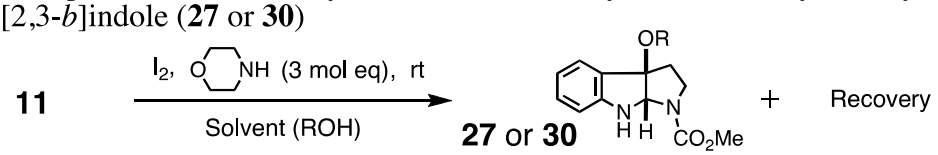
Entry	Iodine (mol eq)	Solvent (ROH)	Reaction Time (h)	Product 29	Product R	Yield (%) of Product	Recovery (%)	Total Yield (%)
1	1.5	MeOH	21	**24**	Me	36	45	81
2	1.6	EtOH	5	**20**	Et	37	55	92
3	"		5	**29a**		17	79	96
4	1.5		24	**29b**		28	26	54
5	"		24	**29c**		11	48	59
6	10	MeOH	1/6	**24**	Me	98	0	98
7	"	EtOH	1/6	**20**	Et	97	0	97
8	"		1/2	**29a**		96	0	96
9	"		1/6	**29b**		97	0	97
10	"		3/2	**29c**		92	0	92
11	"		1/3	**29d**		90	0	90
12	"		1.5	**29e**		89	0	89
13	"	Me_2CHOH	1/3	**29f**	$CHMe_2$	90	0	90
14	"	Me_3COH	1/3	**29g**	CMe_3	80	0	80

We next aimed at the direct one step conversion of **9** into 3a-alkoxy-1,2,3,3a,8,8a-hexahydro-1-methoxycarbonylpyrrolo[2,3-*b*]indole (**29**, Table 5). After various trials including Br_2, Br_2/NaOAc, 4-(*N*,*N*-dimethylamino)pyridinium tribromide, NIS, iodine/triethylamine, iodine/K_2CO_3, iodine/$NaHCO_3$, iodine/pyridine, iodine/NaI, iodine/NH_4Cl, and iodine only in various solvents, we succeeded in finding that the treatment of **9** with iodine and morpholine in an appropriate alcoholic

solvent at room temperature met our end. In these reactions, we also found that suitable quantity of the concomitant base (morpholine) was 3 mol eq. As can be seen from Table 5, the quantity of iodine governs the yields of the desired products. Thus, treatment of **9** with about 1.5 mol eq. of iodine generated **20**, **24**, **29a-c** in the range of 11—37% yields in addition to the recovery (Entries 1—5). With an aim to convert the unreacted **9** to product, the amount of iodine was increased to 10 mol eq. (Entries 6—10). Consequently, the yields of desired products were dramatically improved. Thus, using MeOH, EtOH, allyl alcohol, benzyl alcohol, and ethylene glycol as a solvent, **24**, **20**, **29a**, **29b**, and **29c** are now available in 98, 97, 96, 97, and 92% yields, respectively. 2-Chloroethanol, 1,4-butanediol, *i*-PrOH, and *t*-BuOH were also successfully employed to give **29d**, **29e**, **29f**, and **29g** in 90, 89, 90, and 80% yields, respectively.

Even when the above best reaction conditions with iodine (10 mol eq.) and morpholine (3 mol eq.) were employed for the reaction of **11** (Table 6) in MeOH and allyl alcohol, the yields of **27** and **30** were 60 and 4% (Entries 2 and 4), respectively, together with much quantity of tars. Again N(1)–OMe tryptamine is proved to be a superior substrate to N(1)–H tryptamine for producing 3a-alkoxy-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole derivatives.

Table 6. Preparation of 3a-alkoxy-1,2,3,3a,8,8a-hexahydro-1-methoxycarbonyl-pyrrolo[2,3-*b*]indole (**27** or **30**)



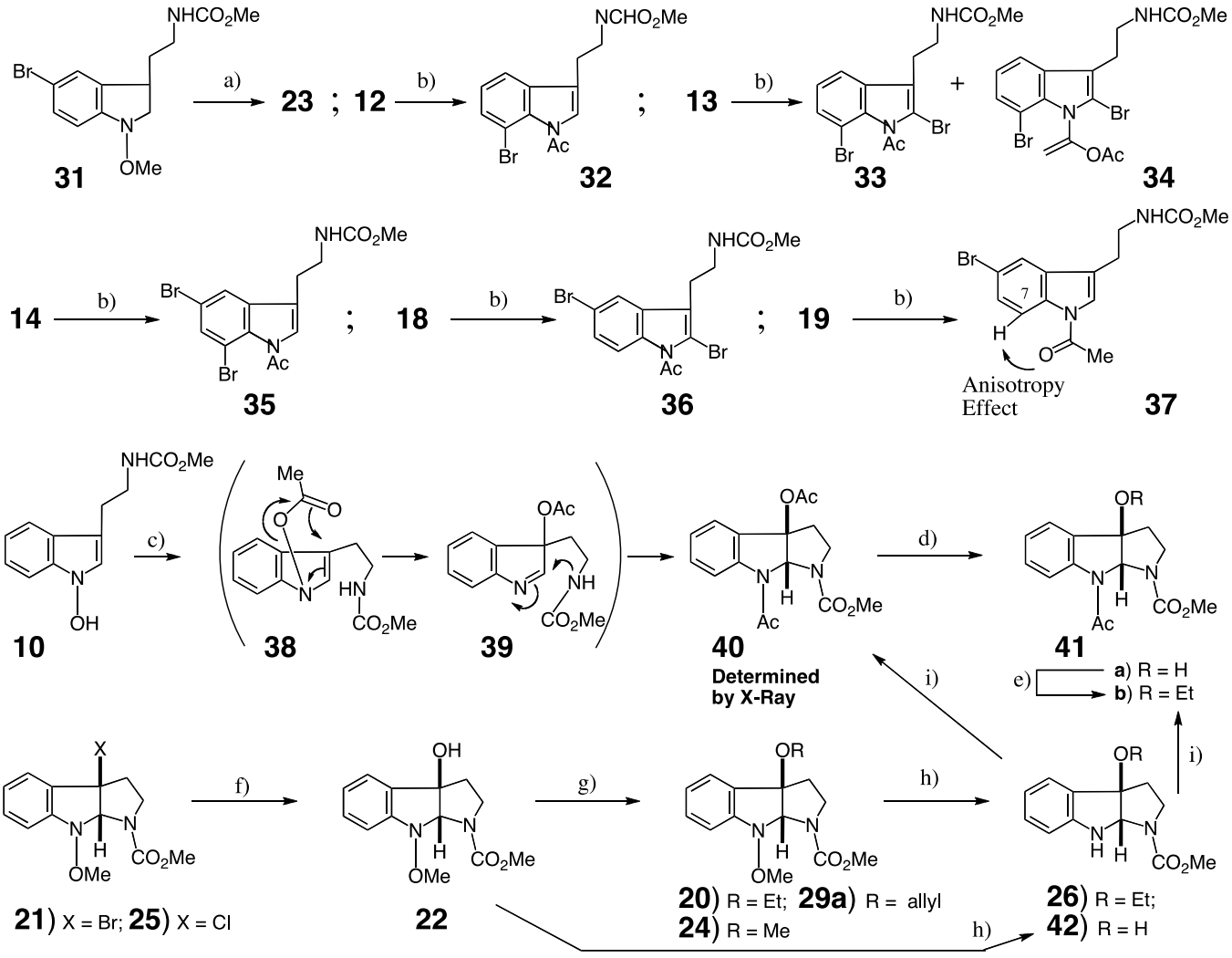
Entry	Iodine (mol eq)	Solvent (ROH)	Reaction Time (h)	Product **27** or **30**	R	Yield (%) of Product	Recovery (%)	Total Yield (%)
1	1.5	MeOH	21	**27**	Me	28	12	40
2	10	"	1/3	**27**	"	60	0	60
3	1.6		5	**30**		8	47	55
4	10	"	1/2	**30**	"	4	0	4

II. Structure determination of products

Structures of various products reported in the previous sections were determined spectroscopically. In cases where spectroscopically more than two structures were possible candidates, the product was led to suitable derivative which could prove its structure.

The structure of **23** was proved by the fact that the treatment of 5-bromo-1-methoxy-*N*b-methoxy-carbonyltryptamine[1b,14] (**31**) with NBS in ethanol free $CHCl_3$ afforded 93% yield of **23**. Structural proof of **19** was obtained by converting it to 1-acetyl compound (**37**) by reacting with NaH/AcCl in 65% yield. In their ^{1}H-NMR spectra, the C7-proton (d, *J*=8.8 Hz, ortho coupling) of **37** shifted to lower field by ca.

0.94 ppm compared with that of **19** by the anisotropy effect of 1-acetyl carbonyl group. This is the proof that **19** has the proton at the 7-position of indole nucleus. Since the same anisotropy effect was observed in the pair of **18** and **36**, **18** is proved to have bromine at the 5-position. Similarly, **12**, **13**, and **14** were led to the corresponding 1-acetyl compounds, **32**, **33**, and **35** in 40, 23, and 58% yields. In these cases any of their aromatic protons did not show the anisotropy effect, proving that these compounds have no proton at the 7-posion. It is interesting to note that the above acetylation of **13** produced enol acetate compound (**34**) in 15% yield.



a) NBS, $CHCl_3$; b) NaH, AcCl; c) Ac_2O, NaOAc; d) $NaHCO_3$, H_2O;
e) NaH, DMF, then EtI; f) AgCN, MeCN, H_2O; g) NaH, DMF, then MeI, EtI, or allyl bromide; h) H_2, 10% Pd/C; i) Ac_2O, pyridine.

Scheme 3

Treatment of 1-hydroxy-*N*b-methoxycarbonyltryptamine (**10**) in refluxing Ac_2O afforded 3a-acetoxy-8-acetyl-1-methoxycarbonyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (**40**) in 72% yield. The reaction can be explained by a [3,3] sigmatropic rearrangement[15] of the 1-acetoxy group of **38** to the 3-position providing the imine (**39**), followed by ring closure. The structure of **40** was unequivocally

proved by X-ray single-crystal analysis[10] as shown in Figure 2 (Experimental part). Mild hydrolysis of **40** produced 96% yield of 8-acetyl-3a-hydroxy-1-methoxycarbonyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]-indole (**41a**). Subsequent alkylation of the 3a-hydroxy group of **41a** with ethyl iodide and NaH afforded **41b** in 93% yield.

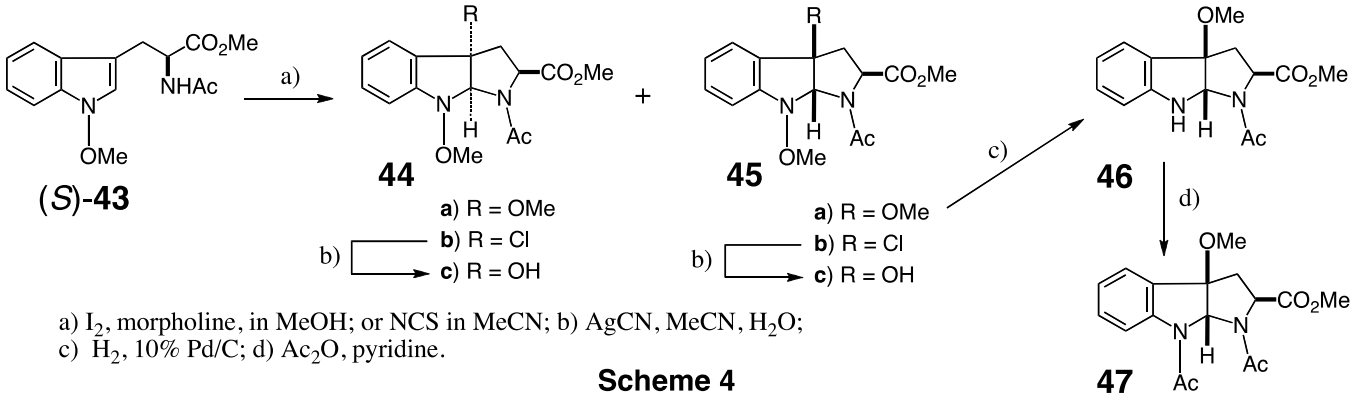
We next tried to convert **21** and **25** into 3a-hydroxy compound (**22**) with silver salt. Among the examined reagents, silver cyanide was found to be the reagent of choice. In MeCN/H_2O, **21** and **25** were transformed to **22** in the respective yields of 94 and 85%. Subsequent treatments of **22** with EtI, MeI, and allyl bromide in the presence of NaH afforded **20**, **24**, and **29a** in 68, 94, and 92% yields, respectively.

The structure of **20** was confirmed by leading it to **41b**. First, **20** was hydrogenated to **26** in 81% yield in the presence of 10% Pd/C at room temperature and 1 atm hydrogen. Subsequent treatment of **26** with Ac_2O/pyridine provided 76% yield of **41b**, which was identical with the sample derived from **40**. Alternative structural proof was obtained by catalytic hydrogenation of **22** giving **42** in 93% yield. Subsequent acetylation with Ac_2O afforded **40** in 95% yield.

Thus, all of the 1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole structures were correlated to **40** and determined unequivocally.

III. Application of iodine/morpholine method to optically active compound

For the preparation of optically active methyl 1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole-2-carboxylates having a halogen or an oxygen functional group at the 3a-position, we further applied the above iodine/morpholine method to *N*b-acetyl-1-methoxy-L-tryptophan methyl ester ((*S*)-**43**).



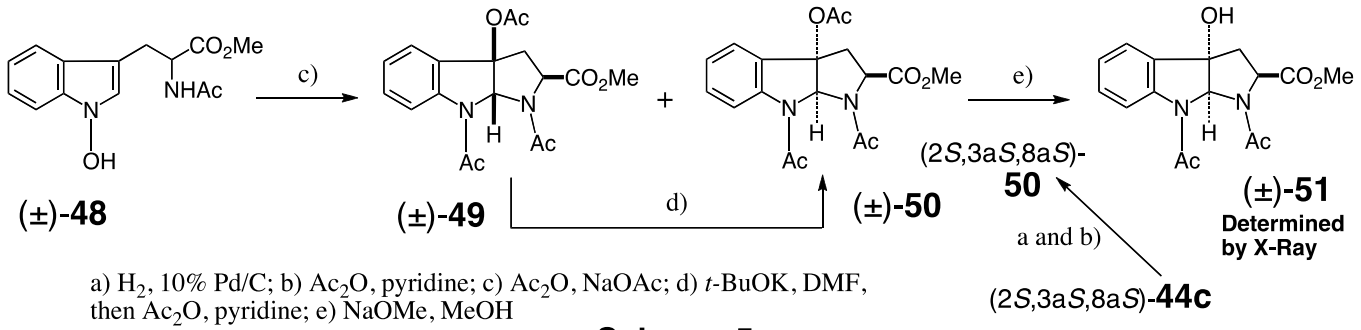
a) I_2, morpholine, in MeOH; or NCS in MeCN; b) AgCN, MeCN, H_2O;
c) H_2, 10% Pd/C; d) Ac_2O, pyridine.

Scheme 4

Treatment of (*S*)-**43**[16,17] with iodine (10 mol eq.) and morpholine (3 mol eq.) in MeOH resulted in the formations of (2*S*,3a*S*,8a*S*)- (**44a**) and (2*S*,3a*R*,8a*R*)-methyl 1-acetyl-1,2,3,3a,8,8a-hexahydro-3a,8-dimethoxypyrrolo[2,3-*b*]indole-2-carboxylates (**45a**) in 6 and 48% yield. The reaction of (*S*)-**43** with NCS in MeCN generated (2*S*,3a*S*,8a*S*)- (**44b**) and (2*S*,3a*R*,8a*R*)-methyl 1-acetyl-3a-chloro-1,2,3,3a,8,8a-hexahydro-8-methoxypyrrolo[2,3-*b*]indole-2-carboxylates (**45b**) in 43 and 44% yields, respectively.

Conversions of 3a-halogen of **44b** and **45b** to hydroxy group was successfully realized by employing AgCN in MeCN/H_2O to give (2*S*,3a*S*,8a*S*)- (**44c**) and (2*S*,3a*R*,8a*R*)-methyl 1-acetyl-3a-hydroxy-8-methoxy-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole-2-carboxylates (**45c**) in the respective yields of 96 and 88% yields.

The stereochemistries of **44a**—**c** and **45a**—**c** were first deduced based on the ^{1}H-NMR spectral data. Thus, the methyl proton in the 2-methoxycarbonyl group of **44a**—**c** appeared at higher magnetic field by ca. 0.20—0.24 ppm than that of **45a**—**c** showing the methyl group is located above the benzene ring and the protons feel the shielding effect of π-electron ring currents. Hydrogenation of **45a** with 1 atm hydrogen afforded (2*S*,3a*R*,8a*R*)-**46** in 97% yield in the presence of 10% Pd/C at room temperature, and subsequent acetylation of (2*S*,3a*R*,8a*R*)-**46** with Ac_2O provided 68% yield of (2*S*,3a*R*,8a*R*)-**47**.



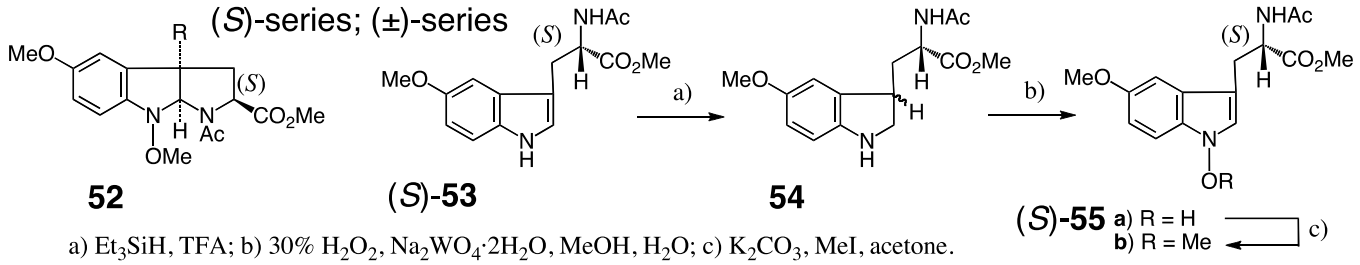
a) H_2, 10% Pd/C; b) Ac_2O, pyridine; c) Ac_2O, NaOAc; d) *t*-BuOK, DMF, then Ac_2O, pyridine; e) NaOMe, MeOH

Scheme 5

In order to obtain unequivocal proof for the above structures, the following sequence of reactions were carried out. First, (2*S*,3a*S*,8a*S*)-**44c** was hydrogenated with 1 atm hydrogen in the presence of 10% Pd/C at room temperature, and subsequent treatment of the product with Ac_2O provided 78% overall yield of (2*S*,3a*S*,8a*S*)-**50** (Scheme 5). On the other hand, (±)-*N*b-acetyltryptophan methyl ester ((±)-**48**) was converted to (±)-methyl 3a-acetoxy-1,8-diacetyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole-2-carboxylates ((±)-**49** and (±)-**50**) in 21 and 23% yields, respectively, by the reaction with Ac_2O at 120 °C in the presence of NaOAc. Isomerization of (±)-**49** to thermodynamically stable (±)-**50** occurred easily in 51% yield by the treatment with KO*t*Bu in DMF, followed by acetylation with Ac_2O. Subsequent hydrolysis of the 3a-acetoxy group of (±)-**50** with NaOMe in MeOH provided (±)-methyl 1,8-diacetyl-3a-hydroxy-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole-2-carboxylates ((±)-**51**) in 96% yields, respectively. Luckily, (±)-**51** became suitable prisms for X-ray single crystallographic analysis.[11] The results shown in Figure 3 (Experimental part) clearly proved the structure and the presence of the methyl moiety in the 2-methoxycarbonyl group above the benzene ring. Consequently, stereochemistry of the 8a-proton and the 2-methoxycarbonyl group in (±)-**49** and (±)-**50** are proved to be *cis* and *trans*, respectively. The ^{1}H-NMR spectrum and TLC behavior of (±)-**50** were identical with those of (2*S*,3a*S*,8a*S*)-**50** derived from (2*S*,3a*S*,8a*S*)-**44c**.

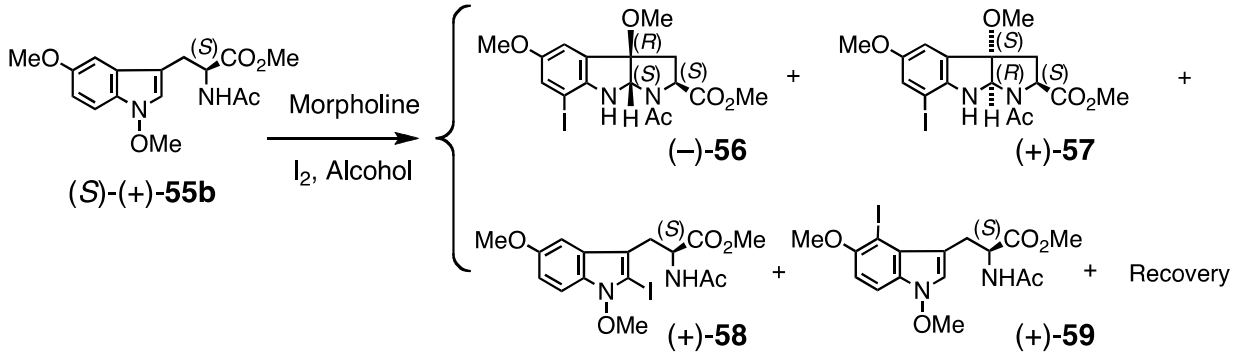
IV. Application of iodine/morpholine method to 5-methoxytryptophane derivatives

Attempt was then made to get new methyl 1,2,3,3a,8,8a-hexahydro-5-methoxypyrrolo[2,3-*b*]indole-2-carboxylates (**52**) having a 3a substituent (Scheme 6). To meet our end we needed 1,5-dimethoxytryptophan derivative ((*S*)-(+)-**55b**) as a starting material. It was prepared from (*S*)-*N*b-acetyl-5-methoxytryptophan methyl ester ((*S*)-**53**) according to our synthetic method for 1-hydroxyindole.[1b,13,14] Thus, reduction of (*S*)-**53** with Et_3SiH afforded a mixture of diastereomers (**54**) in 87% yield. Without separation of diastereomers the mixture was oxidized with 30% H_2O_2 in the presence of $Na_2WO_4 \cdot 2H_2O$[1b,12,13,14] to give the corresponding (*S*)-**55a** in 85% yield. Subsequent methylation with MeI/K_2CO_3 gave the desired (*S*)-**55b** in 83% yield. Under similar reactions, (±)-**55a** was obtained from (±)-**54** in 60% yield, and (±)-**55b** was prepared in 90% yield from (±)-**55a**.



Scheme 6

Table 7. Application to (*S*)-1,5-dimethoxytryptophan derivative ((*S*)-(+)-**55b**)



Entry	Alcohol	Iodine (mol eq.)	Morpholine (mol eq.)	Reaction Time (h)	Yield (%) of (–)-**56**	(+)-**57**	(+)-**58**	(+)-**59**	Recovery
1	MeOH	10	3	0.5	0	0	13	0	16
2	"	10	3	1	7	7	6	0	0
3	"	1	3	1	0	0	0	0	100
4	*i*-Propanol	10	3	3	0	0	33	7	20
5	*t*-BuOH	10	3	3	0	0	23	5	19
6	"	10	10	3	0	0	0	0	100

(±)-**55b** —Morpholine, I_2, MeOH, 1 h→ (±)-**56** 11% + (±)-**57** 9% + (±)-**58** 15% + Tar

It is interesting to note that the treatment of (*S*)-(+)-**55b** with iodine and morpholine in alcoholic solvent proceeded quite different way from the expectation and the results are summarized in Table 7. In the reaction in MeOH for 0.5 h, *N*b-acetyl-1,5-dimethoxy-2-iodotryptophan methyl ester ((*S*)-**58**) was isolated in 13% yield as a sole product with tar (Entry 1). Longer reaction time produced (*S*)-**58** in 6% yield together with (–)-**56** and (+)-**57**[17] in the respective yields of 7 and 7% (Entry 2). As in the cases of (±)-**49** and (±)-**50**, stereochemistries of (–)-**56** and (+)-**57** were determined due to the fact that the methyl proton in the 2-methoxycarbonyl group of (+)-**57** appeared at higher magnetic field by ca. 0.45 ppm than that of (–)-**56** proving the methyl group is located above the benzene ring.

Under similar reaction conditions in *i*-PrOH, (*S*)-**55b** provided (*S*)-**58** and (*S*)-**59** in 33 and 7% yields, respectively. In *t*-BuOH, similar results were obtained. However, excess amount of morpholine blocked the desired reaction (Entry 6). On the other hand, under similar reaction conditions the reaction of (±)-**55b** in MeOH afforded (±)-**56,** (±)-**57**, and (±)-**58** in 11, 9, and 15% yields, respectively.

These results seem to suggest that introduction of electron donating group into the benzenoid part of indole nucleus prefer iodination of indole part to the formation of 1,2,3,3a,8,8a-hexahydro-5-methoxypyrrolo[2,3-*b*]indole skeleton.

In conclusion, 3a-halogeno-, 3a-hydroxy-, and 3a-alkoxy-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indoles are now readily available from **9**. We have also established simple synthetic method for optically active methyl 3a-halogeno-, 3a-hydroxy-, and 3a-alkoxy-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole-2-carboxylates. Evaluations of their biological activity and potential as synthetic intermediates for natural products are now in progress.

EXPERIMENTAL

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared (IR) spectra were determined with a Shimadzu IR-420 or Horiba FT-720 spectrophotometer, and proton nuclear magnetic resonance (^{1}H-NMR) spectra with a JEOL JNM-GSX 500 or FX100S spectrometer with tetramethylsilane as an internal standard. Mass spectra (MS) were recorded on a Hitachi M-80 or JEOL SX-102A spectrometer. Preparative thin-layer chromatography (p-TLC) was performed on Merck Kiesel-gel GF_{254} (Type 60) (SiO_2). Column chromatography was performed on silica gel (SiO_2, 100–200 mesh, from Kanto Chemical Co. Inc.) throughout the present study.

7-Bromo- (12), 2-bromo- (17), 2,7-dibromo- (13), 5,7-dibromo- (14), and 2,5-dibromo-*N*b-methoxycarbonytryptamine (18), *N*b-methoxycarbonyl- (16) and -7-bromo-2-oxytryptamine (15) from 1-methoxy-*N*b-methoxycarbonyltryptamine (9) — [Table 1, Entry 1] : General Procedure: 0.55 M Br_2 in AcOH (0.27 mL, 0.15 mmol) was added to a solution of **9** (52.0 mg, 0.21 mmol) in AcOH (3.0 mL) and the mixture was stirred at rt for 1 h. After addition of $Na_2S_2O_3$ (1.0 mL) and H_2O, the whole

was made basic with 40% NaOH under ice cooling and extracted with $CHCl_3$–MeOH (4:1, v/v). The extract was washed with brine, dried over Na_2SO_4 and evaporated under reduced pressure to leave an oil, which was purified by p-TLC on SiO_2 developed three times with EtOAc–hexane (1:1, v/v). Extraction of the band having an *Rf* value of 0.97—0.86 with EtOAc–MeOH (95:5, v/v) gave a mixture of **13**, **17**, and **18** (18.3 mg). Extraction of the bands having an *Rf* value of 0.85—0.80, 0.57—0.50, and 0.42—0.31 with EtOAc–MeOH (95:5, v/v) gave **12** (14.3 mg, 23%), **15** (0.9 mg, 1%), and **16** (4.2 mg, 9%), respectively. The mixture of **13**, **17**, and **18** was separated by p-TLC on SiO_2 developed twice with $CHCl_3$-MeOH (99:1, v/v). Extraction of the bands having an *Rf* value of 0.81—0.73, 0.60—0.55, and 0.54—0.46 with $CHCl_3$–MeOH (95:5, v/v) afforded **13** (7.4 mg, 9%), **17** (5.0 mg. 8%), and **18** (5.2 mg. 7%), respectively. **12**: 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, br t, *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 and 296 (M^+). *Anal.* Calcd for $C_{12}H_{13}BrN_2O_3$: C, 48.51; H, 4.41; N, 9.43. Found: C, 48.59; H, 4.42; N, 9.31. **13**: colorless oil. IR (film): 3303, 2941, 1695, 1670, 1564, 1489, 1427 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.93 (2H, t, *J*=6.6 Hz), 3.44 (2H, q, *J*=6.6 Hz), 3.67 (3H, s), 4.71 (1H, br s, disappeared on addition of D_2O), 7.01 (1H, t, *J*=7.8 Hz), 7.33 (1H, d, *J*=7.8 Hz), 7.49 (1H, d, *J*=7.8 Hz), 8.23 (1H, br s, disappeared on addition of D_2O). HR–MS *m/z*: Calcd for $C_{12}H_{12}Br_2N_2O_2$: 377.9224, 375.9245, and 373.9265. Found: 377.9215, 375.9229, and 373.9281. **15**: mp 171—172 °C (colorless prisms, recrystallized from $CHCl_3$–hexane). IR (KBr): 3309, 1714, 1693, 1614, 1547, 1277 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.00 (1H, dq, *J*=14.2, 7.1 Hz), 2.15 (1H, dq, *J*=14.2, 7.1 Hz), 3.31 (1H, dq, *J*=13.2, 7.1 Hz), 3.39 (1H, dq, *J*=13.2, 7.1 Hz), 3.55 (1H, t, *J*=6.8 Hz), 3.58 (3H, s), 5.05 (1H, br s, disappeared on addition of D_2O), 6.88 (1H, t, *J*=7.8 Hz), 7.17 (1H, d, *J*=7.8 Hz), 7.28 (1H, d, *J*=7.8 Hz), 7.71 (1H, br s, disappeared on addition of D_2O). MS *m/z*: 314, 312 (M^+). *Anal*. Calcd for $C_{12}H_{13}BrN_2O_3$: C, 46.03; H, 4.18; N, 8.95. Found: C, 46.20; H, 4.31; N, 8.80. **16**: 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. **17**: 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, *J*=7.6, 1.2 Hz), 7.08 (1H, td, *J*=7.6, 1.2 Hz), 7.20 (1H, br t, *J*=5.6 Hz), 7.28 (1H, d, *J*=7.8 Hz), 7.50 (1H, d, *J*=7.8 Hz). HR–MS *m/z*: Calcd for $C_{12}H_{13}BrN_2O_2$: 298.0139 and 296.0160. Found: 298.0117 and 296.0151.

[Entry 2] In the general procedure, 0.60 M Br_2 in AcOH (0.39 mL, 0.24 mmol) and **9** (49.0 mg, 0.20 mmol) in AcOH (3.0 mL) were used. After the same work-up as Entry 1, the products were separated by p-TLC on SiO_2 developed twice with $CHCl_3$–MeOH (97:3, v/v). Extraction of the band having an *Rf* value of 0.88—0.79, 0.77—0.64, 0.50—0.41, 0.34—0.27, and 0.25—0.15 with $CHCl_3$–MeOH (9:1, v/v) gave **13** (16.0 mg, 22%), **14** (8.8 mg, 12%), **15** (2.1 mg, 3%), **16** (2.3 mg, 5%), and **18** (7.2 mg, 10%). **14**: colorless oil. IR (film): 3427, 3319, 1701, 1525, 1464 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.91 (2H, t, *J*=6.8 Hz), 3.48 (2H, q, *J*=6.8 Hz), 3.68 (3H, s), 4.71 (1H, br s, disappeared on addition of D_2O), 7.11 (1H, s), 7.48 (1H, d, *J*=1.5 Hz), 7.67 (1H, d, *J*=1.5 Hz), 8.22 (1H, br s, disappeared on addition of D_2O). HR–MS *m/z*: Calcd for $C_{12}H_{12}Br_2N_2O_2$: 377.9224, 375.9242, and 373.9253. Found: 377.9225, 375.9245, and 373.9216. **18**: colorless oil. IR (film): 3417, 3265, 1701, 1525, 1450, 1290, 1267 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.91 (2H, t, *J*=6.7 Hz), 3.44 (2H, q, *J*=6.7 Hz), 3.68 (3H, s), 4.70 (1H, br s, disappeared on addition of D_2O), 7.16 (1H, d, *J*=8.7 Hz), 7.27 (1H, dd, *J*=8.7, 1.7 Hz), 7.64 (1H, br s), 8.16 (1H, br s, disappeared on addition of D_2O). HR–MS *m/z*: Calcd for $C_{12}H_{12}Br_2N_2O_2$: 377.9224, 375.9240, and 373.9230. Found: 377.9225, 375.9246, and 373.9265.

[Entry 4] In the general procedure, 0.57 M Br_2 in AcOH (1.83 mL, 1.04 mmol) and **10** (203.0 mg, 0.86 mmol) in AcOH (10.0 mL) were used and the mixture was stirred at rt for 1.0 h. After the same work-up as Entry 1, the products were column-chromatographed on SiO_2 with $CHCl_3$–MeOH (99:1, v/v) to give **13** (34.8 mg, 11%), **14** (32.6 mg, 10%), and **18** (29.5 mg, 8%).

[Entry 5] In the general procedure, 0.57M Br_2 in AcOH (0.49 mL, 0.27 mmol) and **11** (50.5 mg, 0.23 mmol) in AcOH (3.0 mL) were used. After the same work-up as Entry 1, the products were column-chromatographed on SiO_2 with EtOAc–hexane (1:2, v/v) to give **14** (3.0 mg, 3%), **16** (24.0 mg, 44%), **18** (3.4 mg, 4%), and **19** (2.3 mg, 3%). **19**: 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, br t, *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*=2.0 Hz). HR–MS *m/z*: Calcd for $C_{12}H_{13}BrN_2O_2$: 298.0140 and 296.0161. Found: 298.0138 and 296.0178.

11, 12, 15, 16, 17, 19, 3a-Ethoxy- (20), 3a-bromo- (21), 3a-hydroxy- (22), and 3a,5-dibromo-8-methoxy-1-methoxycarbonyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (23) from 9 — [**Table 2, Entry 2**] 4-(*N*,*N*-Dimethylamino)pyridinium tribromide (51.0 mL, 0.14 mmol) was added to a solution of **9** (49.8 mg, 0.20 mmol) in $CHCl_3$ (3.0 mL, containing EtOH as a stabilizer) and the mixture was stirred at rt for 20 min. After addition of $Na_2S_2O_3$ (1.0 mL) and H_2O, 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 (3:1, v/v), $CHCl_3$, EtOAc–hexane (1:2,

v/v), and EtOAc to give **12** (9.3 mg, 15%), **15** (3.6 mg, 6%), **17** (1.2 mg, 2%), **19** (1.2 mg, 2%), **20** (4.1 mg, 7%), **21** (5.2 mg, 8%), **22** (5.4 mg, 10%), and unreacted **9** (0.8 mg, 2%). **20**: colorless oil. IR (film): 2976, 1716, 1448, 1383, 1196 cm^{-1}. ^{1}H-NMR ($CDCl_3$, rotational isomers exist in a ratio of 1:1) δ: 1.14 (3H, t, *J*=7.0 Hz), 2.11—2.18 (1H, m), 2.30—2.40 (1H, m), 3.13—3.20 (1H, m), 3.25—3.32 (2H, m), 3.75—4.01 (7H, m), 5.58 (1/2H, br s), 5.66 (1/2H, br s), 7.10 (1H, td, *J*=7.7, 1.0 Hz), 7.11 (1H, dd, *J*=7.7, 1.0 Hz), 7.22 (1H, dd, *J*=7.7, 1.0 Hz), 7.32 (1H, td, *J*=7.7, 1.0 Hz). MS *m/z*: 292 (M^+). HR–MS *m/z*: Calcd for $C_{15}H_{20}N_2O_4$: 292.1425. Found: 292.1423. **21**: colorless oil. IR (film): 1716, 1464, 1448, 1381 cm^{-1}. ^{1}H-NMR (DMSO–d_6) δ: 2.40—2.50 (1H, m), 2.57—2.68 (1H, m), 3.30 (1H, br d), 3.67—3.81 (4H, m), 3.84 (3H, s), 5.63 (1H, s), 7.13 (1H, d, *J*=7.7 Hz), 7.18 (1H, t, *J*=7.7 Hz), 7.39 (1H, t, *J*=7.7 Hz), 7.43 (1H, d, *J*=7.7 Hz). MS *m/z*: 326 (M^+, ^{79}Br), 328 (M^+, ^{81}Br). HR–MS *m/z*: Calcd for $C_{13}H_{15}BrN_2O_3$: 326.0266 and 328.0246. Found: 326.0250 and 328.0262. **22**: colorless oil. IR (film): 3419, 1689, 1452, 1383 cm^{-1}. ^{1}H-NMR (CD_3OD, rotational isomers exist in a ratio of 1:1) δ: 1.97—2.05 (1H, m), 2.22—2.29 (1H, m), 3.44—3.56 (1H, m), 3.77—3.85 (4H, m), 3.87 (3H, s), 5.35 (1/2H, br s), 5.38 (1/2H, br s), 7.01 (1H, dd, *J*=7.7, 0.7 Hz), 7.06 (1H, t, *J*=7.7 Hz), 7.28 (1H, td, *J*=7.7, 0.7 Hz), 7.29 (1H, d, *J*=7.7 Hz). HR–MS *m/z*: Calcd for $C_{13}H_{16}N_2O_4$: 264.1110. Found: 264.1124.

[**Table 2, Entry 3**] 0.57 M Br_2 in EtOH (0.56 mL, 0.30 mmol) was added to a solution of **9** (107.5 mg, 0.43 mmol) in $CHCl_3$ (6.0 mL) and the mixture was stirred at rt for 20 min. After the same work-up and separation as Entry 2, **9** (5.4 mg, 5%), **11** (4.9 mg, 5%), **12** (31.5 mg, 25%), **16** (8.8 mg, 9%), **17** (6.6 mg, 5%), **19** (4.9 mg, 4%), and **23** (0.7 mg, 0.4%) were obtained. **23**: colorless oil. IR (film): 1716, 1446, 1381 cm^{-1}. ^{1}H-NMR ($CDCl_3$, rotational isomers exist in a ratio of 1:1) δ: 2.42—2.50 (1H, m), 2.64—2.71 (1H, m), 3.45—3.53 (1H, m), 3.81 (3/2H, br s), 3.85 (3/2H, br s), 3.86 (3/2H, br s), 3.92 (3/2H, br s), 3.79—3.93 (1H, m), 5.88 (1/2H, br s), 5.96 (1/2H, br s), 6.91 (1H, br s), 7.40 (1H, dd, *J*=8.5, 2.0 Hz), 7.47 (1H, *J*=2.0 Hz). MS *m/z*: 404 (M^+, $^{79}Br_2$), 406 (M^+, ^{79}Br, ^{81}Br), 408 (M^+, $^{81}Br_2$). HR–MS *m/z*: Calcd for $C_{13}H_{14}Br_2N_2O_3$: 406.0729. Found: 406.0720.

[**Table 2, Entry 4**] 0.57 M Br_2 in EtOH (0.51 mL, 0.29 mmol) was added to a solution of **9** (102.5 mg, 0.41 mmol) in EtOH (6.0 mL) and the mixture was stirred at rt for 20 min. After the same work-up and separation as Entry 2, **20** (15.5 mg, 13%), **21** (32.3 mg, 24%), and unreacted **9** (43.7 mg, 43%) were obtained.

[Table 2, Entry 5] *N*-Bromosuccinimide (NBS, 32.2 mg, 0.18 mmol) was added to a solution of **9** (49.8 mg, 0.21 mmol) in EtOH (3.0 mL) and the mixture was stirred at rt for 1 h. After the same work-up and separation as Entry 2, **20** (23.1 mg, 39%), **21** (5.3 mg, 8%), and unreacted **9** (4.3 mg, 9%) were obtained.

Halogenation of 9 with NBS, *N*-iodosuccinimide (NIS), and *N*-chlorosuccinimide (NCS): 20, 21, 24, and 25 from 9 — [**Table 3, Entry 1**] NBS (36.4 mg, 0.20 mmol) was added to a solution of **9** (56.3 mg,

0.23 mmol) in MeOH (5.0 mL) and the mixture was stirred at rt for 1 h. The solvent was evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with EtOAc–hexane (1:4, v/v) to give **21** (9.0 mg, 12%), **24** (36.9 mg, 59%), and unreacted **9** (1.4 mg, 3%). **24**: colorless oil. IR (film): 1716, 1608, 1596, 1448, 1384, 1195, 802, 757 cm^{-1}. ^{1}H-NMR (CD_3OD, rotational isomers exist in a ratio of 1:1) δ: 2.09—2.15 (1H, m), 2.28—2.37 (1H, m), 3.09 (3H, s), 3.19—3.26 (1H, m), 3.75—3.84 (1H, m), 3.77 (3/2H, br s), 3.83 (3/2H, br s), 3.91 (3H, s), 5.56 (1/2H, s), 5.60 (1/2H, s), 7.10 (1H, d, *J*=7.5 Hz), 7.13 (1H, t, *J*=7.5 Hz), 7.23 (1H, d, *J*=7.5 Hz), 7.35 (1H, t, *J*=7.5 Hz). HR–MS *m/z*: Calcd for $C_{14}H_{18}N_2O_4$: 278.1267. Found: 278.1254.

[Table 3, Entry 3] NIS (48.2 mg, 0.21 mmol) was added to a solution of **9** (59.0 mg, 0.24 mmol) in MeOH (5.0 mL) and the mixture was stirred at rt for 1 h. The solvent was evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with EtOAc–hexane (1:4, v/v) to give **24** (38.3 mg, 58%) and unreacted **9** (19.5 mg, 33%).

[Table 3, Entry 5] NCS (63.5 mg, 0.48 mmol) was added to a solution of **9** (118.0 mg, 0.48 mmol) in MeOH (10.0 mL) and the mixture was stirred at rt for 2 h. After the same work-up and separation as Entry 1, **24** (5.3 mg, 4%), **25** (86.2 mg, 64%), and unreacted **9** (8.3 mg, 7%) were obtained. **25**: colorless oil. IR (film): 1716, 1462, 1448, 1383, 754 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.38—2.45 (1H, m), 2.58—2.65 (1H, m), 3.40—3.56 (1H, m), 3.78—3.92 (4H, m), 3.89 (3H, s), 5.68 (1H, s), 7.07 (1H, d, *J*=7.2 Hz), 7.14 (1H, t, *J*=7.2 Hz), 7.35 (1H, t, *J*=7.2 Hz), 7.36 (1H, d, *J*=7.2 Hz). MS *m/z*: 283 (M^+). HR–MS *m/z*: Calcd for $C_{13}H_{15}ClN_2O_3$: 282.0771, 284.0741. Found: 282.0765, 284.0744.

[Table 3, Entry 6] NCS (11.4 mg, 0.09 mmol) was added to a solution of **9** (23.6 mg, 0.10 mmol) in MeCN (2.0 mL) and the mixture was stirred at rt for 30 min. After the same work-up and separation as Entry 1, **25** (23.4 mg, 87%) was obtained.

[Table 3, Entry 7] NBS (14.5 mg, 0.08 mmol) was added to a solution of **9** (22.4 mg, 0.09 mmol) in MeCN (2.0 mL) and the mixture was stirred at rt for 30 min. After the same work-up and separation as Entry 1, **21** (25.1 mg, 85%) was obtained.

3a-Ethoxy- (26) and 3a-methoxy-1-methoxycarbonyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (27) from 11 — **[Table 4, Entry 2]** NCS (60.6 mg, 0.45 mmol) was added to a solution of **11** (109.9 mg, 0.50 mmol) in EtOH (10.0 mL) and the mixture was stirred at rt for 1 h. The solvent was evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with EtOAc–hexane (1:2, v/v) to give **26** (19.1 mg, 15%) and unreacted **11** (70.8 mg, 64%). **26**: colorless oil. IR (film): 3363, 2974, 1699, 1612, 1481, 1469, 1454, 1387 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.09 (3H, t, *J*=7.1 Hz), 2.32—2.42 (1H, m), 2.36 (1H, dd, *J*=7.1, 3.2 Hz), 2.98—3.07 (1H, m), 3.15—3.22 (1H, m), 3.27—3.37 (1H, m), 3.74 (4H, m), 5.31 (1H, d, *J*=9.8 Hz), 6.64 (1H, d, *J*=7.5 Hz), 6.77 (1H, t, *J*=7.5 Hz), 7.14 (1H, td, *J*=7.5, 1.2

Hz), 7.20 (1H, d, *J*=7.5 Hz). MS *m/z*: 262 (M^+). HR–MS *m/z*: Calcd for $C_{14}H_{18}N_2O_3$: 262.1317. Found: 262.1319.

[Table 4, Entry 5] NCS (34.4 mg, 0.26 mmol) was added to a solution of **11** (50.6 mg, 0.23 mmol) in MeOH (10.0 mL) and the mixture was stirred at rt for 4 h. After the same work-up and separation as Entry 2, **27** (28.3 mg, 49%) and unreacted **11** (10.4 mg, 20%) were obtained. **27**: mp 114—118 °C (colorless prisms, recrystallized from EtOAc). IR (KBr): 3365, 1693, 1678, 1456, 1389, 1207 cm^{-1}. ^{1}H-NMR (CD_3OD, rotational isomers exist in a ratio of 1:1) δ: 2.32—2.43 (2H, m), 3.00—3.13 (1H, m), 3.08 (3/2H, s), 3.09 (3/2H, s), 3.70 (3/2H, s), 3.69—3.80 (1H, m), 3.77 (3/2H, s), 5.32 (1/2H, s), 5.34 (1/2H, s), 6.65 (1H, d, *J*=7.6 Hz), 6.78 (1H, t, *J*=7.6 Hz), 7.15 (1H, td, *J*=7.6, 1.0 Hz), 7.20 (1H, d, *J*=7.6 Hz). MS *m/z*: 248 (M^+). *Anal*. Calcd for $C_{13}H_{16}N_2O_3$: C, 62.89; H, 6.50; N, 11.28. Found: C, 62.92; H, 6.53; N, 11.25.

[Table 4, Entry 7] NCS (27.8 mg, 0.21 mmol) was added to a solution of **11** (50.4 mg, 0.23 mmol) in MeCN (5.0 mL) and the mixture was stirred at rt for 1 h. After addition of H_2O, the whole was extracted with EtOAc. The extract was washed with brine, dried over Na_2SO_4 and evaporated under reduced pressure to leave a tar, which was a complex mixture. 31% yield of unreacted **11** was obtained.

20, 24, or 29 from 9 — [Table 5, Entry 1] General Procedure: Morpholine (0.03 mL, 0.31 mmol) was added to a solution of **9** (26.2 mg, 0.11 mmol) and I_2 (42.9 mg, 0.17 mmol) in distilled MeOH (1.0 mL) under ice cooling and the mixture was stirred at rt for 21 h. After addition of 10% aqueous $Na_2S_2O_3$ (excess), H_2O was added to the residue and 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 (1:4, v/v) to give **24** (10.6 mg, 36%) and unreacted **9** (11.8 mg, 45%).

[Table 5, Entry 3] In the general procedure, morpholine (0.06 mL, 0.68 mmol), **9** (55.9 mg, 0.23 mmol), I_2 (91.5 mg, 0.36 mmol), and distilled allyl alcohol (3.0 mL) were used. After the same work-up and separation as described in Entry 1, **29a** (11.9 mg, 17%) and unreacted **9** (43.3 mg, 79%) were obtained.

[**Table 5, Entry 6]** In the general procedure, morpholine (0.04 mL, 0.42 mmol), **9** (35.0 mg, 0.14 mmol), I_2 (358.2 mg, 1.41 mmol), and MeOH (3.0 mL) were used. After the same work-up and separation as described in Entry 1, **24** (37.9 mg, 98%) was obtained.

[Table 5, Entry 7] In the general procedure, morpholine (0.04 mL, 0.42 mmol), **9** (36.0 mg, 0.15 mmol), I_2 (368.4 mg, 1.45 mmol), and EtOH (3.0 mL) were used. After the same work-up and separation as described in Entry 1, **20** (41.1 mg, 97%) was obtained.

[Table 5, Entry 8] In the general procedure, morpholine (0.03 mL, 0.36 mmol), **9** (30.1 mg, 0.12 mmol), I_2 (308.1 mg, 1.21 mmol), and distilled allyl alcohol (3.0 mL) were used. After the same work-up and separation as described in Entry 1, **29a** (35.4 mg, 96%) was obtained. **29a**: colorless oil. IR (film): 1716,

1608, 1597, 1473, 1462, 1448, 1383 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.11—2.18 (1H, m), 2.33—2.43 (1H, m), 3.20—3.30 (1H, m), 3.70 (1H, ddt, *J*=12.9, 5.1, 1.7 Hz), 3.76—3.85 (5H, m), 3.91 (3H, br s), 5.08 (1H, dq, *J*=10.5, 1.7 Hz), 5.21 (1H, dq, *J*=17.1, 1.7 Hz), 5.58 (1H, d, *J*=17.6 Hz), 5.84 (1H, dquin, *J*=17.1, 10.5, 5.1 Hz), 7.10 (1H, d, *J*=7.6 Hz), 7.13 (1H, t, *J*=7.6 Hz), 7.25 (1H, d, *J*=7.6 Hz), 7.35 (1H, t, *J*=7.6 Hz). MS *m/z*: 304 (M^+). HR–MS *m/z*: Calcd for $C_{16}H_{20}N_2O_4$: 304.1423. Found: 304.1426.

[Table 5, Entry 9] In the general procedure, morpholine (0.04 mL, 0.42 mmol), **9** (34.7 mg, 0.14 mmol), I_2 (355.1 mg, 1.40 mmol), and distilled benzyl alcohol (3.0 mL) were used. After the same work-up and separation as described in Entry 1, **29b** (48.0 mg, 97%) was obtained. **29b**: colorless oil. IR (film): 1716, 1448, 1382^{-1}. ^{1}H-NMR (CD_3OD, rotational isomers exist in a ratio of 1:1) δ: 2.14—2.23 (1H, m), 2.39—2.48 (1H, m), 3.25—3.34 (1H, m), 3.77 (3H, s), 3.81—3.88 (1H, m), 3.90 (3/2H, s), 3.93 (3/2H, s), 4.18—4.33 (2H, m), 5.61 (1/2H, s), 5.70 (1/2H, s), 7.14 (1H, d, *J*=8.1 Hz), 7.16 (1H, t, *J*=7.6 Hz), 7.21—7.26 (3H, m), 7.27—7.33 (3H, m), 7.38 (1H, td, *J*=7.7, 1.2 Hz). HR–MS *m/z*: Calcd for $C_{20}H_{22}N_2O_4$: 354.1589. Found: 354.1574.

[Table 5, Entry 10] In the general procedure, morpholine (0.05 mL, 0.53 mmol), **9** (43.3 mg, 0.18 mmol), I_2 (443.1 mg, 17.5 mmol), and distilled ethylene glycol (3.0 mL) were used. The reaction time was 90 min. After the same work-up and separation as described in Entry 1, **29c** (49.3 mg, 92%) was obtained. **29c**: colorless oil. IR (film): 3450, 1705, 1456, 1387 cm^{-1}. ^{1}H-NMR (DMSO-d_6, rotational isomers exist in a ratio of 1:1) δ: 2.08 (1H, ddd, *J*=13.2, 7.3, 5.1 Hz), 2.25—2.35 (1H, m), 3.08 (1H, dt, *J*=9.9, 5.1 Hz), 3.10—3.20 (1H, m), 3.19 (1H, dt, *J*=9.9, 5.1 Hz), 3.40—3.45 (2H, m), 3.67—3.75 (4H, m), 3.84 (3H, s), 4.60 (1H, t, *J*=5.6 Hz), 5.50 (1H, br s), 7.11 (1H, d, *J*=7.6 Hz), 7.14 (1H, t, *J*=7.6 Hz), 7.29 (1H, d, *J*=7.6 Hz), 7.36 (1H, t, *J*=7.6 Hz). MS *m/z*: 308 (M^+). HR–MS *m/z*: Calcd for $C_{15}H_{20}N_2O_5$: 308.1419. Found: 308.1423.

[Table 5, Entry 11] In the general procedure, morpholine (0.06 mL, 0.68 mmol), **9** (56.5 mg, 0.23 mmol), I_2 (578.9 mg, 2.28 mmol), and distilled 2-chloroethanol (3.0 mL) were used. The reaction time was 20 min. After the same work-up and separation as described in Entry 1, **29d** (66.9 mg, 90%) was obtained. **29d**: colorless oil. IR (film): 1716, 1709, 1448, 1385, 1196, 1103 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.12—2.20 (1H, m), 2.33—2.45 (1H, m), 3.24—3.31 (1H, m), 3.42 (1H, dt, *J*=10.4, 5.5 Hz), 3.50 (1H, dt, *J*=10.4, 5.5 Hz), 3.59 (2H, t, *J*=5.5 Hz), 3.77 (3H, br s), 3.78—3.85 (1H, m), 3.91 (3H, s), 5.61 (1H, br s), 7.11 (1H, d, *J*=7.6 Hz), 7.14 (1H, t, *J*=7.6 Hz), 7.28 (1H, d, *J*=7.6 Hz), 7.36 (1H, t, *J*=7.6 Hz). MS *m/z*: 326 (M^+). HR–MS *m/z*: Calcd for $C_{15}H_{19}ClN_2O_4$: 326.1033 and 328.1004. Found: 326.1013 and 328.1017.

[Table 5, Entry 12] In the general procedure, morpholine (0.06 mL, 0.69 mmol), **9** (57.0 mg, 0.23 mmol), I_2 (583.4 mg, 2.30 mmol), and distilled 1,4-butanediol (3.0 mL) were used. The reaction time was 90 min. After the same work-up and separation as described in Entry 1, **29e** (68.5 mg, 89%) was obtained. **29e**:

colorless oil. IR (film): 2949, 1714, 1456, 1387, 1196 cm^{-1}. ^{1}H-NMR ($CDCl_3$, rotational isomers exist in a ratio of 1:1) δ: 1.58—1.63 (4H, m), 1.70 (1/2H, br s, disappeared on addition of D_2O), 1.79 (1/2H, br s, disappeared on addition of D_2O), 2.15 (1H, quint, J=7.3 Hz), 2.30—2.40 (1H, m), 3.12—3.18 (1H, m), 3.27 (1H, t, *J*=7.3 Hz), 3.29 (1H, t, *J*=7.3 Hz), 3.58—3.65 (2H, m), 3.78 (3/2H, br s), 3.84 (3/2H, br s), 3.91 (3/2H, br s), 3.97 (3/2H, br s), 3.75—4.00 (1H, m), 5.57 (1/2H, br s), 5.66 (1/2H, br s), 7.09 (1H, d, *J*=7.3 Hz), 7.10 (1H, t, *J*=7.3 Hz), 7.21 (1H, d, *J*=7.3 Hz), 7.33 (1H, t, *J*=7.3 Hz). HR–MS *m/z*: Calcd for $C_{17}H_{24}N_2O_5$: 336.1685. Found: 336.1681.

[Table 5, Entry 13] In the general procedure, morpholine (0.05 mL, 0.62 mmol), **9** (50.8 mg, 0.21 mmol), I_2 (519.9 mg, 2.05 mmol), and distilled *i*-PrOH (3.0 mL) were used. The reaction time was 20 min. After the same work-up and separation as described in Entry 1, **29f** (56.4 mg, 90%) was obtained. **29f**: colorless oil. IR (film): 1716, 1448, 1385, 1196 cm^{-1}. ^{1}H-NMR (CD_3OD, rotational isomers exist in a ratio of 1:1) δ: 1.02 (3H, d, *J*=6.1 Hz), 1.09 (3H, d, *J*=6.1 Hz), 2.02—2.11 (1H, m), 2.23—2.33 (1H, m), 3.22—3.35 (1H, m), 3.61(1H, dq, *J*=6.1, 6.1 Hz), 3.73—3.85 (4H, m), 3.90 (3H, s), 5.57 (1/2H, br s), 5.63 (1/2H, br s), 7.09 (1H, d, *J*=7.3 Hz), 7.11 (1H, t, *J*=7.3 Hz), 7.28 (1H, d, *J*=7.3 Hz), 7.33 (1H, t, *J*=7.3 Hz). HR–MS *m/z*: Calcd for $C_{16}H_{22}N_2O_4$: 306.1580. Found: 306.1581.

[Table 5, Entry 14] In the general procedure, morpholine (0.06 mL, 0.68 mmol), **9** (56.0 mg, 0.23 mmol), I_2 (573.4 mg, 2.26 mmol), and distilled *t*-butanol (3.0 mL) were used. The reaction time was 20 min. After the same work-up and separation as described in Entry 1, **29g** (65.0 mg, 80%) and two unknown products were obtained. **29g**: colorless oil. IR (film): 1716, 1448, 1383, 1180, 1095, 1041 cm^{-1}. ^{1}H-NMR (CD_3OD, rotational isomers exist in a ratio of 1:1) δ: 1.13 (9H, s), 1.87—1.96 (1H, m), 2.21—2.30 (1H, m), 3.36—3.43 (1H, m), 3.69—3.85 (4H, m), 3.89 (3H, s), 5.96 (1/2H, br s), 6.04 (1/2H, br s), 7.00 (1H, d, *J*=7.3 Hz), 7.04 (1H, t, *J*=7.3 Hz), 7.26 (1H, d, *J*=7.3 Hz), 7.27 (1H, t, *J*=7.3 Hz). HR–MS *m/z* : Calcd for $C_{17}H_{24}N_2O_4$: 320.1736. Found: 320.1733.

Application of I_2 and morpholine (3.0 mol eq.) Method to 11 — [Table 6, Entry 2] Morpholine (0.06 mL, 0.69 mmol) was added to a solution of **11** (50.3 mg, 0.23 mmol) and I_2 (585,6 mg, 2.31 mmol) in distilled MeOH (3.0 mL) under ice cooling and the mixture was stirred at rt for 20 min. After addition of 10% aqueous $Na_2S_2O_3$ (excess), H_2O was added to the residue 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 EtOAc to give **27** (34.6 mg, 60%).

[Table 6, Entry 3] Morpholine (0.06 mL, 0.74 mmol) was added to a solution of **11** (54.0 mg, 0.25 mmol) and I_2 (100.6 mg, 0.40 mmol) in distilled allyl alcohol (3.0 mL) under ice cooling and the mixture was stirred at rt for 5 h. After the same work-up and separation as described in Entry 2, **30** (5.1 mg, 8%)

and unreacted **11** (25.6 mg, 47%) were obtained. **30**: colorless oil. IR (film): 2954, 1697, 1612, 1483, 1469, 1454, 1387 cm^{-1}. ^{1}H-NMR (CD_3OD, rotational isomers exist in a ratio of 1:1) δ: 2.35—2.48 (2H, m), 2.99—3.10 (1H, m), 3.71 (3/2H, s), 3.77 (3/2H, s), 3.65—3.84 (3H, m), 5.05 (1H, dd, *J*=10.4, 1.8 Hz), 5.18 (1H, dq, *J*=17.1, 1.8 Hz), 5.32 (2/1H, s), 5.34 (2/1H, s), 5.83 (1H, dquin, *J*=17.1, 10.4, 5.5 Hz), 6.66 (1H, d, *J*=7.3 Hz), 6.78 (1H, t, *J*=7.3 Hz), 7.16 (1H, t, *J*=7.3 Hz), 7.21 (1H, d, *J*=7.3 Hz). HR–MS *m/z*: Calcd for $C_{15}H_{18}O_3N_2$: 274.1317. Found: 274.1322.

23 from 5-bromo-1-methoxy-*N*b-methoxycarbonyltryptamine (31) — NBS (6.5 mg, 0.04 mmol) was added to a solution of **31** (13.3 mg, 0.04 mmol) in $CHCl_3$ (1.0 mL, EtOH free) and the mixture was stirred at rt for 1.5 h. The solvent was evaporated under reduced pressure to leave an oil, which was purified by column-chromatography on SiO_2 with $CHCl_3$ to give **23** (15.4 mg, 93%).

1-Acetyl-7-bromo-*N*b-methoxycarbonyltryptamine (32) from 12 — A solution of **12** (20.5 mg, 0.07 mmol) in dry DMF (2.0 mL) was added to 60% NaH (6.6 mg, 0.14 mmol) at 0 °C with stirring. After additional stirring for 15 min at rt, a solution of AcCl (20.8 mg, 0.21 mmol) in dry DMF (1.0 mL) was added to the resultant solution. The mixture was stirred at rt for 3 h under N_2 atmosphere. After addition of saturated $NaHCO_3$, 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 subjected to p-TLC on SiO_2 with EtOAc–hexane (1:1, v/v). Extraction of the band having an *Rf* value of 0.39—0.30 with $CHCl_3$–MeOH–28% aq. NH_3 (100:10:0.1, v/v) gave **32** (9.4 mg, 40%). From the band having an *Rf* value of 0.60—0.54, unreacted **12** (5.0 mg, 24%) was obtained. **32**: 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), 3.32 (2H, dt, *J*=7.0, 5.7 Hz), 3.53 (3H, s), 7.23 (1H, t, *J*=7.7 Hz), 7.30 (1H, br t, *J*=5.7 Hz), 7.54 (1H, d, *J*=7.7 Hz), 7.64 (1H, d, *J*=7.7 Hz), 7.74 (1H, s). HR–MS *m/z*: Calcd for $C_{14}H_{15}BrN_2O_3$: 340.0245 and 338.9266. Found: 340.0241 and 338.0278.

1-Acetyl- (33) and 1-[(1-acetoxy)ethen-1-yl]-2,7-dibromo-*N*b-methoxycarbonyltryptamine (34) from 13 — In the same procedure for the preparation of **32**, **13** (25.0 mg, 0.06 mmol) in DMF (2.0 mL), 60% NaH (5.3 mg, 0.13 mmol), and AcCl (0.01 mL, 0.16 mmol) in benzene (0.5 mL) were used. After the same work-up as for **32**, the reaction products were subjected to p-TLC on SiO_2 with EtOAc–hexane (1:4, v/v). Extraction of the band having an *Rf* value of 0.47—0.42 with EtOAc–MeOH (9:1, v/v) gave **33** (6.3 mg, 23%). Extraction of the band having an *Rf* value of 0.53—0.50 with EtOAc–MeOH (9:1, v/v) gave **34** (4.5 mg, 15%). Extraction of the band having an *Rf* value of 0.60—0.56 with EtOAc–MeOH (9:1, v/v) gave unreacted **13** (13.1 mg, 52%). **33**: colorless oil. IR (film): 3336, 2947, 1716, 1701, 1525 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.75 (3H, s), 2.95 (2H, t, *J*=6.8 Hz), 3.43 (2H, q, *J*=6.8 Hz), 3.67 (3H, s), 4.75 (1H, br s, disappeared on addition of D_2O), 7.11 (1H, t, *J*=7.8 Hz), 7.43 (1H, d, *J*=7.8 Hz), 7.52 (1H, d, *J*=7.8

Hz). HR–MS *m/z*: Calcd for $C_{14}H_{14}Br_2N_2O_3$: 415.9350, 417.9340, and 419.9316. Found: 415.9371, 417.9350, and 419.9330. **34**: colorless oil. IR (film): 3342, 2951, 1774, 1705, 1525, 1414, 1255, 1174 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.13 (3H, s), 2.97 (2H, t, *J*=6.4 Hz), 3.44 (2H, br s), 3.68 (3H, s), 4.77 (1H, br s, disappeared on addition of D_2O), 5.22 (1H, d, *J*=2.3 Hz), 5.84 (1H, d, *J*=2.3 Hz), 7.03 (1H, t, *J*=7.8 Hz), 7.40 (1H, d, *J*=7.8 Hz), 7.51 (1H, d, *J*=7.8 Hz). HR–MS m/z: Calcd for $C_{16}H_{16}Br_2N_2O_4$: 457.9477, 459.9417, and 461.9462. Found: 457.9477, 459.9456, and 461.9436.

1-Acetyl-5,7-dibromo-*N*b-methoxycarbonyltryptamine (35) from 14 — In the same procedure for the preparation of **33** and **34**, **14** (30.0 mg, 0.08 mmol) in dry DMF (2.0 mL), 60% NaH (6.4 mg, 0.16 mmol), and AcCl (0.014 mL, 0.20 mmol) in benzene (0.5 mL) were used. After the same work-up and separation by column-chromatography on SiO_2 with EtOAc–hexane (1:3, v/v), **35** (19.3 mg, 58%) and unreacted **14** (2.4 mg, 8%) were obtained. **35**: colorless oil. IR (film): 3332, 2924, 2852, 1716, 1539, 1441, 1246, 1223 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.64 (3H, s), 2.87 (2H, t, *J*=6.3 Hz), 3.50 (2H, q, *J*=6.3 Hz), 3.69 (3H, s), 4.76 (1H, br s, disappeared on addition of D_2O), 7.32 (1H, br s), 7.62 (1H, d, *J*=1.5 Hz), 7.71 (1H, d, *J*=1.5 Hz). HR–MS *m/z*: Calcd for $C_{14}H_{14}Br_2N_2O_3$: 415.9350, 417.9340, and 419.9316. Found: 415.9371, 417.9350, and 419.9330.

1-Acetyl-2,5-dibromo-*N*b-methoxycarbonyltryptamine (36) from 18 — In the same procedure for the preparation of **33** and **34**, **18** (23.0 mg, 0.06 mmol) in dry DMF (2.0 mL), 60% NaH (4.9 mg, 0.12 mmol), and AcCl (0.012 mL, 0.16 mmol) in benzene (0.5 mL) were used. After the same work-up and purification by column-chromatography on SiO_2 with EtOAc–hexane (1:3, v/v), **36** (12.5 mg, 49%) and **18** (4.1 mg, 18%) were obtained. **36**: colorless oil. IR (film): 3338, 3010, 2945, 1701, 1531, 1441, 1369, 1292 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.86 (3H, s), 2.96 (2H, t, *J*=7.3 Hz), 3.44 (2H, q, *J*=7.3 Hz), 3.69 (3H, s), 4.76 (1H, br s, disappeared on addition of D_2O), 7.42 (1H, dd, *J*=9.0, 2.0 Hz), 7.63 (1H, br s), 8.18 (1H, d, *J*=9.0 Hz). HR–MS *m/z*: Calcd for $C_{14}H_{14}Br_2N_2O_3$: 415.9350, 417.9340, and 419.9316. Found: 415.9371, 417.9350, and 419.9330.

1-Acetyl-5-bromo-*N*b-methoxycarbonyltryptamine (37) from 19 — In the same procedure for the preparation of **33** and **34**, **19** (28.5 mg, 0.09 mmol) in dry DMF (3.0 mL), 60% NaH (9.5 mg, 0.19 mmol), and AcCl (24.3 mg, 0.28 mmol) in dry DMF (2.0 mL) were used. After the same work-up and purification by column-chromatography on SiO_2 with EtOAc–hexane (1:3, v/v), **37** (21.1 mg, 65%) was obtained. **37**: mp 131—132 °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 and 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.

3a-Acetoxy-8-acetyl-1-methoxycarbonyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (40) from 10 — Anhydrous NaOAc (35.7 mg, 0.44 mmol) was added to a solution of **10** (51.0 mg, 0.22 mmol) in Ac_2O (3.0 mL) and the mixture was stirred at 100 °C for 3.5 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 EtOAc–hexane (1:2, v/v) to give **40** (43.7 mg, 72%). **40**: mp 137—138 °C (colorless prisms, recrystallized from $CHCl_3$–hexane). IR (KBr): 1743, 1700, 1665, 1480, 1457, 1370, 1281 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.02 (3H, s), 2.48 (1H, td, *J*=10.0, 6.3 Hz), 2.55 (3H, br s), 2.76 (1H, dd, *J*=10.0, 5.0 Hz), 2.88 (1H, td, *J*=10.0, 5.0 Hz), 3.74 (3H, br s), 3.93 (1H, br t, *J*=6.3 Hz), 6.23 (1H, br s), 7.14 (1H, t, *J*=6.3 Hz), 7.37 (1H, t, *J*=6.3 Hz), 7.51 (1H, d, *J*=6.3 Hz), 8.07 (1H, br s). MS *m/z*: 318 (M^+). *Anal*. Calcd for $C_{16}H_{18}N_2O_5$: C, 60.37; H, 5.70; N, 8.80. Found: C, 60.17; H, 5.71; N, 8.79.

40 from 42 — Ac_2O (1.0 mL) was added to a solution of **42** (29.0 mg, 0.12 mmol) in pyridine (2.0 mL) and the mixture was stirred at rt for 1 h. After addition of H_2O, the whole was made alkaline with 40% aqueous NaOH and 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 (9:1, v/v) to give **40** (37.4 mg, 95%).

8-Acetyl-3a-hydroxy-1-methoxycarbonyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (41a) from 40 — Saturated aq. $NaHCO_3$ (5.0 mL) was added to a solution of **40** (94.7 mg, 0.30 mmol) in MeOH (5.0 mL) and the mixture was stirred at 90 °C for 1 h. After addition of H_2O, 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 **41a** (79.1 mg, 96%). **41a**: mp 199—200 °C (colorless prisms, recrystallized from EtOAc–hexane). IR (KBr): 3320, 1710, 1708, 1650, 1647, 1449, 1440, 1372, 1345, 1078 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.12 (3H, s), 2.40—2.44 (1H, m), 2.80—2.86 (1H, m), 3.62—3.68 (1H, m), 3.67 (3H, br s), 3.78 (1H, br s), 4.20 (1H, br s, disappeared on addition of D_2O), 5.66 (1H, br s), 7.19 (1H, t, *J*=6.3 Hz), 7.36 (1H, d, *J*=6.3 Hz), 7.43 (1H, d, *J*=6.3 Hz), 7.94 (1H, br d, *J*=6.3 Hz). MS *m/z*: 276 (M^+). *Anal*. Calcd for $C_{14}H_{16}N_2O_4$: C, 59.57; H, 5.95; N, 9.92. Found: C, 59.32; H, 5.67; N, 9.81.

8-Acetyl-3a-ethoxy-1-methoxycarbonyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (41b) from 26 — Ac_2O (0.5 mL) was added to a solution of **26** (27.3 mg, 0.10 mmol) in pyridine (1.0 mL) and the mixture was stirred at 60 °C for 6 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 (1:2, v/v) to give **41b** (24.0 mg, 76%). **41b**: colorless oil. IR (film): 1707, 1670, 1475, 1450, 1398, 1371 cm^{-1}. ^{1}H-NMR

($CDCl_3$) δ: 1.12 (3H, t, *J*=7.1 Hz), 2.30—2.40 (1H, m), 2.35 (1H, dd, *J*=11.5, 7.1 Hz), 2.56 (3H, br s), 2.85 (1H, ddd, *J*=11.5, 7.1 Hz), 3.17 (1H, dq, *J*=8.6, 7.1 Hz), 3.24 (1H, dq, *J*=8.6, 7.1 Hz), 3.74 (3H, br s), 3.88 (1H, br t), 5.99 (1H, br s), 7.17 (1H, td, *J*=7.3, 1.2 Hz), 7.33 (1H, dd, *J*=7.3, 1.2 Hz), 7.38 (1H, td, *J*=7.3, 1.2 Hz), 8.11 (1H, br s). HR–MS *m/z*: Calcd for $C_{16}H_{20}N_2O_4$: 304.1423. Found: 304.1420.

41b from 41a — A mixture of **41a** (34.5 mg, 0.13 mmol), NaH (3.6 mg, 0.15 mmol), and EtI (0.03 mL, 0.38 mmol) in anhydrous DMF (2.0 mL) was stirred at rt for 6 h under argon atmosphere. After addition of H_2O, the whole was extracted with EtOAc–MeOH (9:1, v/v). The extract was washed with brine, dried over Na_2SO_4 and evaporated under reduced pressure to leave an oil, which was purified by column-chromatography on SiO_2 with EtOAc–hexane (1:2, v/v) to give **41b** (35.3 mg, 93%).

42 from **22** — 10% Pd/C (21.3 mg) was added to a solution of **22** (52.8 mg, 0.20 mmol) in MeOH (3.0 mL) and the mixture was stirred at rt for 30 min under hydrogen atmosphere. Precipitates were filtered off and the filtrate was evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with EtOAc–hexane (1:1, v/v) to give **42** (10.4 mg, 93%). **42**: colorless hard oil. IR (film): 3367, 1695, 1684, 1466, 1458 cm^{-1}. ^{1}H-NMR ($CDCl_3$, rotational isomers exist in a ratio of 1:1) δ: 2.25 (1/2H, br s, disappeared on addition of D_2O), 2.27 (1/2H, br s, disappeared on addition of D_2O), 2.36—2.51 (2H, m), 3.14 (1H, td, *J*=10.1, 7.0 Hz), 3.67—3.85 (4H, m), 5.15 (1H, br s, disappeared on addition of D_2O), 5.19 (1/2H, br s), 5.23 (1/2H, br s), 6.64 (1H, d, *J*=7.5 Hz), 6.82 (1H, q, *J*=7.5 Hz), 7.18 (1H, t, *J*=7.5 Hz), 7.30 (1H, d, *J*=7.5 Hz). HR–MS *m/z*: Calcd for $C_{12}H_{14}N_2O_3$: 234.1005. Found: 234.1011.

22 from 25 — Silver cyanide (32.9 mg, 0.25 mmol) was added to a solution of **25 (**69.6 mg, 0.25 mmol**)** in MeCN–H_2O (3:2, v/v, 4.0 mL) and the mixture was stirred at rt for 30 min. 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 (1:2, v/v) to give **22** (55.2 mg, 85%) was obtained.

22 from 21 — Silver cyanide (6.4 mg, 0.05 mmol) was added to a solution of **21 (**15.7 mg, 0.05 mmol**)** in MeCN-H_2O (3:2, v/v, 1.0 mL) and the mixture was stirred at rt for 15 min. After the same work-up and separation as described from **25**, **22** (12.0 mg, 94%) was obtained.

20 from **22** — A mixture of **22** (10.7 mg, 0.04 mmol), NaH (5.8 mg, 0.12 mmol), and EtI (0.016 mL, 0.20 mmol) in anhydrous DMF (1.0 mL) was stirred for 30 min at rt. After addition of H_2O, 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 (1:4, v/v) to give **20** (8.0 mg, 68%).

24 from 22 — In the same procedure for **20** from **22, 22** (16.2 mg, 0.06 mmol), NaH (8.8 mg, 0.18 mmol), and MeI (0.02 mL, 0.30 mmol) in anhydrous DMF (1.0 mL) were used. After the same work-up

and purification, **24** (16.0 mg, 94%) was obtained.

29a from 22: In the same procedure for **20** from **22, 22** (10.7 mg, 0.04 mmol), NaH (5.8 mg, 0.12 mmol), and allyl bromide (0.02 mL, 0.20 mmol) in anhydrous DMF (1.0 mL) were used. After the same work-up and purification, **29a** (11.4 mg, 92%) was obtained.

26 from 20 — 5% Pd/C (10.4 mg) was added to a solution of **20** (14.3 mg, 0.05 mmol) in MeOH (4.0 mL) and the mixture was stirred at rt for 1.5 h under hydrogen atmosphere. Precipitates were filtered off and the filtrate was 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 **26** (10.4 mg, 81%).

(*2S,3aR,8aR*)-Methyl (44a) and (*2S,3aS,8aS*)-Methyl 1-acetyl-1,2,3,3a,8,8a-hexahydro-3a,8-dimethoxypyrrolo[2,3-*b*]indole-2-carboxylate (45a) from (*S*)-*N*b-acetyl-1-methoxytryptophan methyl ester ((*S*)-43) — Morpholine (0.04 mL, 0.46 mmol) was added to a solution of (*S*)-**43** (41.2 mg, 0.14 mmol) and I_2 (360.9 mg, 1.42 mmol) in MeOH (3.0 mL), and the mixture was stirred at rt for 2 h. After addition of 10% aqueous $Na_2S_2O_3$ (excess), H_2O was added and 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 (1:4, v/v) to give **44a** (2.8 mg, 6%), **45a** (22.0 mg, 48%), and unknown product (7.6 mg, 15.2%, MS *m/z*: 352 (M^+). **44a**: mp 129—130 °C (colorless prisms, recrystallized from EtOAc–hexane). IR (KBr): 1757, 1664 cm^{-1}. ^{1}H-NMR ($CDCl_3$, rotational isomers exist in a ratio of 4:1) δ: 2.13 (3/5H, s), 2.18 (4/5H, dd, *J*=13.7, 8.7 Hz), 2.37 (12/5H, s), 2.55 (1/5H, dd, *J*=13.7, 4.9 Hz), 2.65 (4/5H, *J*=13.7, 8.7 Hz), 2.75 (1/5H, dd, *J*=13.7, 9.0 Hz), 3.11 (3/5H, s), 3.21 (12/5H, s), 3.52 (3/5H, s), 3.65 (12/5H, s), 3.97 (3/5H, s), 4.03 (12/5H, s), 4.67 (1/5H, dd, *J*=9.0, 4.9 Hz), 4.93 (4/5H, t, *J*=8.7 Hz), 5.65 (4/5H, s), 5.98 (1/5H, s), 7.00—7.09 (2H, m), 7.16—7.19 (1/5H, m), 7.17 (4/5H, d, *J*=7.6 Hz), 7.29—7.34 (1/5H, m), 7.31 (4/5H, td, *J*=7.6, 1.2 Hz). $[\alpha]_D^{29}$ +45.5° (*c*=0.302, $CHCl_3$). MS *m/z*: 320 (M^+). *Anal.* Calcd for $C_{16}H_{20}N_2O_5$: C, 59.99; H, 6.29; N, 8.75. Found: C, 60.25; H, 6.45; N, 8.66. **45a**: mp 123—124 °C (colorless needles, recrystallized from EtOAc–hexane). IR (KBr): 1734, 1664 cm^{-1}. ^{1}H-NMR ($CDCl_3$, rotational isomers exist in a ratio of 2:1) δ: 2.11 (1H, s), 2.33 (1/3H, dd, *J*=13.4, 8.8 Hz), 2.34 (2/3H, dd, *J*=13.9, 9.5 Hz), 2.43 (2H, s), 2.46 (2/3H, dd, *J*=13.9, 2.7 Hz), 2.68 (1/3H, d, *J*=13.4 Hz), 3.10 (1H, s), 3.20 (2H, s), 3.75 (2H, s), 3.80 (1H, s), 3.94 (2H, s), 3.95 (1H, s), 4.61 (1/3H, d, *J*=8.8 Hz), 4.72 (2/3H, dd, *J*=9.5, 2.7 Hz), 5.76 (2/3H, s), 5.96 (1/3H, s), 7.03—7.11 (2H, m), 7.15 (1/3H, d, *J*=7.3 Hz), 7.18 (2/3H, d, *J*=6.8 Hz), 7.31—7.36 (1H, m). $[\alpha]_D^{30}$ –167.2 (*c* 0.301, $CHCl_3$). MS *m/z*: 320 (M^+). *Anal.* Calcd for $C_{16}H_{20}N_2O_5$: C, 59.99; H, 6.29; N, 8.75. Found: C, 60.08; H, 6.37; N, 8.68.

(*2S,3aS,8aS*)-Methyl (44b) and (*2S,3aR,8aR*)-methyl 1-acetyl-3a-chlolo-1,2,3,3a,8,8a-hexahydro-8-methoxypyrrolo[2,3-*b*]indole-2-carboxylate (45b) from (*S*)-43 — NCS (139.2 mg, 1.04 mmol) was

added to a solution of (*S*)-**43** (300.9 mg, 1.04 mmol) in MeCN (10.0 mL) and the mixture was stirred at rt for 20 h. H_2O was added and 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 (1:1, v/v) to give **44b** (144.3 mg, 43%) and **45b** (148.5 mg, 44%). **44b**: mp 113—114 °C (colorless prisms, recrystallized from EtOAc–hexane). IR (KBr): 1757, 1672 cm^{-1}. ^{1}H-NMR ($CDCl_3$, rotational isomers exist in a ratio of 9:1) δ: 2.14 (3/10H, s), 2.38 (27/10H, s), 2.47 (9/10H, dd, *J*=14.2, 8.8 Hz), 2.83—2.93 (1/10H, m), 2.90 (9/10H, dd, *J*=14.2, 8.8 Hz), 3.04 (1/10H, dd, *J*=13.8, 8.0 Hz), 3.55 (3/10H, s), 3.69 (27/10H, s), 3.96 (3/10H, s), 4.02 (27/10H, s), 4.74 (1/10H, dd, *J*=8.0, 6.5 Hz), 5.01 (9/10H, t, *J*=8.8 Hz), 5.71 (9/10H, s), 6.11 (1/10H, s), 7.00 (9/10H, d, *J*=8.1 Hz), 7.04—7.10 (11/10H, m), 7.29—7.35 (2H, m). $[\alpha]_D^{29}$ +5.9 (*c* 0.314, $CHCl_3$). MS *m/z*: 324, 326 (M^+). *Anal.* Calcd for $C_{15}H_{17}ClN_2O_4$: C, 55.48; H, 5.28; N, 8.63. Found: C, 55.39; H, 5.30; N, 8.62. **45b**: mp 114—115 °C (colorless needles, recrystallized from EtOAc–hexane). IR ($CHCl_3$): 1759, 1668 cm^{-1}. ^{1}H-NMR ($CDCl_3$, rotational isomers exist in a ratio of 4:1) δ: 2.14 (3/5H, s), 2.43 (12/5H, s), 2.67 (1/5H, dd, *J*=14.5, 9.0 Hz), 2.71 (4/5H, dd, *J*=14.5, 9.3 Hz), 2.76 (4/5H, dd, *J*=14.5, 3.4 Hz), 3.02 (1/5H, d, *J*=14.5 Hz), 3.78 (12/5H, s), 3.85 (3/5H, s), 3.91 (12/5H, s), 3.92 (3/5H, s), 4.71 (1/5H, d, *J*=9.0 Hz), 4.74 (4/5H, dd, *J*=9.3, 3.4 Hz), 5.85 (4/5H, s), 6.09 (1/5H, s), 7.01—7.16 (2H, m), 7.28—7.37 (2H, m). $[\alpha]_D^{30}$ –105.3 (*c* 0.314, $CHCl_3$). MS *m/z*: 324, 326 (M^+). *Anal.* Calcd for $C_{15}H_{17}ClN_2O_4$: C, 55.48; H, 5.28; N, 8.63. Found: C, 55.34; H, 5.01; N, 8.77.

(*2S,3aS,8aS*)-Methyl 1-acetyl-1,2,3,3a,8,8a-hexahydro-3a-hydroxy-8-methoxypyrrolo[2,3-*b*]indole 2-carboxylate (44c) from 44b — AgCN (19.2 mg, 0.14 mmol) was added to a solution of **44b** (23.1 mg, 0.07 mmol) in MeCN (1.5 mL) and H_2O (1.0 mL). The mixture was stirred at rt for 19 h. The whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was purified by column-chromatography on SiO_2 with EtOAc–hexane (7:3, v/v) to give **44c** (20.9 mg, 96%). **44c**: colorless oil. IR (film): 3356, 1747, 1645 cm^{-1}. ^{1}H-NMR ($CDCl_3$, rotational isomers exist in a ratio of 6:1) δ: 2.12 (3/7H, s), 2.18 (6/7H, dd, *J*=13.7, 8.9 Hz), 2.32 (18/7H, s), 2.45 (1/7H, dd, *J*=14.4, 6.1 Hz), 2.65 (6/7H, dd, *J*=13.7, 8.9 Hz), 2.78 (1/7H, dd, *J*=14.4, 9.2 Hz), 3.13 (1H, br s), 3.59 (3/7H, s), 3.67 (18/7H, s), 3.90 (3/7H, s), 4.00 (18/7H, s), 4.75 (1/7H, dd, *J*=9.2, 6.1 Hz), 4.98 (6/7H, t, *J*=8.9 Hz), 5.40 (6/7H, s), 5.69 (1/7H, s), 6.99 (6/7H, d, *J*=7.6 Hz), 7.00—7.07 (2/7H, m), 7.03 (6/7H, d, *J*=7.6 Hz), 7.27—7.33 (2H, m). $[\alpha]_D^{29}$ +37.6 (*c* 0.344, $CHCl_3$). HR–MS *m/z*: Calcd for $C_{15}H_{18}N_2O_5$: 306.1215. Found: 306.1216.

(*2S,3aR,8aR*)-Methyl 1-acetyl-1,2,3,3a,8,8a-hexahydro-3a-hydroxy-8-methoxypyrrolo[2,3-*b*]indole-2-carboxylate (45c) from 45b — AgCN (18.9 mg, 0.14 mmol) was added to a solution of **45b** (22.5 mg, 0.07 mmol) in MeCN (1.5 mL) and H_2O (1.0 mL). The mixture was stirred at rt for 67 h. The whole

was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was purified by column-chromatography on SiO_2 with EtOAc–hexane (7:3, v/v) to give **45c** (18.7 mg, 88%). **45c**: mp 167—168 °C (colorless prisms, recrystallized from EtOAc–hexane). IR ($CHCl_3$): 3338, 1761, 1635 cm^{-1}. ^{1}H-NMR ($CDCl_3$, rotational isomers exist in a ratio of 97:3) δ: 2.23 (1H, d, *J*=14.3 Hz), 2.37 (1H, dd, *J*=14.3, 9.8 Hz), 2.38 (3H, s), 3.84 (3H, s), 3.92 (3H, s), 4.52 (1H, s, disappeared on addition of D_2O), 4.70 (1H, d, *J*=9.8 Hz), 5.55 (1H, s), 6.99 (1H, d, *J*=7.6 Hz), 7.06 (1H, t, *J*=7.6 Hz), 7.29—7.34 (2H, m). $[\alpha]_D^{28}$ –110.7 (*c* 0.317, $CHCl_3$). MS *m/z*: 306 (M^+). *Anal.* Calcd for $C_{15}H_{18}N_2O_5$: C, 58.81; H, 5.92; N, 9.15. Found: C, 58.57; H, 5.99; N, 9.16.

(*2S,3aS,8aR*)-Methyl 1-acetyl-1,2,3,3a,8,8a-hexahydro-3a-methoxypyrrolo[2,3-*b*]indole-2-carboxylate (46) from 45a — 10% Pd/C (96.4 mg) was added to a solution of **45a** (91.8 mg, 0.28 mmol) in MeOH (9.0 mL) and the mixture was stirred at rt for 2h under hydrogen atmosphere. The solvent was 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 **46** (80.5 mg, 97%). **46**: mp 193—194 °C (colorless prisms, recrystallized from EtOAc). IR (KBr): 3347, 1749, 1653 cm^{-1}. ^{1}H-NMR ($CDCl_3$, rotational isomers exist in a ratio of 5:1) δ: 2.02 (5/2H, s), 2.24 (1/2H, s), 2.56—2.64 (1/3H, m), 2.61 (5/6H, dd, *J*=13.4, 8.6 Hz), 2.73 (5/6H, dd, *J*=13.4, 2.4 Hz), 3.10 (5/2H, s), 3.13 (1/2H, s), 3.75 (1/2H, s), 3.81 (5/2H, s), 4.40—4.46 (1/6H, m), 4.44 (5/6H, dd, *J*=8.6, 2.4 Hz), 4.57 (1/6H, br s, disappeared on addition of D_2O), 5.23 (5/6H, br s, disappeared on addition of D_2O), 5.67 (1/6H, br d, *J*=1.2 Hz, collapsed to s on addition of D_2O), 5.81 (5/6H, d, *J*=2.4 Hz, collapsed to s on addition of D_2O), 6.61 (5/6H, d, *J*=7.6 Hz), 6.70 (1/6H, d, *J*=7.6 Hz), 6.79 (5/6H, d, *J*=7.6 Hz), 6.90 (1/6H, d, *J*=7.6 Hz), 7.14—7.24 (2H, m). $[\alpha]_D^{27}$ –261.9 (*c* 0.320, $CHCl_3$). MS *m/z*: 290 (M^+). *Anal.* Calcd for $C_{15}H_{18}N_2O_4$: C, 62.05; H, 6.25; N, 9.65. Found: C, 62.21; H, 6.29; N, 9.64.

(*2S,3aR,8aR*)-Methyl 1,8-diacetyl-1,2,3,3a,8,8a-hexahydro-3a-methoxypyrrolo[2,3-*b*]indole-2-carboxylate (47) from 46 — Ac_2O (2.0 mL) was added to a solution of **46** (52.2 mg, 0.18 mmol) in pyridine (4.0 mL) and stirred at 60—65 °C for 48 h. After evaporation of the solvent under reduced pressure, sat. aq. $NaHCO_3$ was added to the residue 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 purified by column-chromatography on SiO_2 with CH_2Cl_2–MeOH (99:1, v/v) to give **47** (40.8 mg, 68%). **47:** mp 133—134 °C (colorless needles, recrystallized from EtOAc–hexane). IR (KBr): 1757, 1672, 1660 cm^{-1}. ^{1}H-NMR ($CDCl_3$, rotational isomers exist in a ratio of 7:3) δ: 1.78 (9/10H. s), 2.21 (21/10H, s), 2.39 (27/10H, s), 2.44 (7/10H, t, *J*=12.0 Hz), 2.45—2.54 (3/10H, m), 2.63 (9/10H, s), 2.75 (7/10H, dd, *J*=12.0, 6.8 Hz), 2,93—3.02 (3/10H, m), 3.06 (9/10H, s), 3.11 (21/10H, s), 3.73 (21/10H, s),

3.81 (9/10H, s), 3.89 (7/10H, dd, *J*=12.0, 6.8 Hz), 4.08—4.17 (3/10H, m), 5.98 (3/10H, s), 6.52 (7/10H, s), 7.16—7.48 (37/10H, m), 8.05 (3/10H, d, *J*=7.5 Hz). $[\alpha]_D^{30}$ –36.1 (*c* 0.329, $CHCl_3$). HR–MS *m/z*: Calcd for $C_{17}H_{20}N_2O_5$: 332.1372. Found: 332.1377.

(±)-2,3a-*cis*- ((±)-49) and (±)-2,3a-*trans*-3a-Acetoxy-1,8-diacetyl-2-methoxycarbonyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole ((±)-50) from (±)-48 — Sodium acetate (373.4 mg, 4.55 mmol) was added to a solution of (±)-**48** (622.9 mg, 2.26 mmol) in Ac_2O (25.0 mL) and stirred at 120 °C for 12 h. H_2O was added to the reaction mixture, and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to column-chromatography on SiO_2 with $CHCl_3$–MeOH–29% aq. NH_3 (100:1:0.1, v/v) as an eluent to afford (±)-**49** (170.0 mg, 21%) and (±)-**50** (187.3 mg, 23%) in the order of elution. (±)-**49**: mp 156—157 °C (colorless prisms, recrystallized from MeOH–H_2O. IR (KBr): 3475, 2950, 1742, 1678, 1602, 1478, 1403, 1368, 1231, 1043, 760 cm^{-1}. ^{1}H-NMR (5%CD_3OD in $CDCl_3$, 27 °C, rotational isomers existed in a ratio of 4:1) δ: 1.81 (3/5H, s), 2.00 (3H, s), 2.25 (12/5H, s), 2.41 (12/5H, s), 2.51 (1H, dd, *J*=12.2, 10.7 Hz), 2.63 (3/5H, s), 3.24 (4/5H, dd, *J*=12.2, 6.4 Hz), 3.61–3.66 (1/5H, m), 3.73 (12/5H, s), 3.83 (3/5H, s), 3.91 (4/5H, dd, *J*=10.7, 6.4 Hz), 4.20–4.23 (1/5H, m), 6.15 (1/5H, s), 6.64 (4/5H, s), 7.16 (1/5H, t, *J*=7.8 Hz), 7.26–7.28 (8/5H, m), 7.39–7.47 (1H, m), 7.62-7.68 (1H, m), 7.97 (1/5H, d, *J*=7.8 Hz). MS *m/z*: 360 (M^+). *Anal.* Calcd for $C_{18}H_{20}N_2O_6$: C, 60.00; H, 5.59; N, 7.77. Found: C, 60.09; H, 5.60; N, 7.76. (±)-**50**: mp 130—132 °C (colorless prisms, recrystallized from MeOH–H_2O. IR (KBr): 3460, 2950, 1747, 1661, 1478, 1403, 1383, 1233, 763 cm^{-1}. ^{1}H-NMR (CD_3OD, 27 °C, rotational isomers existed in a ratio of 4:1) δ: 2.05 (3H, s), 2.08 (12/5H, s), 2.43 (3/5H, s), 2.45 (3/5H, s), 2.67 (12/5H, s), 2.90 (1/5H, dd, *J*=12.7, 9.3 Hz), 3.00 (4/5H, dd, *J*=12.7, 9.3 Hz), 3.13 (1/5H, d, *J*=12.7 Hz), 3.19 (3/5H, s), 3.24 (12/5H, s), 4.90 (1H, d, *J*=9.3 Hz), 4.98 (1/5H, d, *J*=9.3 Hz), 6.43 (4/5H, s), 6.68 (1/5H, s), 7.20 (4/5H, t, *J*=7.8 Hz), 7.26 (1/5H, t, *J*=7.8 Hz), 7.39–7.45 (1H, m), 7.48–7.56 (6/5H, m), 7.86 (4/5H, d, *J*=7.8 Hz). MS *m/z*: 360 (M^+). *Anal.* Calcd for $C_{18}H_{20}N_2O_6 \cdot H_2O$: C, 57.14; H, 5.86; N, 7.40. Found: C, 57.06; H, 5.91; N, 7.39.

(±)-50 from (±)-49 — KO*t*Bu (23.1 mg, 0.20 mmol) was added to a solution of (±)-**49** (29.6 mg, 0.08 mmol) in anhydrous *N*,*N*-dimethylformamide (5.0 mL) and stirred at rt for 10 min under Ar atmosphere. Then Ac_2O (5.0 mL) and pyridine (5.0 mL) were added under ice-cooling and stirring was continued at rt for 4 h. H_2O was added to the reaction mixture, and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was purified by column-chromatography on Al_2O_3 with EtOAc–hexane (1:1, v/v) as an eluent to give (±)-**50** (15.0 mg, 51%).

(±)-2,3a-*trans*-1,8-Diacetyl-3a-hydroxy-2-methoxycarbonyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]-indole ((±)-51) from (±)-50 — Sodium (1.4 mg, 0.06 mmol) was dissolved in anhydrous MeOH (1.0 mL) at 0 °C, and a solution of (±)-**50** (5.1 mg, 0.01 mmol) in anhydrous MeOH (1.0 mL) was added. After stirring at rt for 1 h, H_2O was added to the reaction mixture, and the whole was acidified with 10% citric acid and extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was purified by column-chromatography on SiO_2 with CH_2Cl_2–MeOH (95:5, v/v) as an eluent to afford (±)-**51** (4.3 mg, 96%). (±)-**51**: mp 274—275 °C (colorless plates, recrystallized from MeOH). IR (KBr): 3285, 3012, 2931, 1702, 1668, 1635, 1597, 1479, 1125, 763 cm^{-1}. ^{1}H-NMR (CD_3OD, 27 °C, rotational isomers existed in a ratio of 4:1) δ: 2.00 (12/5H, s), 2.33 (3/5H, s), 2.44 (3/5H, s), 2.61 (12/5H, s), 2.67 (1/5H, dd, *J*=12.7, 9.8 Hz), 2.80 (4/5H, dd, *J*=12.7, 9.1 Hz), 2.82 (1/5H, d, *J*=12.7 Hz), 2.98 (4/5H, d, *J*=12.7 Hz), 3.15 (3/5H, s), 3.19 (12/5H, s), 4.79 (4/5H, d, *J*=9.1 Hz), 4.81 (1/5H, d, *J*=9.8 Hz), 5.90 (4/5H, s), 6.26 (1/5H, s), 7.16 (4/5H, td, *J*=7.6, 1.2 Hz), 7.21 (1/5H, t, *J*=7.6 Hz), 7.33 (4/5H, td, *J*=7.6, 1.2 Hz), 7.37 (4/5H, dd, *J*=7.6, 1.2 Hz), 7.41 (1/5H, d, *J*=7.6 Hz), 7.43 (1/5H, t, *J*=7.6 Hz), 7.86 (1H, d, *J*=7.6 Hz). MS *m/z*: 318 (M^+). *Anal.* Calcd for $C_{16}H_{18}N_2O_5$: C, 60.37; H, 5.70; N, 8.80. Found: C, 60.37; H, 5.76; N, 8.75.

(*2S,3aS,8aS*)-Methyl 3a-acetoxy-1,8-diacetyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole-2-carboxylate (50) from (*2S,3aS,8aS*)-44c — 10% Pd/C (15.9 mg) was added to a solution of (*2S,3aS,8aS*)-**44c** (13.0 mg, 0.04 mmol) in MeOH (2.0 mL) and the mixture was stirred at rt for 2 h under hydrogen atmosphere. The solvent was evaporated under reduced pressure to leave an oil, which was dissolved in pyridine (2.0 mL). Ac_2O (1.0 mL) was added to the resultant solution and stirred at 50—60 °C for 3 h. After evaporation of the solvent under reduced pressure, sat. aq. $NaHCO_3$ was added to the residue 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 purified by column-chromatography on SiO_2 with EtOAc–hexane (7:3, v/v) to give (*2S,3aS,8aS*)-**50** (11.9 mg, 78%). (*2S,3aS,8aS*)-**50**: mp 195—197 °C (colorless needles, recrystallized from EtOAc–hexane). IR (KBr): 1747, 1666 cm^{-1}. $[\alpha]_D^{30}$ +112.5 (*c* 0.275, $CHCl_3$). ^{1}H-NMR is the same with that of (±)-**50**.

***N*b-Acetyl-2,3-dihydro-5-methoxytryptophan methyl ester (54) from (*S*)-(+)-*N*b-acetyl-5-methoxytryptophan methyl ester ((*S*)-(+)-53)** — Et_3SiH (240.1 mg, 2.07 mmol) was added to a solution of (*S*)-(+)-**53** (200.1 mg, 0.69 mmol) in CF_3CO_2H (3.0 mL) under ice cooling 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 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 (9:1, v/v) to give unreacted (*S*)-(+)-**53** (6.0 mg,

3%) and **54** (175.8 mg, 87%) in the order of elution. **54** is a mixture of diastereomers.

(*S*)-(+)-*N*b-Acetyl-1-hydroxy-5-methoxytryptophan methyl ester ((*S*)-(+)-55a) from the mixture of diastereomers (54) — 30% H_2O_2 (1.3 mL, 11.5 mmol) was added to a solution of **54** (335.0 mg, 1.15 mmol) and $Na_2WO_4 \cdot 2H_2O$ (75.7 mg, 0.23 mmol) in MeOH (35.0 mL) and H_2O (3.5 mL) under ice cooling. The mixture was stirred at 0 °C 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 column-chromatographed on SiO_2 with EtOAc–hexane (7:3, v/v) to give (*S*)-(+)-**55a** (299.0 mg, 85%). (*S*)-(+)-**55a**: colorless oil. IR (film): 1743, 1653, 1439, 1375, 1223, 1093 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.82 (3H, s), 2.97 (1H, dd, *J*=14.6, 8.4 Hz), 3.08 (1H, dd, *J*=14.6, 5.8 Hz), 3.59 (3H, s), 3.77 (3H, s), 4.47 (1H, ddd, *J*=8.4, 7.6, 5.8 Hz, collapsed to dd, *J*=8.4, 5.8 Hz, on addition of D_2O), 6.79 (1H, dd, *J*=8.8, 2.2 Hz), 6.99 (1H, d, *J*=2.2 Hz), 7.19 (1H, s), 7.22 (1H, d, *J*=8.8 Hz), 8.30 (1H, br d, *J*=7.6 Hz, disappeared on addition of D_2O), 11.05 (1H, br s, disappeared on addition of D_2O). $[\alpha]_D^{30}$ +36.3 ($CHCl_3$, *c* 0.211). HR–MS *m/z*: *Anal.* Calcd for $C_{15}H_{18}N_2O_5$: 306.1215. Found: 306.1215.

(*S*)-(+)-*N*b-Acetyl-1,5-dimethoxytryptophan methyl ester ((*S*)-(+)-55b) from (*S*)-(+)-55a — Excess CH_2N_2 in Et_2O was added to a solution of (*S*)-(+)-**55a** (38.0 mg, 0.12 mmol) in MeOH (1.0 mL) and the mixture was stirred at rt for 2 h. The solvent was evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with EtOAc–hexane (2:1, v/v) to give (*S*)-(+)-**55b** (32.9 mg, 83%). (*S*)-(+)-**55b**: mp 127.0—127.5 °C (colorless powder recrystallized from EtOAc). IR (KBr): 3313, 1726, 1630, 1552, 1441, 1377, 1271, 1092 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.98 (3H, s), 3.22 (1H, dd, *J*=5.3, 15.0 Hz), 3.27 (1H, dd, *J*=5.3, 15.0 Hz), 3.71 (3H, s), 3.84 (3H, s), 4.02 (3H, s), 4.92 (1H, td, *J*=5.3, 7.8 Hz, collapsed to t, *J*=5.3 Hz, on addition of D_2O), 5.99 (1H, br d, *J*=7.8 Hz, disappeared on addition of D_2O), 6.90 (1H, dd, *J*=2.2, 8.8 Hz), 6.94 (1H, d, *J*=2.2 Hz), 6.99 (1H, s), 7.29 (1H, d, *J*=8.8 Hz). $[\alpha]_D^{27}$ +53.0 ($CHCl_3$, *c* 0.200). *Anal.* Calcd for $C_{16}H_{20}N_2O_5$: C, 59.99; H, 6.29; N, 8.74. Found: C, 60.01; H, 6.39; N, 8.82.

A mixture of diastereomers of *N*b-acetyl-2,3-dihydro-5-methoxytryptophan methyl ester ((±)-54) from (±)-*N*b-acetyl-5-methoxytryptophan methyl ester ((±)-53) — In the same procedure for the optically active **54**, Et_3SiH (447.2 mg, 3.86 mmol) and (±)-**53** (372.7 mg, 1.29 mmol) in CF_3CO_2H (4.0 mL) were used. After the same work-up and separation, (±)-**54** (260.1 mg, 69%) was obtained.

(±)-*N*b-Acetyl-1-hydroxy-5-methoxytryptophan methyl ester ((±)-55a) from the mixture of diastereomer ((±)-54) — In the same procedure for the optically active (*S*)-**55a**, 30% H_2O_2 (0.86 mL, 7.6 mmol), (±)-**54** (220.1 mg, 0.76 mmol), and $Na_2WO_4 \cdot 2H_2O$ (50.1 mg, 0.15 mmol) in MeOH (20.0 mL) and H_2O (2.0 mL) were used. After the same work-up and separation, (±)-**55a** (138.2 mg, 60%) was

obtained. (±)-**55a**: mp 179—180 °C (decomp., colorless fine needles recrystallized from EtOAc). IR (KBr): 3398, 1732, 1626, 1531, 1232 cm^{-1}. ^{1}H-NMR spectrum was identical with that of (*S*)-(+)-**55a**. MS *m/z*: 306 (M^+). *Anal.* Calcd for $C_{15}H_{18}N_2O_5 \cdot 1/4H_2O$: C, 57.96; H, 6.00; N, 9.01. Found: C, 58.20; H, 5.85; N, 9.17.

***N*b-Acetyl-1,5-dimethoxytryptophan methyl ester ((±)-55b) from *N*b-acetyl-1-hydroxy-5-methoxytryptophan methyl ester ((±)-55a)** — MeI (384.8 mg, 2.71 mmol) was added to a solution of K_2CO_3 (187.0 mg, 1.35 mmol) and (±)-**55a** (187.0 mg, 0.45 mmol) in acetone (10.0 mL) under ice cooling, and the mixture was 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 column-chromatographed on SiO_2 with $CHCl_3$–MeOH (99:1, v/v) to give (±)-**55b** (130.2 mg, 90%). (±)-**55b**: mp 102—103 °C (pale yellow fine needles recrystallized from EtOAc). IR ($CHCl_3$): 3428, 1741, 1674, 1518, 1481,1439, 1254, 1093 cm^{-1}. ^{1}H-NMR spectrum was identical with that of (*S*)-(+)-**55a**. MS *m/z*: 320 (M^+). *Anal.* Calcd for $C_{16}H_{20}N_2O_5$: C, 59.99; H, 6.29; N, 8.74. Found: C, 59.69; H, 6.19; N, 8.74.

(2*S*,3a*R*,8a*S*) ((–)-56), (2*S*,3a*S*,8a*R*)-1-Acetyl-7-iodo-3a,5-dimethoxy-2-methoxycarbonyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3*b*]indole ((+)-57), (*S*)-(+)-*N*b-acetyl-2-iodo- ((+)-58), and (*S*)-(+)-*N*b-acetyl-4-iodo-1,5-dimethoxytryptophan methyl ester ((+)-59) from (*S*)-(+)-55b — [Table 7, Entry 1] Morpholine (0.046 mL, 0.53 mmol) was added to a solution of (+)-**55b** (56.4 mg, 0.18 mmol) and I_2 (447.7 mg, 1.76 mmol) in MeOH (3.0 mL), and the mixture was stirred at rt for 0.5 h. After addition of 10% aqueous $Na_2S_2O_3$ (excess) and H_2O, 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 (1:1, v/v) to give (+)-**58** (10.1 mg, 13%) and unreacted (+)-**55b** (9.2 mg, 16%) in the order of elution. (+)-**58**: mp 152—153 °C (colorless powder, recrystallized from $CHCl_3$–hexane). IR (KBr): 3357, 1726, 1668, 1437, 1223, 1018 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.98 (3H, s), 3.17 (1H, dd, *J*=14.6, 6.0 Hz), 3.21 (1H, dd, *J*=14.6, 6.0 Hz), 3.70 (3H, s), 3.85 (3H, s), 4.02 (3H, s), 4.89 (1H, td, *J*=7.6, 6.0 Hz, collapsed to t, *J*=6.0 Hz, on addition of D_2O), 6.04 (1H, br d, *J*=7.6 Hz, disappeared on addition of D_2O), 6.84 (1H, dd, *J*=8.8, 2.4 Hz), 7.01 (1H, d, *J*=2.4 Hz), 7.30 (1H, d, *J*=8.8 Hz). $[\alpha]_D^{29}$ +22.4 ($CHCl_3$, *c* 0.125). MS *m/z*: 446 (M^+). *Anal.* Calcd for $C_{16}H_{19}IN_2O_5 \cdot 1/4H_2O$: C, 42.63; H, 4.36; N, 6.21. Found: C, 42.71; H, 4.31; N, 6.28.

[**Table 7, Entry 2]** Morpholine (0.07 mL, 0.81 mmol), (+)-**55b** (86.7 mg, 0.27 mmol), I_2 (688.2 mg, 2.71 mmol), and MeOH (4.0 mL) were used. The reaction time was 1 h. After the same work-up and separation as Entry 1, (–)-**56** (8.3 mg, 7%), (+)-**58** (7.0 mg, 6%), and (+)-**57** (9.0 mg, 7%) were obtained in the order of elution. (–)-**56**: colorless oil. IR (film): 2951, 1747, 1653, 1477, 1437, 1201, 1039 cm^{-1}.

^{1}H-NMR ($CDCl_3$, rotational isomers exist in a ratio of 5:1) δ: 2.04 (5/2H, s), 2.27 (1/2H, s), 2.51—2.59 (1/3H, m), 2.56 (5/6H, dd, *J*=13.5, 8.9 Hz), 2.70 (5/6H, dd, *J*=13.5, 1.0 Hz), 3.12 (5/2H, s), 3.14 (1/2H, s), 3.74 (5/2H, s), 3.75 (1/2H, s), 3.76 (1/2H, s), 3.80 (5/2H, s), 4.37 (1/6H, br d, *J*=4.2 Hz, disappeared on addition of D_2O), 4.45—4.50 (1/6H, m), 4.47 (5/6H, dd, *J*=8.8, 1.7 Hz), 4.99 (5/6H, br d, *J*=4.2 Hz, disappeared on addition of D_2O), 5.71 (1/6H, d, *J*=4.2 Hz, collapsed to s on addition of D_2O), 5.89 (5/6H, d, *J*=4.2 Hz, collapsed to s on addition of D_2O), 6.74 (5/6H, d, *J*=2.4 Hz), 6.78 (1/6H, d, *J*=2.4 Hz), 7.10 (5/6H, d, *J*=2.4 Hz) 7.16 (1/6H, d, *J*=2.4 Hz). $[\alpha]_D^{29}$ –120.5 ($CHCl_3$, *c* 0.161). MS *m/z*: 446 (M^+). HR–MS *m/z*: Calcd for $C_{16}H_{19}IN_2O_5$: 446.03390. Found: 446.03249. (+)-**57**: colorless oil. IR (film): 2951, 1736, 1653, 1574, 1477, 1205, 1109, 1039 cm^{-1}. ^{1}H-NMR ($CDCl_3$, rotational isomers exist in a ratio of 4:1) δ: 2.05 (12/5H, s), 2.29 (3/5H, s), 2.61 (1/5H, dd, *J*=13.7, 9.2 Hz), 2.68 (1/5H, dd, *J*=13.7, 1.9 Hz), 2.76 (4/5H, dd, *J*=12.9, 8.5 Hz), 2.82 (4/5H, dd, *J*=12.9, 1.3 Hz), 3.11 (12/5H, s), 3.13 (3/5H, s), 3.30 (3H, s), 3.72 (12/5H, s), 3.74 (3/5H, s), 4.30 (1/5H, br s, disappeared on addition of D_2O), 4.52 (4/5H, dd, *J*=8.5, 1.3 Hz), 4.97 (1/5H, dd, *J*=9.2, 1.9 Hz), 5.03 (4/5H, br s, disappeared on addition of D_2O), 5.44 (1/5H, s), 5.51 (4/5H, s), 6.75 (4/5H, d, *J*=2.2 Hz), 6.73 (1/5H, d, *J*=2.2 Hz), 7.11 (4/5H, d, *J*=2.2 Hz), 7.15 (1/5H, d, *J*=2.2 Hz). $[\alpha]_D^{30}$ +160.4 ($CHCl_3$, *c* 0.106). MS *m/z*: 446 (M^+). HR–MS *m/z*: Calcd for $C_{16}H_{19}IN_2O_5$: 446.03390. Found: 446.03739.

[Table 7, Entry 4] Morpholine (0.02 mL, 0.19 mmol) was added to a solution of (+)-**55b** (20.3 mg, 0.063 mmol) and I_2 (161.1 mg, 0.63 mmol) in *i*-PrOH (2.0 mL) and the mixture was stirred at rt for 3 h. After the same work-up and separation as Entry 1, (+)-**58** (9.3 mg, 33%), unreacted (+)-**55b** (4.1 mg, 20%), and (+)-**59** (1.9 mg, 7%) were obtained in the order of elution. (+)-**59**: colorless solid. IR (film): 1743, 1653, 1554, 1541, 1458, 1437, 1061, 756 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.94 (3H, s), 3.53 (1H, dd, *J*=15.3, 7.9 Hz), 3.71 (1H, dd, *J*=15.3, 5.5 Hz), 3.73 (3H, s), 3.91 (3H, s), 4.02 (3H, s), 4.99 (1H, td, *J*=7.9, 5.5 Hz, collapsed to dd, *J*=7.9, 5.5 Hz, on addition of D_2O), 6.00 (1H, br d, *J*=7.9 Hz, disappeared on addition of D_2O), 6.92 (1H, d, *J*=9.2 Hz), 7.18 (1H, s), 7.34 (1H, d, *J*=9.2 Hz). $[\alpha]_D^{24}$ +12.2 ($CHCl_3$, *c* 0.049). HR–MS *m/z*: Calcd for $C_{16}H_{19}IN_2O_5$: 446.03390. Found: 446.03410.

[Table 7, Entry 5] Morpholine (0.02 mL, 0.19 mmol) was added to a solution of (+)-**55b** (20.1 mg, 0.06 mmol) and I_2 (159.5 mg, 0.63 mmol) in *t*-BuOH (2.0 mL) and the mixture was stirred at rt for 3 h. After the same work-up and separation as Entry 1, (+)-**58** (6.5 mg, 23%), unreacted (+)-**55b** (3.8 mg, 19%), and (+)-**59** (1.5 mg, 5%) were obtained in the order of elution

[Table 7, Entry 6] Morpholine (0.06 mL, 0.64 mmol) was added to a solution of (+)-**55b** (20.5 mg, 0.06 mmol) and I_2 (162.7 mg, 0.64 mmol) in *t*-BuOH (2.0 mL) and the mixture was stirred at rt for 3 h. After the same work-up and separation as Entry 1, (+)-**55b** (20.5 mg, 100%) was obtained.

(±)-2,3a-*cis*- ((±)-56), (±)-2,3a-*trans*-1-acetyl-7-iodo-3a,5-dimethoxy-2-methoxycarbonyl-1,2,3,3a,8,-

8a-hexahydropyrrolo[2,3b]indole ((±)-57), and (±)-58 from (±)-55b — Morpholine (0.04 mL, 0.48 mmol) was added to a solution of (±)-**55b** (51.5 mg, 0.16 mmol) and I_2 (408.8 mg, 1.61 mmol) in MeOH (3.0 mL) and the mixture was stirred at rt for 1 h. After addition of 10% aqueous $Na_2S_2O_3$ (excess) and H_2O, 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 successively with $CHCl_3$–MeOH (99:1, v/v) and EtOAc–hexane (1:1, v/v) to give (±)-**56** (7.9 mg, 11%), (±)-**58** (10.7 mg, 15%), and (±)-**57** (6.7 mg, 9%) in the order of elution. (±)-**56**: pale yellow oil. IR (film): 1747, 1655, 1574, 1477, 1439, 1406, 1201 cm^{-1}. ^{1}H-NMR was identical with that of (–)-**56**. HR–MS *m/z*: Calcd for $C_{16}H_{19}IN_2O_5$: 446.03390. Found: 446.03442. (±)-**57**: pale yellow oil. IR (film): 2951, 1743, 1655, 1574, 1477, 1437, 1410, 1203 cm^{-1}. ^{1}H-NMR was identical with that of (+)-**57**. HR–MS *m/z*: Calcd for $C_{16}H_{19}IN_2O_5$: 446.03390. Found: 446.03387. (±)-**58**: pale yellow oil. IR (film): 1743, 1655, 1473, 1437, 1223, 756 cm^{-1}. ^{1}H-NMR was identical with that of (+)-**58**. HR–MS *m/z*: Calcd for $C_{16}H_{19}IN_2O_5$: 446.03390. Found: 446.03365.

X-Ray single crystal analysis of 40

A single crystal (0.30x0.30x0.30 mm) of **40** was obtained by recrystallization from $CHCl_3$-hexane. All measurements were made on a Rigaku AFC5R diffractometer with graphite monochromated Cu-$K\alpha$ radiation (λ=1.54178 Å). Crystal data: $C_{16}H_{18}N_2O_5$, M=318.33, orthorhombic, space group $P2_12_12_1$ (#19), a=12.0955 (9)Å, b=15.231 (1)Å, c=8.4361 (5)Å, V=1554.1 (2)Å^3, Z=4, D_{calc}=1.360 g/cm^3, F(000)=672, and μ(Cu$K\alpha$)=8.12 cm^{-1}. The structure was solved by direct methods using MITHRIL.[18] The non-hydrogen atoms were refined anisotropically. The final cycle of full-matrix least-squares refinement was based on 1265 observed reflections (I>3.00σ (I), 2θ <120.1°) and 280 variable parameters. The final refinement converged with R=0.033 and Rw=0.041.

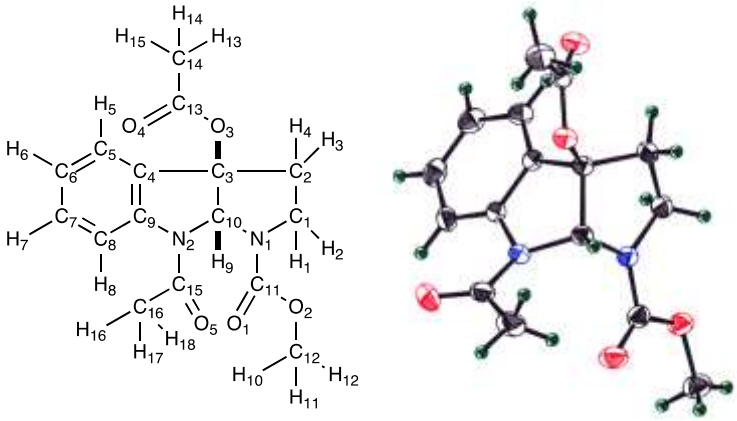


Figure 2

Table 8. Positional Parameters and *B* (eq) for 40

atom	x	y	z	B (eq)	atom	x	y	z	B (eq)
O (1)	0.7124 (2)	–0.0009 (2)	0.6232 (3)	4.8 (1)	C (15)	0.9343 (3)	0.1224 (2)	0.6971 (4)	3.8 (1)

O (2)	0.5444 (2)	0.0440 (1)	0.5384 (3)	4.1 (1)	C (16)	0.9710 (4)	0.0351 (3)	0.6366 (6)	4.8 (2)
O (3)	0.9129 (2)	0.2341 (1)	0.2879 (2)	3.15 (8)	H (1)	0.572 (3)	0.141 (2)	0.307 (4)	5.17 (3)
O (4)	0.8690 (2)	0.3614 (1)	0.1690 (3)	4.1 (1)	H (2)	0.581 (3)	0.220 (3)	0.427 (4)	4.65 (2)
O (5)	0.9758 (2)	0.1556 (2)	0.8137 (3)	5.8 (1)	H (3)	0.731 (3)	0.180 (2)	0.163 (4)	4.36 (2)
N (1)	0.6920 (2)	0.1186 (1)	0.4650 (3)	3.1 (1)	H (4)	0.683 (3)	0.277 (2)	0.211 (4)	3.94 (2)
N (2)	0.8537 (2)	0.1658 (1)	0.6144 (3)	3.0 (1)	H (5)	0.737 (3)	0.404 (2)	0.401 (4)	4.32 (2)
C (1)	0.6229 (3)	0.1752 (2)	0.3640 (4)	3.6 (1)	H (6)	0.726 (4)	0.487 (3)	0.635 (5)	6.54 (4)
C (2)	0.7073 (3)	0.2196 (2)	0.2571 (4)	3.3 (1)	H (7)	0.789 (3)	0.421 (2)	0.875 (5)	5.24 (2)
C (3)	0.8058 (2)	0.2287 (2)	0.3661 (3)	2.7 (1)	H (8)	0.843 (3)	0.278 (2)	0.878 (5)	4.24 (2)
C (4)	0.7956 (2)	0.2945 (2)	0.4986 (3)	2.7 (1)	H (9)	0.855 (3)	0.095 (2)	0.408 (4)	3.47 (2)
C (5)	0.7594 (3)	0.3808 (2)	0.4963 (4)	3.3 (1)	H (10)	0.430 (4)	–0.032 (3)	0.599 (5)	5.34 (3)
C (6)	0.7560 (3)	0.4268 (2)	0.6367 (5)	4.1 (1)	H (11)	0.495 (7)	–0.015 (3)	0.738 (7)	11.39 (8)
C (7)	0.7879 (3)	0.3878 (2)	0.7768 (4)	4.1 (2)	H (12)	0.540 (3)	–0.081 (3)	0.609 (5)	5.53 (3)
C (8)	0.8233 (3)	0.3014 (2)	0.7817 (4)	3.5 (1)	H (13)	1.091 (3)	0.273 (3)	0.193 (5)	4.95 (2)
C (9)	0.8255 (2)	0.2560 (2)	0.6410 (3)	2.8 (1)	H (14)	1.044 (4)	0.252 (3)	0.058 (5)	6.87 (4)
C (10)	0.8091 (2)	0.1416 (2)	0.4597 (3)	2.8 (1)	H (15)	1.070 (4)	0.356 (3)	0.085 (5)	7.39 (4)
C (11)	0.6552 (3)	0.0488 (2)	0.5482 (4)	3.4 (1)	H (16)	0.911 (3)	–0.001 (3)	0.598 (5)	5.76 (3)
C (12)	0.4946 (4)	–0.0286 (3)	0.6214 (6)	4.7 (2)	H (17)	1.018 (4)	0.011 (3)	0.714 (4)	6.39 (4)
C (13)	0.9351 (3)	0.3044 (2)	0.1957 (3)	3.3 (1)	H (18)	1.011 (4)	0.040 (3)	0.530 (5)	6.32 (3)
C (14)	1.0493 (4)	0.3007 (3)	0.1319 (6)	4.8 (2)					

X-Ray single crystal analysis of 51

A single crystal (0.50x0.30x0.10 mm) of **51** was obtained by recrystallization from MeOH. All measurements were made on a Rigaku AFC5R diffractometer with graphite monochromated Mo-$K\alpha$ radiation (λ=0.71069 Å).

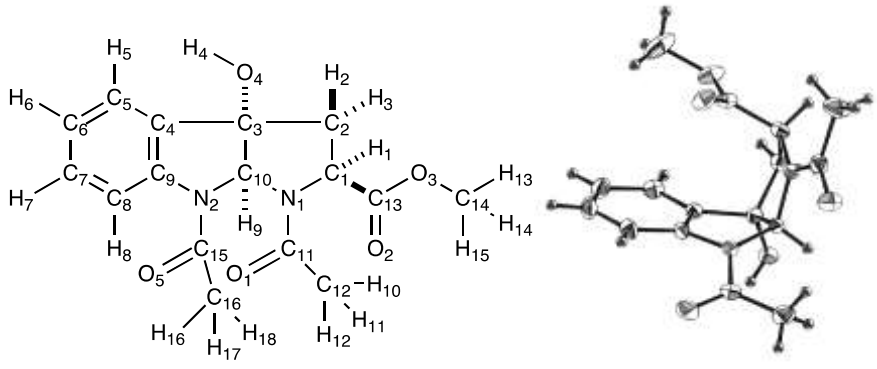


Figure 3

Crystal data: $C_{16}H_{18}N_2O_5$, M=318.33, monoclinic, space group $P2_1/a$ (#14), a=8.230 (5)Å, b=20.75 (1)Å, c=9.607 (6)Å, β=112.86 (5)°, V=1512 (2)Å^3, Z=4, D_{calc}=1.398 g/cm^3, F(000)=672, and μ(Mo$K\alpha$)=0.98 cm^{-1}. The structure was solved by direct methods using MITHRIL.[18] The non-hydrogen atoms were refined anisotropically. The final cycle of full-matrix least-squares refinement was based on 1830 observed reflections (I>3.00σ (I), 2θ <55.0°) and 280 variable parameters. The final refinement converged with R=0.045 and Rw=0.050.

Table 9. Positional Parameters and *B* (eq) for 51

atom	x	y	z	B (eq)	atom	x	y	z	B (eq)
O (1)	0.7200 (3)	0.3296 (1)	0.6974 (2)	4.0 (1)	C (15)	0.9996 (4)	0.4208 (1)	0.5978 (3)	2.8 (1)
O (2)	0.5902 (3)	0.2704 (1)	0.2381 (2)	4.0 (1)	C (16)	0.9947 (6)	0.4357 (2)	0.7470 (4)	4.1 (2)
O (3)	0.3547 (3)	0.3165 (1)	0.0607 (2)	4.4 (1)	H (1)	0.322 (4)	0.329 (1)	0.320 (3)	3.2 (6)
O (4)	0.5443 (3)	0.5186 (1)	0.3237 (2)	2.90 (8)	H (2)	0.313 (4)	0.425 (1)	0.147 (3)	3.4 (7)
O (5)	1.1385 (3)	0.4189 (1)	0.5788 (2)	4.4 (1)	H (3)	0.311 (4)	0.442 (1)	0.309 (3)	3.0 (6)
N (1)	0.5701 (3)	0.3564 (1)	0.4557 (2)	2.35 (9)	H (4)	0.636 (5)	0.536 (2)	0.339 (5)	7 (1)
N (2)	0.8447 (3)	0.4095 (1)	0.4767 (2)	2.17 (8)	H (5)	0.518 (4)	0.445 (1)	0.013 (3)	2.7 (6)
C (1)	0.4226 (4)	0.3501 (1)	0.3092 (3)	2.7 (1)	H (6)	0.726 (4)	0.407 (2)	–0.084 (4)	4.1 (8)
C (2)	0.3816 (4)	0.4200 (1)	0.2592 (4)	2.8 (1)	H (7)	0.993 (4)	0.366 (1)	0.076 (3)	3.8 (7)
C (3)	0.5624 (3)	0.4511 (1)	0.3164 (3)	2.3 (1)	H (8)	1.064 (4)	0.366 (1)	0.339 (3)	2.9 (6)
C (4)	0.6719 (3)	0.4306 (1)	0.2281 (3)	2.2 (1)	H (9)	0.663 (3)	0.441 (1)	0.556 (3)	1.2 (5)
C (5)	0.6286 (4)	0.4306 (1)	0.0741 (3)	3.1 (1)	H (10)	0.458 (5)	0.236 (2)	0.464 (5)	7 (1)
C (6)	0.7498 (5)	0.4080 (2)	0.0188 (4)	3.7 (1)	H (11)	0.375 (7)	0.273 (3)	0.555 (6)	11 (2)
C (7)	0.9106 (5)	0.3847 (2)	0.1172 (4)	3.8 (1)	H (12)	0.531 (6)	0.233 (2)	0.651 (5)	10 (1)
C (8)	0.9556 (4)	0.3835 (2)	0.2708 (4)	3.1 (1)	H (13)	0.341 (6)	0.303 (2)	–0.142 (6)	9 (2)
C (9)	0.8337 (3)	0.4071 (1)	0.3249 (3)	2.3 (1)	H (14)	0.338 (8)	0.239 (3)	–0.065 (6)	12 (2)
C (10)	0.6637 (3)	0.4178 (1)	0.4703 (3)	2.2 (1)	H (15)	0.53 (1)	0.271 (4)	–0.019 (8)	17 (3)
C (11)	0.6016 (4)	0.3174 (1)	0.5763 (3)	2.8 (1)	H (16)	0.925 (8)	0.469 (3)	0.753 (6)	12 (2)
C (12)	0.4885 (6)	0.2587 (2)	0.5560 (5)	4.9 (2)	H (17)	1.099 (6)	0.452 (2)	0.809 (5)	8 (1)
C (13)	0.4696 (4)	0.3075 (1)	0.2007 (3)	2.9 (1)	H (18)	0.954 (6)	0.402 (2)	0.791 (5)	9 (1)
C (14)	0.387 (1)	0.2812 (3)	–0.0562 (5)	6.7 (3)					

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(–)-**57**. Alternatively a mixture sample of (+)-**57** and (–)-**57** in a ratio of 99.5:0.5 was made. After confirming the mixture sample showed resoluted peaks under the above column conditions, (+)-**57** sample was subjected to the column chromatography. Since the peak of (–)-**57** was not observed at all, its ee was determined to be more than 99%.

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