Preparation of Alkyl-Substituted Indoles in the Benzene Portion. Part 13.[1] Enantiospecific Synthesis of Mitosene Analogues Related to FR 900482 and FR 66979

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An acid-catalyzed indole formation reaction previously reported by us was successfully applied to the preparation of variously substituted 4-hydroxy-1*H*-indoles 11a—g having carbon and/or heteroatom substituents at the benzene portion of the indole ring, using as substrates 3-(4,4-dialkoxy-1-oxobutyl)-1*H*-pyrroles 10a—g, which are readily available from simple pyrroles in several steps. Employing one of these indoles, 11g, as a starting intermediate, an enantiospecific synthesis of the mitosene analogues 8, 9a and 9b related to antitumor antibiotics FR 900482 (1) and FR 66979 (2) was achieved by i) condensation of 20 with a chiral aldehyde 21, ii) transformation of 22a and 22b into the tricyclic compounds 29a and 29b, iii) introduction of the additional one-carbon unit as a formyl group, iv) formation of the aziridine ring, and v) removal of the benzyl protecting group. Elimination of the *tert*-butyloxycarbonyl group was also examined to provide the basis for a future project to synthesize 5a, the cross-linkage product of 2 and DNA.

Keywords enantiospecific synthesis; acid-catalyzed indole formation reaction; mitosene analogue; FR 900482; FR66979

FR 900482[2] (**1**) and FR 66979[3] (**2**) are potent antitumor antibiotics isolated from *Streptomyces sandaensis* No. 6897 (Chart 1). Their chemical structures are noteworthy in that they contain an aziridino function and a carbamoyloxymethyl group, together with a framework containing a hydroxylamine hemi-acetal partial structure. These structural features of **1** and **2**, showing striking similarities to mitomycins **3**, led us to speculate that indole derivatives **4** corresponding to the aziridinomitosenes derived from mitomycins **3** might show antitumor activity, although an indoloquinone function is lacking in **4a** and **4b**.[4] Recently biological evidence was presented in support of this speculation,[5] and finally a covalent adduct **5a** was isolated and characterized by spectroscopic means as its heptaacetate **5b** from a hydrolysate of the reaction mixture between FR 66979 (**2**) and synthetic DNA duplexes in the presence of a reducing reagent.[6] This fact strongly suggests that both **1** and **2** cause DNA interstrand cross-linking by incorporating **4a** and **4b** as the reactive species.

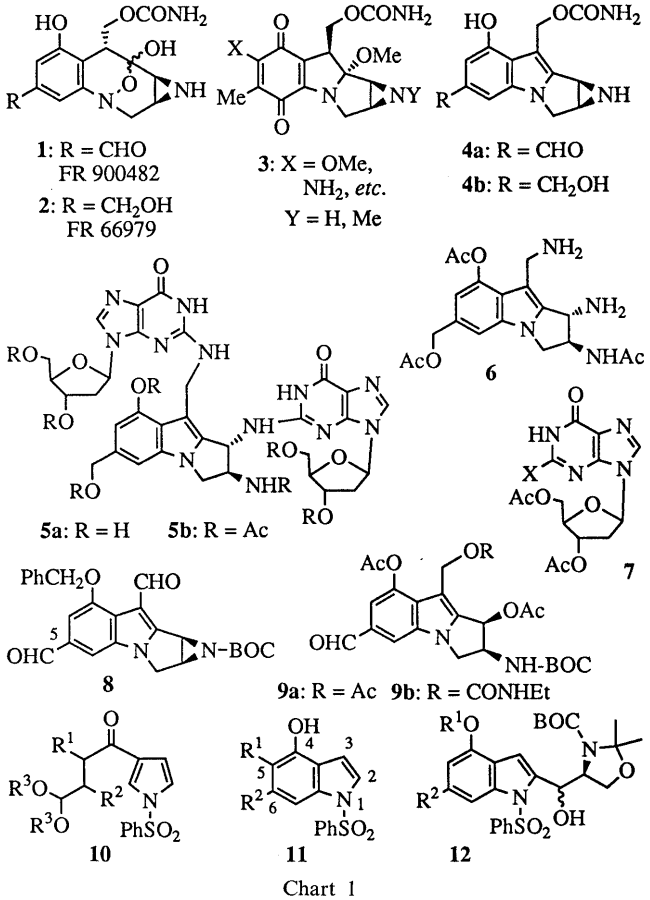


Chart 1

In order to confirm synthetically the proposed structure of the cross-link adduct, we planned an enantioselective synthesis of **5b**, assuming that the absolute configuration of the aziridino part of **1** and **2** is the same as that of mitomycins **3**. Our plan consists of two parts: i) a synthetic pathway for preparation of the indole moiety **6** was designed based on both our preparative procedures for alkyl-substituted 4-hydroxyindole derivatives[7] and the previous enantioselective synthesis of (1a*S*,8b*S*)-1-*tert*-butyloxycarbonyl-8-formyl-1,1a,2,8b-tetrahydroazirino-[2′,3′:3,4]pyrrolo[1,2-*a*]indole (**8** without the benzyloxy and 5-formyl groups)[8]; and ii) 2-haloinosine 2′,3′-diacetate (**7**) would be synthesized and introduced into the two amino groups of **6** in a stepwise manner or in a single step. In this paper, we report some preliminary experiments to establish synthetic pathways leading to the tricyclic indole derivatives **8**, **9a** and **9b**, which are closely related to the supposed mitosenes **4a** and **4b** originating from FR 900482 (**1**) and FR 66979 (**2**). Preparation of **8** and **9** was accomplished by three successive operations as follows. First, variously substituted 3-(4,4-dialkoxy-1-oxobutyl)-1-(phenylsulfonyl)-1*H*-pyrroles **10** were prepared starting from simple pyrroles. Secondly, these were cyclized to 4-hydroxy-1*H*-indoles **11** by means of our indole formation reaction.[7] Thirdly, a three-carbon unit carrying an amino group of defined absolute configuration was

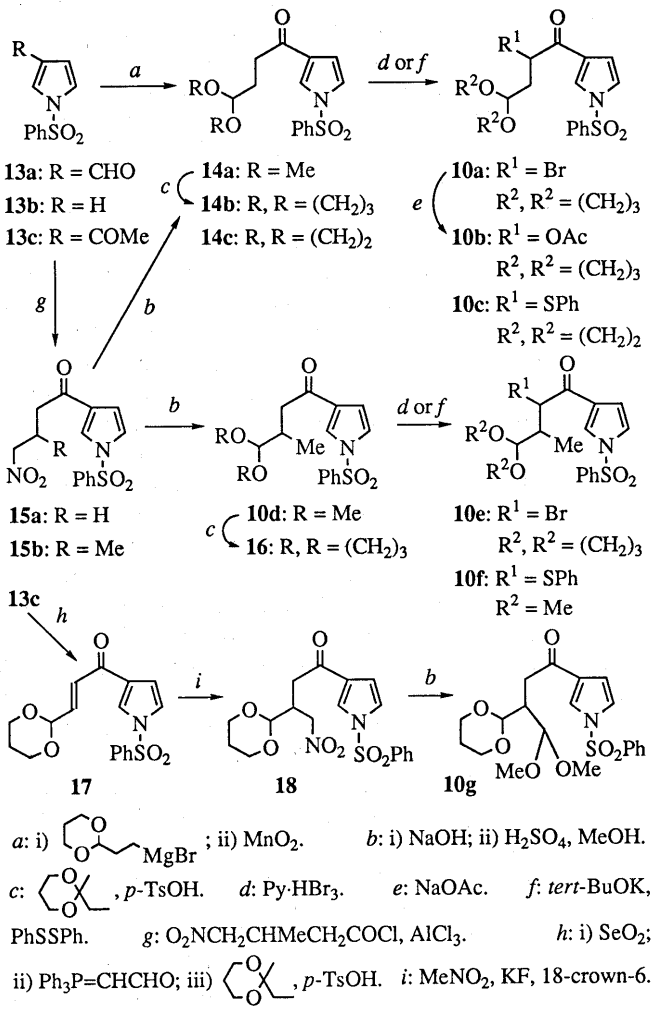
introduced into the C-2 position of **11** to form **12**, followed by construction of the tricyclic carbon skeleton of **8** and **9**, by connecting the terminal methylene group to the indole nitrogen.[8] These transformations directed towards **8** and **9** required timely execution of the following three operations, *i.e.*, introduction of the one-carbon unit at the C-3 position, formation of the aziridine ring to ensure in subsequent opperations the vicinal *trans* arrangement of the diamino functions of **6**, and removal of the benzyl protecting group at the indolol group. The present study includes all these procedures as a preliminary to an effective synthesis of **6** in the near future.

Synthesis of 4-Hydroxyindoles Having Substituents in the Benzene Portion Synthesis of 5- and/or 6-functionalized 4-hydroxy-1-(phenylsulfonyl)-1*H*-inoles **11** was initiated by the formation of pyrrole derivatives **10** from readily available starting materials (Chart 2). The ketoaldehyde derivative **14b** having a trimethylene acetal group was prepared in two ways. The 3-formylpyrrole[9] **13a** was treated with a Grignard reagent prepared from 2-(1,3-dioxan-2-yl)ethyl bromide, and the resulting alcohol was oxidized with manganese(IV) oxide in refluxing dichloromethane to afford **14b** in 91% overall yield. Alternatively the nitro derivative **15a** described in the previous paper[9] was submitted to the Nef reaction using sodium hydroxide in methanol, followed by treatment with diluted sulfuric acid in methanol. The dimethyl acetal **14a** was obtained in 90% yield and its acetal group was exchanged to give **14b** in 89% yield by reaction with 2-ethyl-2-methyl-1,3-dioxane in the presence of a catalytic amount of *p*-toluenesulfonic acid. α-Bromination of the ketoacetal **14b** was effected with pyridinium bromide perbromide in tetrahydrofuran (THF) to afford **10a** in 92% yield. An α-acetoxyketone derivative **10b** was prepared from **10a** by treatment with sodium acetate in dimethyl formamide (DMF) in 96% yield. Similarly, an α-phenylthioketone **10c** was obtained in 93% yield by treatment of **14c**[9] with diphenyl disulfide in the presence of potassium *tert*-butoxide in THF at low temperature.

The other acetals **10d** and **16** having an additional methyl group at the side chain were prepared from the nitro derivative **15b**, produced in 97% yield by the aluminum chloride-catalyzed Friedel–Crafts reaction between 1-(phenylsulfonyl)-1*H*-pyrrole (**13b**) and 3-methyl-4-nitrobutyryl chloride derived from *tert*-butyl crotonate and nitromethane. The product **15b** was changed to **10d** in 82% yield by use of the Nef reaction, and **16** was synthesized from **10d** in 97% yield by the same acetal exchange reaction as above. Bromination of **16** with pyridinium bromide perbromide afforded **10e** in 96% yield and introduction of the phenylthio group into **10d** was carried out with diphenyl disulfide in the presence of potassium *tert*-butoxide to form **10f** in 63% yield.

Preparation of an important intermediate **10g** for the present study was devised on the basis that the selenium(IV) oxide oxidation of the acetylpyrrole[10] **13c** afforded a compound having the α-ketoaldehyde structure in a good yield. This aldehyde could be elongated readily by reaction with the Wittig reagent, (triphenylphosphoranylidene)acetaldehyde. The two carbonyl groups in the resulting ketoenal behaved in different ways, so that a mild trimethylene acetal formation reaction gave only **17** in 58% overall yield from **13c**. Conjugate addition of nitromethane to the enone **17** was performed in 93% yield with the aid of potassium fluoride and 18-crown-6,[11] and the Nef reaction of **18** afforded **10g** in 83% yield. Thus, the substrates **10a**—**g** were in hand for the next indole cyclization process.

The indole formation was effected by azeotropic refluxing of a solution of the ketoacetals **10a**—**g** mostly in 1,2-dichloroethane with *ca.* 30 molar eq of 1,3-propanediol in the presence of concentrated sulfuric acid (*p*-toluenesulfonic acid for **10d**) (Table I).[7] Cyclization of **10d** is the simplest case among the variously substituted 4-hydroxyindoles and proceeded with extreme ease in the presence of a catalytic amount of the sulfonic acid by heating in toluene for a relatively short period, resulting in the formation of **19d** in an excellent yield. Analogously, a 6-mono-substituted indole seems to be formed readily, and the cyclization of **10g** proceeded in a few hours with 0.5 molar eq of 95% sulfuric acid, affording **19g** in 83% yield. On the other hand, for the formation of 5-mono- and 5,6-disubstituted indoles, addition of 3—11 molar eq of sulfuric acid was necessary and a longer refluxing time (14—33 h) was required for completion of the reaction. These phenomena can probably be ascribed to the presence

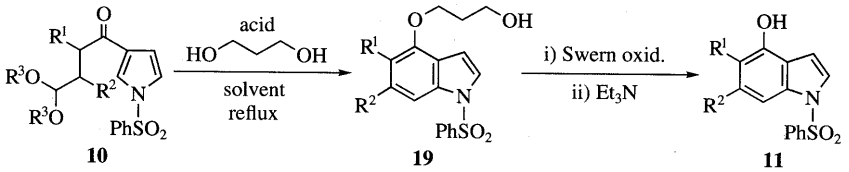


a: i) ; ii) MnO_2. *b*: i) NaOH; ii) H_2SO_4, MeOH.

c: , *p*-TsOH. *d*: Py·HBr_3. *e*: NaOAc. *f*: *tert*-BuOK, PhSSPh. *g*: $O_2NCH_2CHMeCH_2COCl$, $AlCl_3$. *h*: i) SeO_2; ii) Ph_3P=CHCHO; iii) , *p*-TsOH. *i*: $MeNO_2$, KF, 18-crown-6.

Chart 2

TABLE I. Preparation of 4-Hydroxyindoles **11** by an Acid-Catalyzed Cyclization Reaction of **10**, Followed by Removal of the Hydroxypropyl Group of **19**



10 **19** **11**

	R^1	R^2	R^3, R^3	$HO(CH_2)_3OH$ mol eq	Acid (mol eq)	Solvent	Reflux time (h)	**10→19** Yield (%)	**19→11** Yield (%)
a	Br	H	$-(CH_2)_3-$	31	H_2SO_4 (3.2)	$Cl(CH_2)_2Cl$	33	56	93
b	OAc	H	$-(CH_2)_3-$	30	H_2SO_4 (5)	$Cl(CH_2)_2Cl$	14	53 (R^1 = OH)[a]	—
c	SPh	H	$-(CH_2)_2-$	30	H_2SO_4 (3)	$Cl(CH_2)_2Cl$	14	77	94
d	H	Me	Me, Me	29	*p*-TsOH (0.3)	PhMe	5	91	86
e	Br	Me	$-(CH_2)_3-$	30	H_2SO_4 (11)	$Cl(CH_2)_2Cl$	12	14	—
f	SPh	Me	Me, Me	30	H_2SO_4 (6)	$Cl(CH_2)_2Cl$	22	59	92
g	H		Me, Me	30	H_2SO_4 (0.5)	$Cl(CH_2)_2Cl$	3	83	85

a) The resulting acetoxy derivative was converted to the hydroxy derivative for ease of separation from contaminants.

of a substituent adjacent to the ketone group in **10**. When the indole cyclization reaction was checked by thin layer chromatography (TLC), a spot corresponding to a compound bearing trimethylene acetal at the ketone group was observed first, and this gradually disappeared as a new spot of the resulting indole became predominant. The presence of the neighboring substituent might increase steric hindrance around the ketone group and retard the trimethylene acetal formation essential to the subsequent indole cyclization. Nevertheless, yields were good to fairly good except for a low yield for **19e**, for some unknown reason. The hydroxypropyl group of **19** was readily removed by the Swern oxidation, followed by brief treatment with triethylamine to give a variety of 4-hydroxyindoles **11** in very good yields. As a whole, our indole cyclization reaction[7] can be successfully applied to the preparation of 4-hydroxyindoles having a variety of substituents in the benzene portion, when the substrates for the reaction, the pyrrole derivatives **10**, are readily available from simple starting materials.

Enantiospecific Synthesis of Mitosene Analogues 8, 9a and 9b Related to FR 900482 (1) and FR 66979 (2) 6-(1,3-Dioxan-2-yl)-1-(phenylsulfonyl)-1*H*-indol-4-ol (**11g**) was benzylated using sodium hydride and benzyl bromide in a mixture of THF–DMF (2:1) to give **20** in 77% yield (Chart 3). The benzyl ether **20** in THF was treated with lithium diisopropylamide (LDA) at −75 °C, and then reacted with a chiral aldehyde **21** prepared from L-serine.[12] Two diastereomers **22a** and **22b** were obtained in 62% and 11% yields in almost the same ratio as observed in the preliminary experiment.[8] Assignment of the absolute configuration of the newly formed asymmetric center in **22a** was carried out as follows. The diastereomer **22a** was treated with diluted hydrochloric acid in dimethoxyethane (DME)–water (9:1) to remove both the acetonide and acetal groups, and the product was isolated as the diacetate **23** in 83% yield. The formyl group in **23** was protected with 1,2-ethanedithiol to afford **24** in 86% yield, and this was successively treated with potassium carbonate in methanol, followed with 2,2-dimethoxypropane in dichloromethane in the presence of a catalytic amount of *p*-toluenesulfonic acid. An *O*,*O*-acetonide **25** was obtained in 72% yield, together with an *N*,*O*-acetonide **22c** in 18% yield. Removal of the indole protecting group in **25** was effected by treatment with magnesium in methanol to afford **26** in 87% yield. In the ^{1}H-NMR spectra of **25** and **26**, proton signals of C-4′ appeared at 5.53 and 4.92 ppm with coupling constants of 9.5 and 9 Hz, respectively. These coupling values resembled well those of the corresponding compounds (*ca.* 10 Hz) in the preliminary experiment, and indicated that the indole substituent and the urethane group at the C-4′ and C-5′ positions were oriented in the *trans* diequatorial manner. This assignment was definitively verified by single crystal X-ray crystallography.[8] Thus, the orientation of the hydroxy group in **22a** and **22b** was established to be as shown in Chart 3.

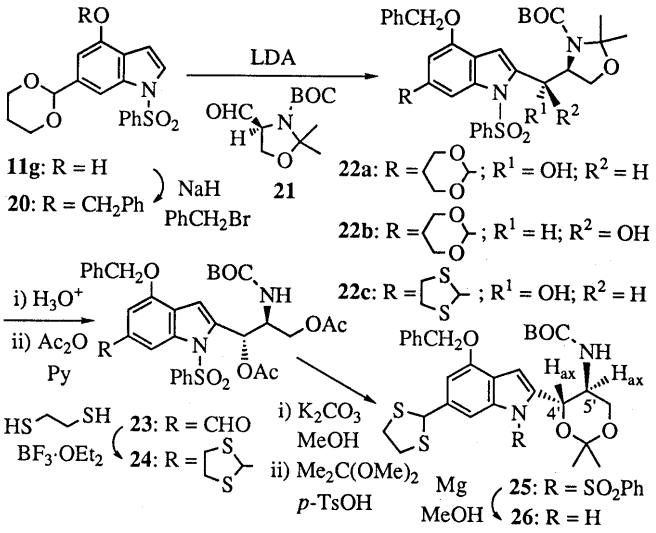


Chart 3

The indole protecting group in **22a** and **22b** was separately removed with magnesium in methanol to afford **27a** and **27b** in 95% and 96% yields, respectively (Chart 4). These were then treated with *ca.* 3% hydrochloric acid in

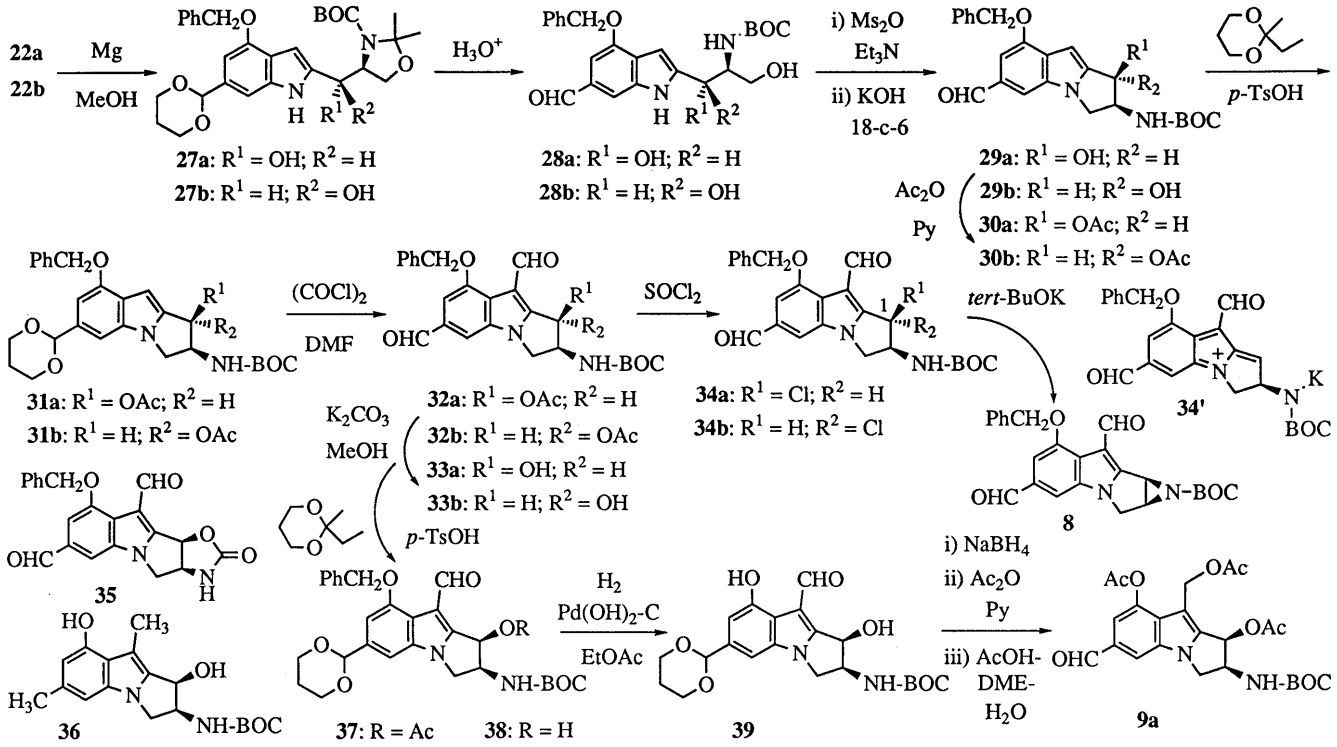


Chart 4

DME–water (5 : 1) to produce the dihydroxyaldehydes **28a** and **28b** in 75% yield, each of these being suitable compounds for the construction of the tricyclic framework. In the model experiment, the 3-formyl group of the indole ring made it possible to realize this process,[8] but in these cases, the 6-formyl group took the role of activating the indole nitrogen to connect with the terminal methylene group. Only the primary alcohols in **28a** and **28b** were mesylated with methanesulfonic anhydride in dichloromethane in the presence of triethylamine at −20 °C and the resulting mesylates in THF were treated with potassium hydroxide in the presence of 18-crown-6 at 0 °C and then at room temperature. The tricyclic compounds **29a** and **29b** were obtained in 43% and 38% yields, respectively, and were converted to their acetates **30a** and **30b** in 98% and 95% yields with acetic anhydride in pyridine.

The next important step is introduction of the one-carbon unit into the C-3 position of the indole ring. For this purpose, the electron-withdrawing group (the 6-formyl group) was protected as the trimethylene acetals **31a** and **31b** by treatment with 2-ethyl-2-methyl-1,3-dioxane in dichloromethane in the presence of *p*-toluenesulfonic acid in 84% and 82% yields. The acetals **31a** and **31b** were then formylated with the Vilsmeier reagent prepared from oxalyl chloride and DMF in dichloromethane. During this reaction, the acetal group was mostly cleaved and **32a** and **32b** were produced in 72% and 81% yields, accompanied with **37** in 6% yield in the former case.

For the formation of the aziridine ring, the acetyl groups of **32a** and **32b** were eliminated by treatment with potassium carbonate in methanol to give **33a** and **33b** in 99% and 90% yields. When one of these, **33a**, was reacted with thionyl chloride in dichloromethane at room temperature, a single chloro compound **34a** was obtained in 84% yield. On the other hand, the same chlorination of **33b** afforded another chloro derivative **34b** in 32% yield, but the major product was a 2-oxazolidone **35** isolated in 52% yield; this result could reasonably be explained by the intramolecular nucleophilic attack of the *tert*-butyloxycarbonyl (BOC) group in an *S*N 2 like manner on the carbon atom bearing an activated hydroxy group in the *trans* situation. Chlorination products **34a** and **34b** seemed to be formed by retention of configuration, since the coupling constant of the NMR proton signal at C-1 of **34a** was 5.5 Hz, which is within the range of 5.5—6 Hz for other compounds of the a series. Another chloro derivative **34b** exhibited the proton signal at C-1 as a singlet, and this shape reflected the tendency of small coupling values (3—4 Hz) for the b series. Aziridino ring formation in compounds **34a** and **34b** was carried out by treatment with potassium *tert*-butoxide in THF at room temperature. The same compound **8** was produced from both chloro compounds in 43% and 31% yields, respectively, and the aforementioned compound **35** was also obtained as a by-product from **34b** in 18% yield. Formation of **8** and **35** from **34b** was readily understood in terms of the *trans* nature of the leaving group. Compound **34a** having the *cis* chlorine group relative to the nitrogen function also afforded the aziridine **8** in better yield than **34b**. This fact might be attributable to the special location of the chlorine atom in **34a**. The indole nitrogen would facilitate elimination of the chlorine atom to provide a reactive species **34′**, which might participate in the subsequent formation of the aziridine ring. As the same species **34′** could be formed from **34b**, this might also be partially responsible for the formation of **8** from **34b**. In any case, one of the target molecules **8** was synthesized in

a straightforward manner from both chiral diastereomers **22a** and **22b**.

Removal of the benzyl group was next examined at the stage of **33a**. When this compound **33a** was simply hydrogenated without any precaution over palladium hydroxide on carbon (Pearlman's catalyst) in methanol, only the dimethyl derivative **36** was obtained in 54% yield together with a complex mixture of reduction products. So one of the formyl groups was protected as the acetal, using the difference of reactivities of the two formyl groups. Thus, both the acetate **32a** and the alcohol **33a** were respectively treated with 2-ethyl-2-methyl-1,3-dioxane in dichloromethane in the presence of a catalytic amount of *p*-toluenesulfonic acid for a short period. Partially protected compounds **37** and **38** were obtained in 63% and 80% yields, and the former compound **37** was hydrolyzed to the latter **38** in 65% yield by stirring with potassium carbonate in methanol at room temperature. As the remaining formyl group was inert to catalytic hydrogenation under the following conditions, successful elimination of the benzyl group was realized when an ethyl acetate solution of **38** was hydrogenated over Pearlman's catalyst at room temperature for several hours to furnish **39** in 91% yield. For preparing the model compound **9a**, **39** was reduced with sodium borohydride in a mixture of methanol–THF (1 : 1), followed by acetylation with acetic anhydride in pyridine and then by removal of the acetal with a mixture of acetic acid–DME–water (1 : 1 : 1) at room temperature to afford **9a** in 60% overall yield. The

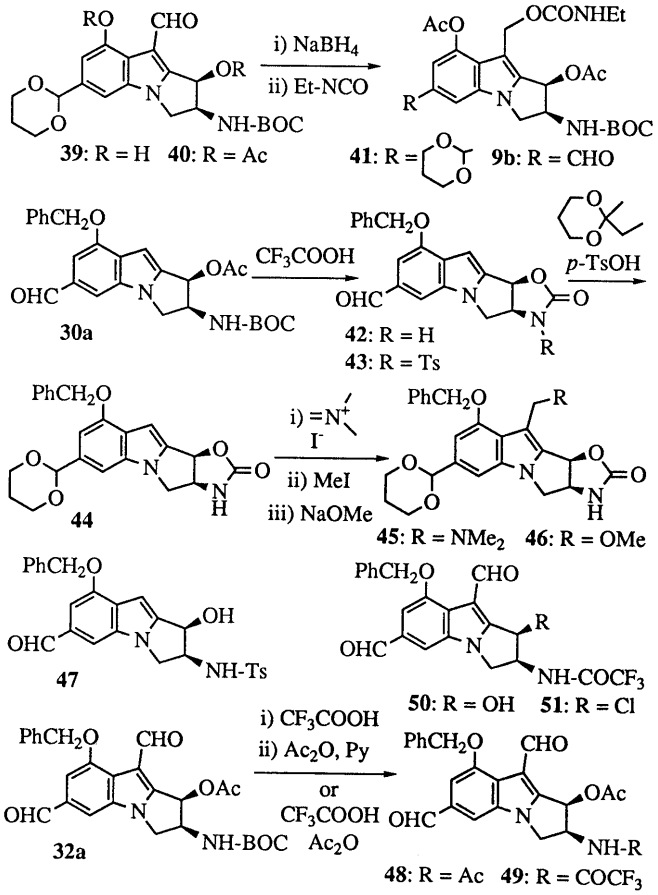


Chart 5

hydrogenolysis product **39** was acetylated to form **40** in 95% yield (Chart 5). This diacetate **40** was reduced with sodium borohydride in THF–methanol (2 : 1) and the resulting alcohol was transformed into the ethylcarbamoyloxy derivative **41** in 66% yield by treatment with ethyl isocyanate in dichloromethane in the presence of triethylamine. Removal of the acetal group from **41** gave another model **9b** in 89% yield.

The final task was to eliminate the BOC group from the amine function. The monoformyl compound **30a** was treated with trifluoroacetic acid in dichloromethane at room temperature. The 2-oxazolidone **42** was the sole compound obtained (63% yield). Introduction of a one-carbon unit into **42** was examined after converting **42** to the acetal **44** in 86% yield, followed by application of the Eschenmoser salt, *N*,*N*-dimethylmethyleneammonium iodide.[13] The resulting dimethylamine **45** formed in 75% yield was further transformed into the methoxy derivative **46** by treatment first with methyl iodide and then with sodium methoxide in methanol, in 51% yield. Cleavage of the 2-oxazolidone ring in **42** was only effected after its conversion to the tosylate **43** by treatment with *p*-toluenesulfonyl chloride in the presence of sodium hydride in THF in 63% yield. Reaction of **43** with potassium carbonate in methanol afforded **47** in 92% yield. However, attempts to execute the reductive removal of the tosyl group from **47** with metal in ammonia were unfruitful.

Elimination of the BOC group in the diformyl compound **32a** proceeded in a different fashion. When **32a** was stirred with trifluoroacetic acid in dichloromethane at room temperature, an *N*,*O*-diacetate **48** was obtained in 68% yield after subsequent acetylation, and no 2-oxazolidone formation was observed in this case. When this BOC elimination of **32a** was conducted by further addition of acetic anhydride in trifluoroacetic acid solution, the trifluoroacetamide **49** was produced in 50% yield. A mixed anhydride formed in the reaction medium trifluoroacetylated the amino group liberated by the reaction with trifluoroacetic acid from the BOC-amino group in **32a**. Methanolysis of **49** catalyzed with potassium carbonate gave the alcohol **50** in 82% yield, and chlorination of **50** with thionyl chloride afforded **51** in 58% yield. Unfortunately, attempts to generate the aziridine ring from **51** ended in failure.

In summary, our indole cyclization reaction from pyrrole derivatives was successfully applied to the preparation of various types of 4-hydroxyindole derivatives **11a**—**g** carrying carbon substituents and/or heteroatom functions in the benzene portion of the indole. One of these, **11g**, served as a suitable starting intermediate for an enantiospecific synthesis of the mitosene analogues **8**, **9a** and **9b** related to FR 900482 (**1**) and FR 66979 (**2**). A chiral aldehyde **21** was condensed with **20** and important intermediates **29a** and **29b** having the tricyclic framework were produced from **22a** and **22b**. Introduction of the one-carbon unit into the 3-position of the indole, formation of the aziridine ring, removal of the benzyl protecting group from the benzyloxyindole, and the elimination of the BOC protecting group were investigated as a preliminary study to approach the indole part **6** re-

quired for synthesizing the cross-link compound **5b** for its structural confirmation. Related studies will be reported in due course.

Experimental

Melting points were determined on a Yanagimoto micro-melting point apparatus and are not corrected. MS and high-resolution MS (HRMS) were recorded on a Hitachi M-80B spectrometer at an ionizing voltage of 70 eV, and figures in parentheses indicate the relative intensities. IR spectra were measured on a Hitachi 215 spectrophotometer. ^{1}H-NMR spectra were obtained on a Varian EM 390 (90 MHz) spectrometer, unless otherwise specified, in $CDCl_3$ with tetramethylsilane (TMS) as an internal reference. ^{1}H-NMR (400 MHz) spectra were measured on a JEOL JNM-GX-400 spectrometer. Column chromatography was conducted on silica gel (Fuji Davison BW 200) and preparative TLC (PTLC) was carried out on glass plates (20 × 20 cm) coated with Merck Silica gel 60 PF_{254} (1 mm thick). Usual work-up refers to washing of the organic layers with water or brine, drying over anhydrous Na_2SO_4, and evaporating off the solvents under reduced pressure.

3-(4,4-Dimethoxy-1-oxobutyl)-1-(phenylsulfonyl)-1*H*-pyrrole (14a) A slurry of **15a** (631 mg, 1.96 mmol) in MeOH (8 ml) was stirred with powdered NaOH (98 mg, 2.45 mmol) at 0 °C for 15 min. The resulting clear solution was poured into cooled (−20 °C) 20% H_2SO_4–MeOH (4 ml) using MeOH (4 ml) and the mixture was stirred at −20 °C for 10 min, then poured into saturated $NaHCO_3$–H_2O. Extraction with CH_2Cl_2, usual work-up and PTLC [hexane–CH_2Cl_2 (1 : 5)] gave **14a** (592 mg, 90%) along with recovered **15a** (15 mg, 2%) and 3-(4,4-dimethoxy-1-oxobutyl)-1*H*-pyrrole (24 mg, 6%), colorless syrup. HRMS Calcd for $C_{10}H_{15}NO_3$: 197.1051. Found: 197.1035. MS *m/z*: 197 (M^+, 2), 166 (13), 109 (34), 106 (38), 94 (100), 89 (75), 75 (79). ^{1}H-NMR δ: 2.01 (2H, dt, J=5.5, 7.5 Hz), 2.85 (2H, t, J=7.5 Hz), 3.34 (6H, s), 4.46 (1H, t, J=5.5 Hz), 6.58—6.72 (1H, m), 6.72—6.87 (1H, m), 7.38—7.53 (1H, m), 9.49 (1H, br s, NH). **14a**: colorless prisms, mp 78—78.5 °C (Et_2O–hexane). *Anal.* Calcd for $C_{16}H_{19}NO_5S$: C, 56.96; H, 5.68; N, 4.15. Found: C, 56.76; H, 5.70; N, 4.24. HRMS Calcd for $C_{16}H_{19}NO_5S$: 337.0983. Found: 337.0985. MS *m/z*: 337 (M^+, 1), 306 (7), 249 (31), 234 (20), 141 (21), 89 (68), 77 (80), 75 (100), 51 (22). IR (KBr) cm^{-1}: 1676. ^{1}H-NMR δ: 1.96 (2H, dt, J=5.5, 7.5 Hz), 2.86 (2H, t, J=7.5 Hz), 3.31 (6H, s), 4.39 (1H, t, J=5.5 Hz), 6.68 (1H, dd, J=3.5, 2 Hz), 7.13 (1H, dd, J=3.5, 2.5 Hz), 7.40—7.71 (3H, m), 7.74 (1H, dd, J=2.5, 2 Hz), 7.83—8.04 (2H, m).

3-[3-(1,3-Dioxan-2-yl)-1-oxopropyl]-1-(phenylsulfonyl)-1*H*-pyrrole (14b) a) A THF solution (4 ml) of **13a** (220 mg, 0.936 mmol) was stirred at −20 °C for 15 min under an Ar atmosphere with a *ca.* 1.25 M THF solution (1.50 ml, 1.88 mmol) of 2-(1,3-dioxan-2-yl)ethylmagnesium bromide. The reaction was quenched with saturated NH_4Cl–H_2O and the mixture was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [benzene–EtOAc (4 : 1)] afforded α-[2-(1,3-dioxan-2-yl)ethyl]-1-(phenylsulfonyl)-1*H*-pyrrole-3-methanol (325 mg, 99%) as colorless prisms, mp 81—83 °C (Et_2O–hexane). *Anal.* Calcd for $C_{17}H_{21}NO_5S$: C, 58.10; H, 6.02; N, 3.99. Found: C, 58.10; H, 6.11; N, 4.21. HRMS Calcd for $C_{17}H_{21}NO_5S$: 351.1139. Found: 351.1136. MS *m/z*: 351 (M^+, 3), 249 (36), 236 (20), 210 (35), 141 (25), 106 (42), 87 (44), 77 (100). ^{1}H-NMR δ: 1.30 (1H, br d, J=13.5 Hz), 1.50—2.33 (5H, m), 2.63 (1H, br s, OH), 3.71 (2H, ddd, J=12, 12, 2 Hz), 4.08 (2H, dd, J=12, 5.5 Hz), 4.45—4.70 (2H, m), 6.24 (1H, dd, J=2.5, 2.5 Hz), 7.06 (2H, d, J=2.5 Hz), 7.31—7.69 (3H, m), 7.74—7.95 (2H, m). A slurry of the above alcohol (198 mg, 0.564 mmol) and MnO_2 (985 mg, 11.3 mmol) in CH_2Cl_2 (10 ml) was stirred under reflux for 1 h. The mixture was filtered through a Celite bed and the Celite was thoroughly washed with CH_2Cl_2. The combined CH_2Cl_2 solution was evaporated *in vacuo* and the residual crystals were recrystallized from CH_2Cl_2–hexane to yield **14b** (182 mg, 92%) as colorless prisms, mp 122—123 °C. *Anal.* Calcd for $C_{17}H_{19}NO_5S$: C, 58.44; H, 5.48; N, 4.01. Found: C, 58.21; H, 5.50; N, 3.97. HRMS Calcd for $C_{17}H_{19}NO_5S$: 349.0983. Found: 349.0986. MS *m/z*: 349 (M^+, 2), 348 (2), 249 (16), 234 (23), 208 (57), 141 (24), 100 (90), 87 (90), 77 (100), 51 (27), 31 (34). IR (KBr) cm^{-1}: 1676. ^{1}H-NMR δ: 1.30 (1H, br d, J=13 Hz), *ca.* 1.80—2.32 (1H, m), 1.94 (2H, dt, J=5, 7.5 Hz), 2.84 (2H, t, J=7.5 Hz), 3.70 (2H, ddd, J=12, 12, 2.5 Hz), 4.07 (2H, dd, J=12, 5.5 Hz), 6.67 (1H, dd, J=3.5, 1.5 Hz), 7.12 (1H, dd, J=3.5, 2 Hz), 7.37—7.70 (3H, m), 7.74 (1H, dd, J=2, 1.5 Hz), 7.83—8.03 (2H, m).

b) A solution of **14a** (200 mg, 0.593 mmol) in 2-ethyl-2-methyl-1,3-dioxane (2.0 ml) was stirred with *p*-TsOH · H_2O (7 mg, 0.037 mmol) at room temperature for 1.5 h. Saturated $NaHCO_3$–H_2O was added to this and the mixture was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [hexane–EtOAc (5 : 2)] afforded **14b** (184 mg, 89%) as colorless prisms, mp 122—123 °C (CH_2Cl_2–hexane), together with recovered **14a** (6.5 mg, 3%) and 2-[2-(1,3-dioxan-2-yl)ethyl]-2-[1-(phenylsulfonyl)-1*H*-pyrrol-3-yl]-1,3-dioxane (9 mg, 4%) as a colorless syrup. HRMS Calcd for $C_{20}H_{25}NO_6S$: 407.1401. Found: 407.1408. MS *m/z*: 407 (M^+, 1), 406 (2), 292 (100), 266 (42), 234 (27), 87 (28), 77 (37). ^{1}H-NMR δ: 1.06—1.40 (2H, m), 1.40—2.29 (6H, m), 3.44—4.17 (8H, m), 4.39 (1H, t, J=4.5 Hz), 6.13—6.26 (1H, m), 7.03—7.18 (2H, m), 7.35—7.72 (3H, m), 7.77—7.99 (2H, m).

3-[2-Bromo-3-(1,3-dioxan-2-yl)-1-oxopropyl]-1-(phenylsulfonyl)-1*H*-pyrrole (10a) Py · HBr_3 (80%, 397 mg, 0.993 mmol) was added to a cooled (0 °C) solution of **14b** (288 mg, 0.825 mmol) in THF (8 ml) and the mixture was stirred at the same temperature for 1 h and at room temperature for 30 min. Saturated $NaHCO_3$–H_2O and saturated $Na_2S_2O_3$–H_2O were added and the whole was extracted with CH_2Cl_2, and then worked up as usual. Purification by PTLC [hexane–CH_2Cl_2 (1 : 3)] afforded **10a** (326 mg, 92%) as a colorless syrup. MS *m/z*: 348 (M^+ − Br, 45), 234 (66), 141 (29), 87 (80), 77 (100), 51 (25) 31 (42). IR ($CHCl_3$) cm^{-1}: 1680. ^{1}H-NMR δ: 1.30 (1H, br d, J=12 Hz), 1.61—2.66 (3H, m), 3.49—4.24 (4H, m), 4.69 (1H, dd, J=5, 5 Hz), 4.98 (1H, dd, J=7, 7 Hz), 6.73 (1H, dd, J=3.5, 1.5 Hz), 7.14 (1H, dd, J=3.5, 2 Hz), 7.41—7.80 (3H, m), 7.80—8.04 (3H, m).

3-[2-Acetoxy-3-(1,3-dioxan-2-yl)-1-oxopropyl]-1-(phenylsulfonyl)-1*H*-pyrrole (10b) NaOAc (315 mg, 3.84 mmol) was added to a solution of **10a** (55 mg, 0.129 mmol) in DMF (3 ml) and the mixture was stirred at room temperature for 20 h. Saturated NH_4Cl–H_2O was added and the whole was extracted with Et_2O and then worked up as usual. Purification by PTLC [hexane–EtOAc (3 : 2)] afforded **10b** (50 mg, 96%) as a colorless syrup. HRMS Calcd for $C_{19}H_{21}NO_7S$: 407.1037. Found: 407.1056. MS *m/z*: 407 (M^+, 1), 347 (21), 234 (100), 141 (23), 77 (72), 43 (63). IR ($CHCl_3$) cm^{-1}: 1740, 1687. ^{1}H-NMR δ: 1.30 (1H, br d, J=12.5 Hz), 1.53—2.33 (3H, m), 2.08 (3H, s), 3.51—3.91 (2H, m), 3.91—4.27 (2H, m), 4.64 (1H, dd, J=5, 5 Hz), 5.66 (1H, dd, J=6.5, 6.5 Hz), 6.72 (1H, dd, J=3.5, 1.5 Hz), 7.13 (1H, dd, J=3.5, 2 Hz), 7.40—7.79 (3H, m), 7.79—8.03 (3H, m).

3-[3-(1,3-Dioxolan-2-yl)-1-oxo-2-(phenylthio)propyl]-1-(phenylsulfonyl)-1*H*-pyrrole (10c) A THF solution (4 ml) of **14c** (80 mg, 0.24 mmol) and PhSSPh (68 mg, 0.31 mmol) was cooled at −18 °C and *tert*-BuOK (62 mg, 0.55 mmol) was added to this. The mixture was stirred at the same temperature under an Ar atmosphere for 20 min. Saturated NH_4Cl–H_2O was added and the whole was extracted with CH_2Cl_2, and then worked up as usual. Purification by PTLC [benzene–EtOAc (19 : 1)] gave **10c** (98 mg, 93%) as a colorless syrup. HRMS Calcd for $C_{22}H_{21}NO_5S_2$: 443.0860. Found: 443.0872. MS *m/z*: 443 (M^+, 2), 357 (4), 334 (17), 234 (39), 141 (14), 77 (50), 73 (100), 45 (26). IR ($CHCl_3$) cm^{-1}: 1672. ^{1}H-NMR δ: 2.11 (1H, ddd, J=13.5, 6.5, 4.5 Hz), 2.39 (1H, ddd, J=13.5, 8, 4.5 Hz), 3.60—3.98 (4H, m), 4.28 (1H, dd, J=8, 6.5 Hz), 4.98 (1H, dd, J=4.5, 4.5 Hz), 6.63 (1H, dd, J=3, 1.5 Hz), 7.08 (1H, dd, J=3, 2 Hz), *ca.* 7.08—7.45 (5H, m), *ca.* 7.45—7.74 (4H, m), 7.74—7.95 (2H, m).

3-Methyl-4-nitrobutyryl Chloride In a similar manner to that described for the preparation of 4-nitrobutyryl chloride,[9] an MeCN solution (30 ml) of *tert*-butyl crotonate (10.00 g, 70.4 mmol) and $MeNO_2$ (19.0 ml, 0.351 mol) containing 18-crown-6 (0.93 g, 3.5 mmol) and KF (0.41 g, 7.1 mmol) was heated under reflux with stirring for 24 h. After cooling, saturated NH_4Cl–H_2O was added and the mixture was extracted with EtOAc. Usual work-up and distillation afforded *tert*-butyl 3-methyl-4-nitrobutyrate (10.82 g, 76%) as a colorless oil, bp 114—117 °C (8 mmHg). GCMS *m/z*: 188 (M^+ − Me, 0.4), 148 (3), 130 (38), 102 (8), 101 (8), 57 (100). IR (neat) cm^{-1}: 1728, 1556, 1371. ^{1}H-NMR δ: 1.07 (3H, d, J=7 Hz), 1.42 (9H, s), 2.18—2.39 (2H, m), 2.46—3.01 (1H, m), 4.27 (1H, dd, J=12, 7 Hz), 4.46 (1H, dd, J=12, 6 Hz). A $CHCl_3$ solution (30 ml) of the above ester (8.95 g, 44.1 mmol) was stirred with 95% H_2SO_4 (205 mg, 1.99 mmol) under reflux for 8 h. After cooling, the mixture was shaken with brine and the brine solution was extracted with Et_2O. The combined organic layer was worked up as usual to leave a residue (6.63 g). The residue was dissolved in $SOCl_2$ (7.60 ml, 0.104 mmol) and the solution was refluxed for 1.5 h. Excess $SOCl_2$ was removed by evaporation, benzene (10 ml) was added to the residue, and the solution was evaporated to dryness. This operation was repeated once more and the residue was submitted to distillation to yield the title chloride (6.28 g, 86%) as a slightly yellow oil, bp 90—91 °C (0.1 mmHg). IR (neat) cm^{-1}: 1811, 1790,

1568, 1556, 1393, 1385. ^{1}H-NMR δ: 1.16 (3H, d, J=7 Hz), 2.60—3.27 (3H, m), 4.31 (1H, dd, J=13, 6 Hz), 4.46 (1H, dd, J=13, 6 Hz).

3-(3-Methyl-4-nitro-1-oxobutyl)-1-(phenylsulfonyl)-1*H*-pyrrole (15b) In the same manner as described for the preparation of **15a**,[9] 1-(phenylsulfonyl)-1*H*-pyrrole (**13b**) (2.000 g, 9.66 mmol) was treated with 3-methyl-4-nitrobutyryl chloride (3.515 g, 21.2 mmol) and $AlCl_3$ (4.246 g, 31.8 mmol) in 1,2-dichloroethane (70 ml) at room temperature for 30 min. The same work-up as before and purification by column chromatography [silica gel: 50 g, hexane–EtOAc (3 : 1)] yielded **15b** (3.149 g, 97%) as colorless prisms, mp 71.5—72.5 °C (Et_2O–hexane). *Anal.* Calcd for $C_{15}H_{16}N_2O_5S$: C, 53.56; H, 4.79; N, 8.33. Found: C, 53.60; H, 4.80; N, 8.53. MS *m/z*: 336 (M^+, 44), 302 (7), 290 (6), 289 (8), 249 (31), 234 (94), 195 (11), 141 (100), 93 (76), 77 (94). IR (KBr) cm^{-1}: 1686, 1560, 1391. ^{1}H-NMR δ: 1.06 (3H, d, J=6.5 Hz), 2.63—3.13 (3H, m), 4.34 (1H, dd, J=16, 6 Hz), 4.47 (1H, dd, J=16, 6 Hz), 6.64 (1H, dd, J=3, 1.5 Hz), 7.12 (1H, dd, J=3, 2 Hz), *ca.* 7.37—7.74 (3H, m), 7.74 (1H, dd, J=2, 1.5 Hz), *ca.* 7.74—8.01 (2H, m).

3-(4,4-Dimethoxy-3-methyl-1-oxobutyl)-1-(phenylsulfonyl)-1*H*-pyrrole (10d) In the same manner as described for the preparation of **14a**, a slurry of **15b** (180 mg, 0.536 mmol) in MeOH (5 ml) was stirred with NaOH (33 mg, 0.83 mmol) at 0 °C for 15 min. This was poured into 20% H_2SO_4 in MeOH (4 ml) using MeOH (3 ml) at −20 °C. The solution was stirred for 15 min at −20 °C and then worked up as before. Purification by PTLC [hexane–CH_2Cl_2 (1 : 5)] gave **10d** (154 mg, 82%) as a colorless syrup, along with recovered **15b** (8 mg, 4%). HRMS Calcd for $C_{17}H_{21}NO_5S$: 351.1139. Found: 351.1137. MS *m/z*: 351 (M^+, 0.4), 320 (3), 260 (2), 234 (15), 141 (11), 102 (62), 77 (40), 75 (100). IR ($CHCl_3$) cm^{-1}: 1677. ^{1}H-NMR δ: 0.93 (3H, d, J=6.5 Hz), 2.25—2.69 (2H, m), 2.75—3.14 (1H, m), 3.31 (3H, s), 3.33 (3H, s), 4.10 (1H, d, J=5 Hz), 6.65 (1H, dd, J=3, 1.5 Hz), 7.11 (1H, dd, J=3, 2 Hz), *ca.* 7.36—7.72 (3H, m), 7.72 (1H, dd, J=2, 1.5 Hz), *ca.* 7.72—8.01 (2H, m).

3-[3-(1,3-Dioxan-2-yl)-1-oxobutyl]-1-(phenylsulfonyl)-1*H*-pyrrole (16) In the same manner as above, **10d** (576 mg, 1.64 mmol) in 2-ethyl-2-methyl-1,3-dioxane (10 ml) was stirred with *p*-TsOH · H_2O (16 mg, 0.084 mmol) at room temperature for 3 h. The same work-up as above and purification by column chromatography (silica gel: 25 g, CH_2Cl_2) afforded **16** (580 mg, 97%) as a colorless syrup. HRMS Calcd for $C_{18}H_{21}NO_5S$: 363.1139. Found: 363.1139. MS *m/z*: 363 (M^+, 1), 234 (11), 222 (13), 114 (100), 87 (83), 77 (37). IR ($CHCl_3$) cm^{-1}: 1677. ^{1}H-NMR δ: 0.95 (3H, d, J=7 Hz), 1.13—1.42 (1H, m), 1.63—2.68 (3H, m), 3.02 (1H, dd, J=14.5, 3.5 Hz), 3.67 (2H, ddd, J=11.5, 11.5, 2 Hz), 3.92—4.22 (2H, m), 4.38 (1H, d, J=3.5 Hz), 6.68 (1H, dd, J=3.5, 1.5 Hz), 7.09 (1H, dd, J=3.5, 2 Hz), 7.37—7.68 (3H, m), 7.73 (1H, dd, J=2, 1.5 Hz), 7.80—8.00 (2H, m).

3-[2-Bromo-3-(1,3-dioxan-2-yl)-1-oxobutyl]-1-(phenylsulfonyl)-1*H*-pyrrole (10e) In the same manner as described for the preparation of **10a**, a THF solution (8 ml) of **16** (224 mg, 0.617 mmol) was stirred with Py · HBr_3 (80%, 296 mg, 0.740 mmol) at 0 °C for 1 h and at room temperature for 1 h. The same work-up as above and purification by PTLC [hexane–CH_2Cl_2 (1 : 5)] yielded **10e** (262 mg, 96%) as a colorless syrup. MS *m/z*: 362 (M^+ − Br, 33), 234 (39), 141 (15), 87 (100), 77 (55). IR ($CHCl_3$) cm^{-1}: 1679. ^{1}H-NMR of major and minor diastereomers δ: 1.14 and 1.00 (total 3H, d each, J=6.5 Hz), *ca.* 1.14—1.44 (1H, m), 1.57—2.18 (1H, m), 2.18—2.64 (1H, m), 3.41—4.26 (4H, m), 4.42 and 4.84 (total 1H, d each, J=5 and 3.5 Hz), 5.12 and 4.80 (total 1H, d each, J=6.5 and 9 Hz), 6.72 (1H, dd, J=3.5, 1.5 Hz), 7.16 (1H, dd, J=3.5, 2 Hz), 7.42—7.81 (3H, m), 7.81—8.07 (3H, m).

3-[4,4-Dimethoxy-3-methyl-1-oxo-2-(phenylthio)butyl]-1-(phenylsulfonyl)-1*H*-pyrrole (10f) In the same manner as described for the preparation of **10c**, a solution of **10d** (103 mg, 0.293 mmol) and PhSSPh (80 mg, 0.37 mmol) in THF (6 ml) was stirred with *tert*-BuOK (76 mg, 0.68 mmol) at −40—−34 °C for 20 min. The same work-up as before and purification by PTLC [hexane–CH_2Cl_2 (2 : 7)] afforded recovered **10d** (5 mg, 5%) and **10f** (85 mg, 63%) as a colorless syrup. HRMS Calcd for $C_{23}H_{25}NO_5S_2$: 459.1173. Found: 459.1176. MS *m/z*: 459 (M^+, 2), 427 (5), 350 (5), 234 (15), 77 (31), 75 (100). IR ($CHCl_3$) cm^{-1}: 1666. ^{1}H-NMR of major and minor diastereomers δ: 0.98 and 1.19 (total 3H, d each, J=7 Hz), 2.19—2.63 (1H, m), 3.31 and 3.14 (total 3H, s each), 3.40 and 3.24 (total 3H, s each), 4.20 and 4.26 (total 1H, d each, J=9 and 7.5 Hz), 6.60 (1H, dd, J=3.5, 1.5 Hz), 6.97—7.10 (1H, m), 7.04—7.72 (9H, m), 7.69—7.90 (2H, m).

3-[(*E*)-3-(1,3-Dioxan-2-yl)-1-oxo-2-propenyl]-1-(phenylsulfonyl)-1*H*-pyrrole (17) SeO_2 (694 mg, 6.25 mmol) was added to a solution of **13c** (388 mg, 1.56 mmol) in dioxane–H_2O (10 : 1, 5.5 ml) and the mixture was stirred under reflux for 5 h, and then allowed to cool. H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up gave a residue (461 mg). Ph_3P=CHCHO (426 mg, 1.40 mmol) was added to a CH_2Cl_2 solution (8 ml) of the above residue, and the mixture was stirred at room temperature for 4 h. 2-Ethyl-2-methyl-1,3-dioxane (3.00 ml, 22.2 mmol) and *p*-TsOH · H_2O (30 mg, 0.16 mmol) were further added to the mixture, and the whole was stirred at room temperature for 15 h. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and purification by column chromatography (silica gel: 30 g, CH_2Cl_2) gave **17** (314 mg, 58%) as slightly yellow prisms, mp 115—116 °C (benzene–hexane). *Anal.* Calcd for $C_{17}H_{17}NO_5S$: C, 58.77; H, 4.93; N, 4.03. Found: C, 59.06; H, 4.92; N, 4.06. HRMS Calcd for $C_{17}H_{17}NO_5S$: 347.0826. Found: 347.0822. MS *m/z*: 347 (M^+, 28), 234 (14), 206 (19), 148 (25), 141 (24), 134 (30), 87 (100), 77 (99), 51 (18). IR (KBr) cm^{-1}: 1672, 1628. ^{1}H-NMR δ: 1.39 (1H, br d, J=13.5 Hz), 1.84—2.43 (1H, m), 3.84 (2H, ddd, J=11.5, 11.5, 2 Hz), 4.19 (2H, dd, J=11.5, 5.5 Hz), 5.13 (1H, d, J=2 Hz), 6.71 (1H, dd, J=16, 2 Hz), 6.72 (1H, dd, J=3.5, 1.5 Hz), 6.91 (1H, d, J=16 Hz), 7.11 (1H, dd, J=3.5, 2.5 Hz), 7.37—7.74 (3H, m), 7.74—7.99 (3H, m).

3-[3-(1,3-Dioxan-2-yl)-4-nitro-1-oxobutyl]-1-(phenylsulfonyl)-1*H*-pyrrole (18) 18-Crown-6 (6 mg, 0.02 mmol) and KF (4 mg, 0.07 mmol) were added successively to a cooled (0 °C) solution of **17** (81 mg, 0.23 mmol) and $MeNO_2$ (0.25 ml, 4.6 mmol) in MeCN (3 ml) and the mixture was stirred at 0 °C for 2 h. Saturated NH_4Cl–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [hexane–EtOAc (2 : 1)] afforded **18** (89 mg, 93%) as colorless needles, mp 97—98 °C (benzene–hexane). *Anal.* Calcd for $C_{18}H_{20}N_2O_7S$: C, 52.93; H, 4.94; N, 6.86. Found: C, 53.04; H, 4.97; N, 6.81. HRMS Calcd for $C_{18}H_{20}N_2O_7S$: 408.0990. Found: 408.1003. MS *m/z*: 408 (M^+, 0.3), 378 (5), 362 (1), 360 (3), 347 (1), 249 (34), 234 (28), 141 (28), 113 (81), 87 (76), 77 (100). IR (KBr) cm^{-1}: 1676. ^{1}H-NMR δ: 1.14—1.45 (1H, m), *ca.* 1.61—2.30 (1H, m), 2.81 (1H, dd, J=18, 9 Hz), *ca.* 2.81—3.28 (1H, m), 3.10 (1H, dd, J=18, 5 Hz), 3.50—3.91 (2H, m), 3.91—4.21 (2H, m), 4.45 (1H, dd, J=13.5, 6 Hz), 4.60 (1H, dd, J=13.5, 5.5 Hz), 4.68 (1H, d, J=3.5 Hz), 6.67 (1H, dd, J=3.5, 1.5 Hz), 7.14 (1H, dd, J=3.5, 2 Hz), 7.41—7.72 (3H, m), 7.74 (1H, dd, J=2, 1.5 Hz), 7.84—8.05 (2H, m).

3-[4,4-Dimethoxy-3-(1,3-dioxan-2-yl)-1-oxobutyl]-1-(phenylsulfonyl)-1*H*-pyrrole (10g) In the same manner as described for the preparation of **10d**, **18** (117 mg, 0.287 mmol) was converted into **10g** (101 mg, 83%) and α-(1,3-dioxan-2-yl)-γ-oxo-1-(phenylsulfonyl)-1*H*-pyrrole-3-butanal (CHO compound) (5 mg, 4.5%), which were separated by PTLC (CH_2Cl_2). **10g**: Colorless syrup. MS *m/z*: 392 (M^+ − OMe, 2), 304 (2), 273 (3), 250 (4), 234 (10), 143 (47), 87 (100), 77 (34), 75 (54), 31 (24). IR ($CHCl_3$) cm^{-1}: 1680. ^{1}H-NMR δ: 1.23 (1H, br d, J=13 Hz), 1.62—2.18 (1H, m), 2.59—3.07 (3H, m), 3.26 (3H, s), 3.31 (3H, s), 3.67 (2H, ddd, J=11.5, 11.5, 2.5 Hz), 3.82—4.16 (2H, m), 4.39 (1H, d, J=5 Hz), 4.64 (1H, d, J=3.5 Hz), 6.69 (1H, dd, J=3.5, 1.5 Hz), 7.12 (1H, dd, J=3.5, 2 Hz), 7.38—7.73 (3H, m), 7.77 (1H, dd, J=2, 1.5 Hz), 7.82—8.01 (2H, m). CHO compound: HRMS Calcd for $C_{18}H_{19}NO_6S$: 377.0932. Found: 377.0946. MS *m/z*: 377 (M^+, 1), 292 (8), 234 (91), 129 (82), 87 (69), 77 (100). IR ($CHCl_3$) cm^{-1}: 1728, 1677. ^{1}H-NMR δ: 1.17—1.46 (1H, m), *ca.* 1.73—2.37 (1H, m), 2.82—3.53 (3H, m), 3.53—3.93 (2H, m), 3.93—4.27 (2H, m), 4.87 (1H, d, J=4 Hz), 6.66 (1H, dd, J=3.5, 1.5 Hz), 7.06—7.19 (1H, m), 7.40—7.69 (3H, m), 7.69—7.81 (1H, m), 7.81—7.99 (2H, m), 9.85 (1H, s).

Indole Cyclization Reaction of 10 to Form 19 Preparation of 5-bromo-4-(3-hydroxypropoxy)-1-(phenylsulfonyl)-1*H*-indole (**19a**) is described as a representative example. A mixture of **10a** (31 mg, 0.072 mmol), 95% H_2SO_4 (24 mg, 0.23 mmol), and 1,3-propanediol (169 mg, 2.22 mmol) in 1,2-dichloroethane (4 ml) was refluxed using a Dean–Stark apparatus for 33 h, and then cooled to 0 °C. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up followed by purification by PTLC [hexane–CH_2Cl_2 (1 : 4)] gave **19a** (16.5 mg, 56%) as a colorless syrup. HRMS Calcd for $C_{17}H_{16}BrNO_4S$: 410.9963, 408.9983. Found: 410.9978, 409.0007. MS *m/z*: 411, 409 (M^+; 31, 30), 353, 351 (33, 31), 212, 210 (73, 75), 141 (22), 77 (100), 51 (32), 31 (68). ^{1}H-NMR δ: 1.84 (1H, br s, OH), 2.06 (2H, tt, J=6, 6 Hz), 3.94 (2H, t, J=6 Hz), 4.24 (2H, t, J=6 Hz), 6.78 (1H, d, J=4 Hz), 7.32—7.65 (3H, m), 7.42 (1H, d, J=8.5 Hz), 7.53 (1H, d, J=4 Hz), 7.65 (1H, d, J=8.5 Hz), 7.79—7.97 (2H, m).

4-(3-Hydroxypropoxy)-1-(phenylsulfonyl)-1*H*-indol-5-ol (19b) Indole cyclization of **10b** (80 mg, 0.20 mmol) was carried out as above. The residual mixture was treated with K_2CO_3 (30 mg) in MeOH (3 ml) at

0 °C for 2 h and **19b** (37 mg, 53%) was isolated as a colorless syrup after purification by PTLC [benzene–EtOAc (3 : 2)]. HRMS Calcd for $C_{17}H_{17}NO_5S$: 347.0826. Found: 347.0815. MS *m/z*: 347 (M^+, 53), 289 (29), 148 (100), 77 (63), 51 (22), 31 (49). ^{1}H-NMR δ: 1.91 (2H, tt, J=5.5, 5.5 Hz), 2.69 (1H, br s, OH), 3.91 (2H, t, J=5.5 Hz), 4.18 (2H, t, J=5.5 Hz), 6.62 (1H, d, J=4 Hz), 6.89 (1H, d, J=8.5 Hz), *ca.* 7.21–7.58 (4H, m containing phenolic OH), 7.44 (1H, d, J=4 Hz), 7.74—7.94 (2H, m).

4-(3-Hydroxypropoxy)-1-(phenylsulfonyl)-5-(phenylthio)-1*H*-indole (19c) A colorless syrup (**19c**, 19 mg, 77%) was obtained from **10c** (25 mg, 0.056 mmol) after purification by PTLC (CH_2Cl_2). HRMS Calcd for $C_{23}H_{21}NO_4S_2$: 439.0911. Found: 439.0896. MS *m/z*: 439 (M^+, 100), 381 (27), 299 (15), 240 (53), 134 (20), 77 (50), 51 (18), 31 (31). ^{1}H-NMR δ: 1.63—2.20 (1H, m, OH), 1.93 (2H, tt, J=6, 6 Hz), 3.80 (2H, t, J=6 Hz), 4.22 (2H, t, J=6 Hz), 6.75 (1H, d, J=3.5 Hz), 7.04—7.31 (5H, m), 7.22 (1H, d, J=8.5 Hz), *ca.* 7.31—7.59 (3H, m), 7.51 (1H, d, J=3.5 Hz), 7.66 (1H, d, J=8.5 Hz), 7.76—7.97 (2H, m).

4-(3-Hydroxypropoxy)-6-methyl-1-(phenylsulfonyl)-1*H*-indole (19d) Cyclization reaction of **10d** (501 mg, 1.43 mmol) was carried out under the conditions described in Table I to afford **19d** (446 mg, 91%) as a colorless syrup after purification by column chromatography [silica gel, 30 g, hexane–EtOAc (1 : 1)]. HRMS Calcd for $C_{18}H_{19}NO_4S$: 345.1034. Found: 345.1034. MS *m/z*: 345 (M^+, 45), 204 (19), 160 (12), 146 (100), 77 (43), 51 (18), 31 (32). ^{1}H-NMR δ: 1.77—2.13 (1H, m, OH), 2.00 (2H, tt, J=6, 6 Hz), 2.40 (3H, s), 3.81 (2H, t, J=6 Hz), 4.12 (2H, t, J=6 Hz), 6.44 (1H, s), 6.64 (1H, d, J=3.5 Hz), 7.19—7.58 (5H, m), 7.66—7.92 (2H, m).

5-Bromo-4-(3-hydroxypropoxy)-6-methyl-1-(phenylsulfonyl)-1*H*-indole (19e) A colorless syrup (**19e**, 6 mg, 14%) was obtained from **10e** (44 mg, 0.10 mmol) after purification by PTLC [benzene–EtOAc (9 : 1)]. HRMS Calcd for $C_{18}H_{18}BrNO_4S$: 425.0120, 423.0139. Found: 425.0112, 423.0130. MS *m/z*: 425, 423 (M^+; 43, 42), 367, 365 (29, 25), 225, 223 (92, 97), 77 (100), 51 (36), 31 (76). ^{1}H-NMR δ: *ca.* 1.77—2.17 (1H, m, OH), 2.06 (2H, tt, J=5.5, 5.5 Hz), 2.50 (3H, s), 3.96 (2H, t, J=5.5 Hz), 4.23 (2H, t, J=5.5 Hz), 6.73 (1H, d, J=3.5 Hz), 7.33—7.63 (4H, m), 7.68 (1H, s), 7.77—7.99 (2H, m).

4-(3-Hydroxypropoxy)-6-methyl-1-(phenylsulfonyl)-5-(phenylthio)-1*H*-indole (19f) A colorless syrup (**19f**, 25 mg, 59%) was obtained from **10f** (43 mg, 0.094 mmol) after purification by PTLC [hexane–CH_2Cl_2 (1 : 4)]. HRMS Calcd for $C_{24}H_{23}NO_4S_2$: 453.1067. Found: 453.1047. MS *m/z*: 453 (M^+, 100), 395 (28), 254 (87), 176 (61), 77 (69), 51 (25), 31 (44). ^{1}H-NMR δ: 1.90 (2H, tt, J=6, 6 Hz), 2.12 (1H, br s, OH), 2.48 (3H, s), 3.77 (2H, t, J=6 Hz), 4.17 (2H, t, J=6 Hz), 6.74 (1H, d, J=3.5 Hz), 6.84—7.28 (5H, m), 7.32—7.62 (3H, m), 7.46 (1H, d, J=3.5 Hz), 7.72 (1H, s), 7.81—8.03 (2H, m).

6-(1,3-Dioxan-2-yl)-4-(3-hydroxypropoxy)-1-(phenylsulfonyl)-1*H*-indole (19g) A colorless syrup (**19g**, 41 mg, 83%) was obtained from **10g** (50 mg, 0.12 mmol) after purification by PTLC [hexane–EtOAc (1 : 1)]. HRMS Calcd for $C_{21}H_{23}NO_6S$: 417.1245. Found: 417.1253. MS *m/z*: 417 (M^+, 100), 359 (16), 331 (15), 276 (44), 218 (52), 160 (62), 132 (56), 87 (38), 77 (87). ^{1}H-NMR δ: 1.30—1.57 (1H, m), *ca.* 1.63—2.54 (1H, m), 1.78 (1H, br s, OH), 2.04 (2H, tt, J=6, 6 Hz), *ca.* 3.67—4.43 (4H, m), 3.81 (2H, t, J=6 Hz), 4.22 (2H, t, J=6 Hz), 5.55 (1H, s), 6.69 (1H, d, J=4 Hz), 6.88 (1H, s), 7.18—7.62 (4H, m), *ca.* 7.62—7.95 (2H, m), 7.73 (1H, s).

Oxidative Deprotection of 19 to Form 4-Hydroxyindoles 11 This transformation was carried out by the procedure already reported.[7]

5-Bromo-1-(phenylsulfonyl)-1*H*-indol-4-ol (11a) Colorless prisms, mp 125.5—126.5 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{14}H_{10}BrNO_3S$: C, 47.74; H, 2.86; N, 3.98. Found: C, 47.78; H, 2.94; N, 3.98. HRMS Calcd for $C_{14}H_{10}BrNO_3S$: 352.9545, 350.9565. Found: 352.9572, 350.9554. MS *m/z*: 353, 351 (M^+; 53, 49), 212, 210 (97, 98), 103 (33), 77 (100), 51 (64). ^{1}H-NMR δ: 5.45 (1H, br s, OH), 6.76 (1H, d, J=4 Hz), 7.22—7.63 (6H, m), 7.73—7.97 (2H, m).

1-(Phenylsulfonyl)-5-(phenylthio)-1*H*-indol-4-ol (11c) Colorless prisms, mp 99.5—101 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{20}H_{15}NO_3S$: C, 62.97; H, 3.96; N, 3.67. Found: C, 63.06; H, 4.08; N, 3.66. HRMS Calcd for $C_{20}H_{15}NO_3S$: 381.0492. Found: 381.0509. MS *m/z*: 381 (M^+, 100), 240 (55), 162 (18), 134 (29), 77 (54), 51 (27). ^{1}H-NMR δ: *ca.* 6.72—6.93 (1H, m, OH), 6.81 (1H, d, J=3.5 Hz), *ca.* 6.93—7.31 (5H, m), 7.31—7.61 (3H, m), 7.42 (1H, d, J=8.5 Hz), 7.52 (1H, d, J=3.5 Hz), 7.61 (1H, d, J=8.5 Hz), 7.81—8.03 (2H, m).

6-Methyl-1-(phenylsulfonyl)-1*H*-indol-4-ol (11d) Colorless prisms, mp 146—147 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{15}H_{13}NO_3S$: C, 62.70; H, 4.56; N, 4.88. Found: C, 62.42; H, 4.49; N, 4.91. HRMS Calcd for $C_{15}H_{13}NO_3S$: 287.0615. Found: 287.0620. MS *m/z*: 287 (M^+, 31), 146 (100), 77 (26), 51 (17). ^{1}H-NMR δ: 2.36 (3H, s), 5.04 (1H, s, OH), 6.41 (1H, s), 6.64 (1H, d, J=4 Hz), 7.20—7.62 (4H, m), 7.44 (1H, s), 7.71—7.99 (2H, m).

6-Methyl-1-(phenylsulfonyl)-5-(phenylthio)-1*H*-indol-4-ol (11f) Colorless syrup. HRMS Calcd for $C_{21}H_{17}NO_3S_2$: 395.0649. Found: 395.0648. MS *m/z*: 395 (M^+, 100), 254 (98), 176 (71), 148 (21), 104 (24), 77 (58), 51 (36). ^{1}H-NMR δ: 2.46 (3H, s), 6.77 (1H, d, J=3.5 Hz), 6.87—7.31 (5H + OH, m), 7.31—7.70 (4H, m), 7.45 (1H, d, J=3.5 Hz), 7.81—8.03 (2H, m).

6-(1,3-Dioxan-2-yl)-1-(phenylsulfonyl)-1*H*-indol-4-ol (11g) Colorless syrup. HRMS Calcd for $C_{18}H_{17}NO_5S$: 359.0826. Found: 359.0841. MS *m/z*: 359 (M^+, 78), 342 (8), 301 (26), 273 (12), 218 (39), 160 (94), 132 (63), 87 (79), 77 (100), 51 (40). ^{1}H-NMR δ: 1.56 (1H, br d, J=13 Hz), 2.19 (1H, dtt, J=13, 12, 6 Hz), 3.94 (2H, ddd, J=12, 12, 2 Hz), 4.23 (2H, br dd, J=12, 6 Hz), 5.49 (1H, s), 6.60 (1H, d, J=3 Hz), 6.77 (1H, s), 7.17—7.50 (4H, m), 7.68 (1H, s), 7.70—7.90 (2H, m).

4-Benzyloxy-6-(1,3-dioxan-2-yl)-1-(phenylsulfonyl)-1*H*-indol (20) A solution of **11a** (281 mg, 0.783 mmol) in THF (4 ml) and DMF (2 ml) was stirred with NaH (60%, 41 mg, 1.0 mmol) under an Ar atmosphere at 0 °C for 10 min. $PhCH_2Br$ (0.12 ml, 1.0 mmol) was added and the mixture was further stirred at room temperature for 45 min. Saturated NH_4Cl–H_2O was added and the whole was extracted with Et_2O, and then worked up as usual. Purification by PTLC [hexane–EtOAc (3 : 1)] afforded **20** (269 mg, 77%) as colorless prisms (benzene–hexane), mp 159—160 °C. *Anal.* Calcd for $C_{25}H_{23}NO_5S$: C, 66.80; H, 5.16; N, 3.12. Found: C, 67.05; H, 5.26; N, 3.08. HRMS Calcd for $C_{25}H_{23}NO_5S$: 449.1296. Found: 449.1279. MS *m/z*: 449 (M^+, 20), 358 (12), 308 (16), 258 (7), 141 (14), 91 (100), 87 (13), 77 (41), 51 (8). ^{1}H-NMR δ: 1.45 (1H, br d, J=13 Hz), 2.25 (1H, dtt, J=13, 12, 6 Hz), 4.00 (2H, ddd, J=12, 12, 2 Hz), 4.29 (2H, br dd, J=12, 6 Hz), 5.14 (2H, s), 5.53 (1H, s), 6.77 (1H, d, J=3 Hz), 6.97 (1H, s), 7.20—7.57 (9H, m), 7.73—7.98 (3H, m).

***tert*-Butyl (4*S*)-4-[(*S*)-Hydroxy[4-benzyloxy-6-(1,3-dioxan-2-yl)-1-(phenylsulfonyl)-1*H*-indol-2-yl]methyl]-2,2-dimethyloxazolidine-3-carboxylate (22a) and *tert*-Butyl (4*S*)-4-[(*R*)-Hydroxy[4-benzyloxy-6-(1,3-dioxan-2-yl)-1-(phenylsulfonyl)-1*H*-indol-2-yl]methyl]-2,2-dimethyloxazolidine-3-carboxylate (22b)** A solution (0.40 ml) of 0.8 M LDA in THF–hexane, prepared from 1.6 M BuLi in hexane (2.00 ml) and iso-Pr_2NH (0.50 ml) in THF (1.50 ml), was added to a THF solution (5 ml) of **20** (112 mg, 0.249 mmol) at −75 °C under an Ar atmosphere. The mixture was stirred at −75—−72 °C for 10 min, and a toluene solution (1 ml) of the chiral aldehyde **21** (95 mg, 0.42 mmol) was added to this. Stirring was continued at −72—−68 °C for 1 h, and then saturated NH_4Cl–H_2O was added while the mixture was cooled. The whole was extracted with CH_2Cl_2 and worked up as usual. Separation by PTLC [hexane–THF (2 : 1)] afforded recovered **20** (19 mg, 17%) and a mixture of **22a** and **22b**. PTLC of the latter twice [CH_2Cl_2 and then CH_2Cl_2–MeOH (199 : 1)] gave **22a** (105 mg, 62%) as a more polar isomer and **22b** (18 mg, 11%) as a less polar isomer. **22a**: Colorless syrup. HRMS Calcd for $C_{36}H_{42}N_2O_9S$: 678.2608. Found: 678.2636. $[\alpha]_D^{24}$ +90.3° (c=1.42, $CHCl_3$). MS *m/z*: 678 (M^+, 0.6), 605 (0.6), 538 (2), 478 (24), 423 (9), 338 (14), 246 (6), 190 (4), 144 (7), 91 (91), 87 (23), 57 (100). IR ($CHCl_3$) cm^{-1}: 1695. ^{1}H-NMR δ: 1.40 (15H, s), 1.81—2.53 (1H, m), 3.80—4.42 (6H, m), 4.42—4.63 (1H, m), 5.07 (2H, s), 5.53 (1H, s), 5.63—5.80 (1H, m), 6.72 (1H, s), 6.91 (1H, s), 7.17—7.53 (8H, m), 7.63—7.80 (2H, m), 7.85 (1H, s). **22b**: Colorless syrup. HRMS Calcd for $C_{36}H_{42}N_2O_9S$: 678.2608. Found: 678.2633. $[\alpha]_D^{24}$ −42.0° (c=0.65, $CHCl_3$). MS *m/z*: 678 (M^+, 0.4), 605 (0.5), 538 (2), 478 (19), 423 (7), 338 (12), 246 (6), 190 (4), 144 (7), 91 (98), 87 (23), 57 (100). IR ($CHCl_3$) cm^{-1}: 1654. ^{1}H-NMR δ: 1.47 (9H, s), 1.50 (3H, s), 1.68 (3H, s), 1.90—2.55 (1H, m), 3.50—4.43 (6H, m), 4.43—4.72 (1H, m), 5.09 (2H, s), 5.29—5.51 (1H, m), 5.51 (1H, s), 6.83 (1H, s), 6.97 (1H, s), 7.20—7.57 (8H, m), 7.77—7.99 (3H, m).

2-[(1*S*,2*S*)-1,3-(Diacetoxy)-2-(*tert*-butyloxycarbonylamino)propyl]-4-benzyloxy-1-(phenylsulfonyl)-1*H*-indole-6-carboxaldehyde (23) A DME solution (4.5 ml) of **22a** (49 mg, 0.072 mmol) and 10% HCl–H_2O (0.5 ml) was stirred at room temperature for 2 h. Saturated $NaHCO_3$–H_2O and NaCl powder were added, and the whole was extracted with 10% MeOH-containing CH_2Cl_2. The extract was worked up as usual, and the dried residue (42 mg) was acetylated with Ac_2O (0.15 ml) in pyridine (0.3 ml) by stirring at room temperature for 3 h. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. The extract was successively washed with 3% HCl–H_2O, H_2O, saturated $NaHCO_3$–H_2O

and H_2O, and worked up as usual. Purification by PTLC [hexane–EtOAc (7:3)] afforded **23** (40 mg, 83%) as a colorless syrup. HRMS Calcd for $C_{34}H_{36}N_2O_{10}S$: 664.2088. Found: 664.2082. $[\alpha]_D^{24}$ +231° (c=1.22, $CHCl_3$). MS m/z: 664 (M^+, 1), 590 (1), 546 (1), 524 (1), 463 (15), 421 (7), 280 (5), 202 (6), 146 (5), 91 (100), 57 (46). IR ($CHCl_3$) cm^{-1}: 1746, 1715, 1696. ^{1}H-NMR δ: 1.20 (9H, s), 2.05 (3H, s), 2.16 (3H, s), 3.97—4.60 (3H, m), 5.12 (2H, s), 5.20—5.50 (1H, br s, NH), 6.62 (1H, d, J=7.5Hz), 6.90 (1H, s), 7.27 (1H, s), 7.27—7.57 (8H, m), 7.90—8.08 (2H, m), 8.12 (1H, s), 9.93 (1H, s).

2-[(1*S*,2*S*)-1,3-(Diacetoxy)-2-(*tert*-butyloxycarbonylamino)propyl]-4-benzyloxy-6-(1,3-dithiolan-2-yl)-1-(phenylsulfonyl)-1*H*-indole (24) $BF_3 \cdot OEt_2$ (30 μl, 0.24 mmol) was added to a CH_2Cl_2 solution (4 ml) of **23** (70 mg, 0.11 mmol) and 1,2-ethanedithiol (88 mg, 0.94 mmol) at 0 °C, and the mixture was stirred at the same temperature for 20 min. Saturated $NaHCO_3$–H_2O was added at 0 °C and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [hexane–EtOAc (7:3)] gave **24** (67 mg, 86%) as a colorless glass. HRMS Calcd for $C_{36}H_{40}N_2O_9S_3$: 740.1893. Found: 740.1872. $[\alpha]_D^{24}$ +189° (c=1.20, $CHCl_3$). MS m/z: 740 (M^+, 0.3), 664 (1), 590 (2), 546 (1), 463 (11), 421 (6), 280 (4), 202 (5), 146 (4), 91 (100), 57 (34). IR ($CHCl_3$) cm^{-1}: 1744, 1714. ^{1}H-NMR δ: 1.27 (9H, s), 2.04 (3H, s), 2.13 (3H, s), 3.17—3.83 (4H, m), 3.92—4.57 (3H, m), 5.07 (2H, s), 5.17—5.45 (1H, br s, NH), 5.67 (1H, s), 6.61 (1H, d, J=7.5 Hz), 6.76 (1H, s), 6.88 (1H, s), 7.18—7.53 (8H, m), 7.83 (1H, s), 7.87—8.10 (2H, m).

(4*S*,5*S*)-4-[4-Benzyloxy-6-(1,3-dithiolan-2-yl)-1-(phenylsulfonyl)-1*H*-indol-2-yl]-5-(*tert*-butyloxycarbonylamino)-2,2-dimethyl-1,3-dioxane (25) A mixture of **24** (66 mg, 0.089 mmol) and K_2CO_3 (10 mg, 0.072 mmol) in MeOH (3 ml) was stirred at room temperature for 30 min. Saturated NaCl–H_2O was added and the whole was extracted with 10% MeOH-containing CH_2Cl_2, and then worked up as usual to give the residue (64 mg). TsOH · H_2O (8 mg, 0.04 mmol) was added to a CH_2Cl_2 solution (5 ml) of the dried residue and 2,2-dimethoxypropane (0.3 ml), and the mixture was stirred at room temperature for 20 min. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2, and then worked up as usual. Purification by PTLC twice [hexane–EtOAc (3:1) and then hexane–EtOAc (7:3)] afforded **25** (45 mg, 72%) as a less polar colorless syrup, along with an *N*,*O*-acetonide **22c** (11 mg, 18%) as a more polar colorless syrup. **25**: HRMS Calcd for $C_{35}H_{40}N_2O_7S_3$: 696.1995. Found: 696.2002. $[\alpha]_D^{24.5}$ +190° (c=0.63, $CHCl_3$). MS m/z: 696 (M^+, 1), 622 (3), 556 (2), 495 (12), 355 (4), 264 (4), 91 (100), 57 (31). IR ($CHCl_3$) cm^{-1}: 1710. ^{1}H-NMR δ: 1.31 (9H, s), 1.37 (3H, s), 1.59 (3H, s), 3.17—3.63 (4H, m), 3.52—4.33 (3H, m), 5.10 (2H, s), 5.53 (1H, d, J=9.5 Hz), 5.70 (1H, s), 6.90 (1H, s), 7.10 (1H, s), 7.21—7.54 (8H, m), 7.72—7.94 (3H, m). *tert*-Butyl (4*S*)-4-[(*S*)-Hydroxy[4-benzyloxy-6-(1,3-dithiolan-2-yl)-1-(phenylsulfonyl)-1*H*-indol-2-yl]methyl]-2,2-dimethyloxazolidine-3-carboxylate (**22c**): HRMS Calcd for $C_{35}H_{40}N_2O_7S_3$: 696.1995. Found: 696.1999. MS m/z: 696 (M^+, 0.7), 622 (4), 556 (3), 496 (14), 441 (6), 356 (8), 264 (6), 200 (5), 144 (9), 91 (100), 57 (94). IR ($CHCl_3$) cm^{-1}: 1694. ^{1}H-NMR δ: 1.43 (15H, s), 1.61 (1H, br s, OH), 3.19—3.67 (4H, m), 4.01 (1H, dd, J=9, 7 Hz), 4.28 (1H, dd, J=9, 3 Hz), 4.47—4.64 (1H, m), 5.07 (2H, s), 5.66—5.84 (1H, m), 5.71 (1H, s), 6.38 (1H, s), 6.95 (1H, s), 7.22—7.60 (8H, m), 7.70—7.89 (3H, m), 7.89 (1H, s).

(4*S*,5*S*)-4-[4-Benzyloxy-6-(1,3-dithiolan-2-yl)-1*H*-indol-2-yl]-5-(*tert*-butyloxycarbonylamino)-2,2-dimethyl-1,3-dioxane (26) A mixture of **25** (36 mg, 0.052 mmol) and Mg (83 mg, 3.5 mg atom) in MeOH (5 ml) was stirred at room temperature for 1.5 h. Saturated NH_4Cl–H_2O was added and the whole was extracted with CH_2Cl_2, and then worked up as usual. Purification by PTLC [hexane–EtOAc (7:3)] gave **26** (25 mg, 87%) as a colorless syrup. HRMS Calcd for $C_{29}H_{36}N_2O_5S_2$: 556.2064. Found: 556.2063. MS m/z: 556 (M^+, 8), 482 (6), 456 (5), 391 (5), 355 (14), 290 (4), 264 (12), 151 (10), 91 (100), 57 (35), 43 (64). IR ($CHCl_3$) cm^{-1}: 1712. ^{1}H-NMR δ: 1.33 (9H, s), 1.43 (3H, s), 1.53 (3H, s), 3.23—3.57 (4H, m), 3.60—4.18 (3H, m), 4.56 (1H, br d, J=7.5 Hz, NH), 4.92 (1H, br d, J=9 Hz), 5.15 (2H, s), 5.73 (1H, s), 6.53 (1H, s), 6.75 (1H, s), 7.13 (1H, s), 7.20—7.57 (5H, m), 8.60 (1H, br s, NH).

***tert*-Butyl (4*S*)-4-[(*S*)-Hydroxy[4-benzyloxy-6-(1,3-dioxan-2-yl)-1*H*-indol-2-yl]methyl]-2,2-dimethyloxazolidine-3-carboxylate (27a)** A mixture of **22a** (96 mg, 0.14 mmol) and Mg (109 mg, 4.54 mg atom) in MeOH (5 ml) was stirred at room temperature for 1.5 h. This was worked up as above, and purification by PTLC [hexane–EtOAc (2:1)] gave **27a** (72 mg, 95%) as a colorless glass. HRMS Calcd for $C_{30}H_{38}N_2O_7$: 538.2677. Found: 538.2685. $[\alpha]_D^{24}$ −19.7° (c=1.28, $CHCl_3$). MS m/z: 538 (M^+, 4), 480 (4), 338 (12), 281 (10), 280 (8), 248 (4), 190 (12), 144 (7), 100 (34), 91 (57), 57 (100). IR ($CHCl_3$) cm^{-1}: 1696. ^{1}H-NMR δ: 1.44 (15H, s), 1.97—2.53 (1H, m), 3.78—4.45 (8H, m), 5.17 (2H, s), 5.55 (1H, s), 6.44 (1H, s), 6.77 (1H, s), 7.11 (1H, s), 7.27—7.60 (5H, m), 8.65 (1H, br s, NH).

***tert*-Butyl (4*S*)-4-[(*R*)-Hydroxy[4-benzyloxy-6-(1,3-dioxan-2-yl)-1*H*-indol-2-yl]methyl]-2,2-dimethyloxazolidine-3-carboxylate (27b)** A mixture of **22b** (93 mg, 0.14 mmol) and Mg (121 mg, 4.98 mg atom) in MeOH (5 ml) was stirred at room temperature for 2 h. It was worked up as above, and purification by PTLC [hexane–EtOAc (5:3)] gave **27b** (71 mg, 96%) as a colorless glass. HRMS Calcd for $C_{30}H_{38}N_2O_7$: 538.2677. Found: 538.2684. $[\alpha]_D^{21}$ +19.5° (c=1.04, $CHCl_3$). MS m/z: 538 (M^+, 8), 403 (7), 375 (4), 338 (34), 299 (5), 248 (10), 190 (12), 144 (7), 100 (32), 91 (77), 57 (100). IR ($CHCl_3$) cm^{-1}: 1664, 1652. ^{1}H-NMR δ: 1.44 (3H, s), 1.21—1.62 (1H, m), 1.51 (12H, s), 1.96—2.50 (1H, m), 3.53—4.40 (7H, m), 4.92 (1H, br d, J=9 Hz), 5.16 (2H, s), 5.51 (1H, s), 6.50 (1H, br s), 6.77 (1H, s), 7.11 (1H, s), 7.23—7.57 (5H, m), 8.93 (1H, br s, NH).

4-Benzyloxy-2-[(1*S*,2*S*)-2-(*tert*-butyloxycarbonylamino)-1,3-(dihydroxy)propyl]-1*H*-indole-6-carboxaldehyde (28a) A mixture of a DME solution (2.5 ml) of **27a** (72 mg, 0.13 mmol) and 10% HCl–H_2O (0.5 ml) was stirred at room temperature for 14 h. Saturated $NaHCO_3$–H_2O and NaCl powder were added, and the whole was extracted with 10% MeOH-containing CH_2Cl_2. Usual work-up and purification by PTLC [benzene–EtOAc (1:1)] gave **28a** (44 mg, 75%) as a colorless glass. HRMS Calcd for $C_{24}H_{28}N_2O_6$: 440.1947. Found: 440.1959. $[\alpha]_D^{23}$ +9.4° (c=1.2, MeOH). MS m/z: 440 (M^+, 2), 384 (2), 366 (4), 281 (9), 201 (8), 190 (8), 91 (65), 59 (100), 57 (30). IR ($CHCl_3$) cm^{-1}: 1688, 1676. ^{1}H-NMR [$CDCl_3$–CD_3OD (10:1)] δ: 1.36 (9H, s), 3.47—4.02 (3H, m), 5.07 (1H, d, J=4.5 Hz), 5.20 (2H, s), 5.66 (1H, br d, J=9 Hz, NH), 6.63 (1H, s), 7.09 (1H, s), 7.27—7.49 (5H, m), 7.49 (1H, s), 9.84 (1H, s).

4-Benzyloxy-2-[(1*R*,2*S*)-2-(*tert*-butyloxycarbonylamino)-1,3-(dihydroxy)propyl]-1*H*-indole-6-carboxaldehyde (28b) A mixture of a DME solution (5 ml) of **27b** (70 mg, 0.13 mmol) and 10% HCl–H_2O (2.5 ml) was stirred at room temperature for 2 h. This was worked up as above and purification by PTLC [5% MeOH–CH_2Cl_2] gave **28b** (43 mg, 75%) as a colorless syrup. HRMS Calcd for $C_{24}H_{28}N_2O_6$: 440.1947. Found: 440.1946. $[\alpha]_D^{21}$ +52.8° (c=1.10, $CHCl_3$). MS m/z: 440 (M^+, 2), 384 (1), 366 (1), 320 (2), 281 (22), 190 (18), 91 (100), 59 (52), 57 (37). IR ($CHCl_3$) cm^{-1}: 1682. ^{1}H-NMR δ: 1.22 (9H, s), 3.57—4.23 (3H, m), 5.06 (2H, br s), 5.17 (1H, br s), 5.40—5.73 (1H, br s, NH), 6.57 (1H, br s), 6.94 (1H, s), 7.15 (1H, s), 7.20—7.52 (5H, m), 9.59 (1H, s), 9.97 (1H, br s, NH).

(1*S*,2*S*)-8-Benzyloxy-2-(*tert*-butyloxycarbonylamino)-2,3-dihydro-1-hydroxy-1*H*-pyrrolo[1,2-*a*]indole-6-carboxaldehyde (29a) Ms_2O (32 mg, 0.18 mmol) was added to a CH_2Cl_2 solution (3 ml) of **28a** (17 mg, 0.039 mmol) and Et_3N (0.3 ml) at −20 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 2 h and 45 min. Saturated $NaHCO_3$–H_2O was added, and the whole was extracted with CH_2Cl_2. The extract was successively washed with 1% HCl–H_2O, H_2O, saturated $NaHCO_3$–H_2O and H_2O, and worked up as usual to yield the residue (21 mg). Powdered KOH (85%, 7 mg, 0.1 mmol) was added to a THF solution (3 ml) of the dried above residue and 18-crown-6 (18 mg, 0.068 mmol) at 0 °C, and the mixture was stirred at room temperature for 30 min. Saturated NH_4Cl–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [hexane–EtOAc (3:2)] afforded **29a** (7 mg, 43%) as a colorless glass. HRMS Calcd for $C_{24}H_{26}N_2O_5$: 422.1840. Found: 422.1822. $[\alpha]_D^{23.5}$ +21.2° (c=1.31, $CHCl_3$). MS m/z: 422 (M^+, 8), 348 (12), 275 (13), 257 (12), 213 (4), 91 (100), 59 (54), 57 (20). IR ($CHCl_3$) cm^{-1}: 1704, 1678. ^{1}H-NMR (400 MHz, 50 °C) δ: 1.50 (9H, s), 2.13 (1H, d, J=3.5 Hz, OH), 3.92 (1H, dd, J=10, 7.5 Hz), 4.55 (1H, dd, J=10, 7.5 Hz), 4.83 (1H, dddd, J=8, 7.5, 7.5, 5.5 Hz), 5.18 (1H, dd, J=5.5, 3.5 Hz), 5.27 (2H, s), 5.47 (1H, br d, J=8 Hz, NH), 6.71 (1H, s), 7.14 (1H, s), 7.25 (1H, s), 7.30—7.35 (1H, m), 7.36—7.42 (2H, m), 7.46—7.51 (2H, m), 9.94 (1H, s).

(1*R*,2*S*)-8-Benzyloxy-2-(*tert*-butyloxycarbonylamino)-2,3-dihydro-1-hydroxy-1*H*-pyrrolo[1,2-*a*]indole-6-carboxaldehyde (29b) A CH_2Cl_2 solution (6 ml) of **28b** (40 mg, 0.091 mmol) and Et_3N (0.5 ml) was mesylated as above with Ms_2O (36 mg, 0.21 mmol) at −20 °C under an Ar atmosphere for 1.5 h. The crude mesylate (47 mg) was further treated as above with KOH powder (85%, 14 mg, 0.21 mmol) and 18-crown-6 (28 mg, 0.11 mmol) in THF (4 ml) at room temperature for 30 min to give, after PTLC twice [hexane–EtOAc (4:3) and CH_2Cl_2–MeOH (19:1)], **29b** (15 mg, 38%) and recovered **28b** (14 mg, 35%). **29b**: Colorless glass. HRMS Calcd for $C_{24}H_{26}N_2O_5$: 422.1840. Found: 422.1840. $[\alpha]_D^{24}$ −34.9° (c=0.65, $CHCl_3$). MS m/z: 422 (M^+, 6), 348 (12), 322 (5), 257 (16), 214 (18), 91 (100), 59 (25), 57 (15). IR ($CHCl_3$) cm^{-1}: 1717, 1692.

^{1}H-NMR δ: 1.46 (9H, s), 3.60—3.92 (1H, m), 4.33—4.65 (2H, m), 5.05—5.35 (1H+NH, m), 5.17 (2H, s), 6.61 (1H, s), 7.01 (1H, s), 7.14 (1H, s), 7.26—7.57 (5H, m), 9.71 (1H, s).

(1*S*,2*S*)-1-Acetoxy-8-benzyloxy-2-(*tert*-butyloxycarbonylamino)-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole-6-carboxaldehyde (30a) A solution of **29a** (67 mg, 0.16 mmol) and Ac_2O (0.3 ml) in pyridine (0.5 ml) was stirred at room temperature for 2 h. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. The extract was successively washed with saturated $CuSO_4$–H_2O, H_2O, saturated $NaHCO_3$–H_2O and H_2O, and worked up as usual. Purification by PTLC [hexane–EtOAc (3:2)] afforded **30a** (72 mg, 98%) as a colorless glass. HRMS Calcd for $C_{26}H_{28}N_2O_6$: 464.1946. Found: 464.1943. $[\alpha]_D^{23.5}$ −148° (c=1.31, $CHCl_3$). MS m/z: 464 (M^+, 29), 373 (4), 348 (6), 317 (39), 214 (21), 190 (7), 91 (100), 59 (9), 57 (44). IR ($CHCl_3$) cm^{-1}: 1746, 1714, 1682. ^{1}H-NMR δ: 1.50 (9H, s), 2.10 (3H, s), 3.90 (1H, dd, J=10, 7.5 Hz), 4.59 (1H, dd, J=10, 7 Hz), 4.94—5.33 (1H+NH, m), 5.24 (2H, s), 6.05 (1H, d, J=5 Hz), 6.77 (1H, s), 7.13 (1H, s), 7.27—7.60 (6H, m), 9.96 (1H, s).

(1*R*,2*S*)-1-Acetoxy-8-benzyloxy-2-(*tert*-butyloxycarbonylamino)-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole-6-carboxaldehyde (30b) Acetylation of **29b** (23 mg, 0.55 mmol) with Ac_2O (0.1 ml) in pyridine (0.3 ml) as above afforded **30b** (24 mg, 95%) as a colorless glass after purification by PTLC [hexane–EtOAc (2:1)]. HRMS Calcd for $C_{26}H_{28}N_2O_6$: 464.1946. Found: 464.1945. [a]$_D^{23.5}$ +100° (c=1.04, $CHCl_3$). MS m/z: 464 (M^+, 6), 390 (12), 299 (8), 256 (9), 214 (27), 91 (100), 59 (24), 57 (16), 43 (31). IR ($CHCl_3$) cm^{-1}: 1745, 1715, 1684. ^{1}H-NMR δ: 1.44 (9H, s), 2.13 (3H, s), 4.06 (1H, dd, J=10.5, 3 Hz), 4.53—4.97 (2H, m), 5.10—5.34 (1H, br s, NH), 5.23 (2H, s), 6.02 (1H, d, J=3 Hz), 6.70 (1H, s), 7.08 (1H, s), 7.28—7.59 (6H, m), 9.93 (1H, s).

(1*S*,2*S*)-1-Acetoxy-8-benzyloxy-2-(*tert*-butyloxycarbonylamino)-6-(1,3-dioxan-2-yl)-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole (31a) A CH_2Cl_2 solution (2 ml) of **30a** (18 mg, 0.039 mmol), 2-ethyl-2-methyl-1,3-dioxane (0.2 ml) and p-TsOH·H_2O (1 mg, 0.005 mmol) was stirred at 0 °C for 1.5 h. aturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2, and then worked up as usual. Purification by PTLC (CH_2Cl_2) afforded **31a** (17 mg, 84%) as colorless needles, mp 233—234.5 °C (MeOH). *Anal.* Calcd for $C_{29}H_{34}N_2O_7$: C, 66.65; H, 6.56; N, 5.36. Found: C, 66.43; H, 6.55; N, 5.28. HRMS Calcd for $C_{29}H_{34}N_2O_7$: 522.2364. Found: 522.2355. $[\alpha]_D^{23.5}$ −109° (c=1.15, $CHCl_3$). MS m/z: 522 (M^+, 24), 448 (10), 431 (14), 375 (35), 357 (20), 315 (9), 214 (9), 91 (100), 59 (32), 57 (36), 43 (43). IR ($CHCl_3$) cm^{-1}: 1736, 1695. ^{1}H-NMR δ: 1.47 (9H, s), 1.32—1.67 (1H, m), 2.04—2.53 (1H, m), 2.08 (3H, s), 3.67—4.62 (6H, m), 4.74—5.28 (1H+NH, m), 5.17 (2H, s), 5.56 (1H, s), 6.02 (1H, d, J=5 Hz), 6.63 (1H, s), 6.74 (1H, s), 7.06 (1H, s), 7.25—7.57 (5H, m).

(1*R*,2*S*)-1-Acetoxy-8-benzyloxy-2-(*tert*-butyloxycarbonylamino)-6-(1,3-dioxan-2-yl)-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole (31b) Similarly, treatment of **30b** (126 mg, 0.297 mmol) with 2-ethyl-2-methyl-1,3-dioxane (0.3 ml) and p-TsOH·H_2O (3 mg, 0.02 mmol) in CH_2Cl_2 (10 ml) at 0 °C for 1 h afforded, after purification by PTLC [hexane–EtOAc (5:3)], **31b** (116 mg, 82%) as a colorless glass and recovered **30b** (7 mg, 6%). HRMS Calcd for $C_{29}H_{34}N_2O_7$: 522.2364. Found: 522.2349. $[\alpha]_D^{23.5}$ +96.6° (c=0.784, $CHCl_3$). MS m/z: 522 (M^+, 20), 431 (11), 406 (25), 375 (20), 315 (19), 272 (14), 214 (10), 91 (100), 59 (23), 57 (42), 43 (45). IR ($CHCl_3$) cm^{-1}: 1740 (sh), 1716. ^{1}H-NMR δ: 1.44 (9H, s), 1.97—2.53 (1H, m), 2.07 (3H, s), 3.77—4.88 (8H, m), 5.09 (1H, br d, J=6 Hz, NH), 5.17 (2H, s), 5.54 (1H, s), 5.88 (1H, d, J=3 Hz), 6.57 (1H, s), 6.74 (1H, s), 7.05 (1H, s), 7.29—7.58 (5H, m).

(1*S*,2*S*)-1-Acetoxy-8-benzyloxy-2-(*tert*-butyloxycarbonylamino)-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole-6,9-dicarboxaldehyde (32a) A CH_2Cl_2 solution (3 ml) of DMF (0.1 ml, 1 mmol) and $(COCl)_2$ (40 μl, 0.57 mmol) was stirred at 0 °C for 10 min under an Ar atmosphere. A CH_2Cl_2 solution (2.5 ml) of **31a** (31 mg, 0.059 mmol) was added to this at 0 °C, and the mixture was stirred at room temperature for 45 min. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [hexane–EtOAc (1:1)] afforded **32a** (21 mg, 72%) as a colorless syrup, together with **37** (*vide infra*) (2 mg, 6%). HRMS Calcd for $C_{27}H_{28}N_2O_7$: 492.1895. Found: 492.1893. $[\alpha]_D^{24}$ −4.7° (c=1.4, $CHCl_3$). MS m/z: 492 (M^+, 4), 463 (2), 418 (3), 389 (3), 345 (4), 286 (7), 242 (4), 226 (4), 91 (100), 59 (15), 57 (19), 43 (25). IR ($CHCl_3$) cm^{-1}: 1754, 1712, 1692, 1655. ^{1}H-NMR δ: 1.47 (9H, s), 2.17 (3H, s), 3.95—4.31 (1H, m), 4.47—4.76 (1H, m), 4.90—5.20 (1H+NH, m), 5.29 (2H, s), 6.65 (1H, d, J=6 Hz), 7.29—7.57 (5H, m), 7.34 (1H, s), 7.50 (1H, s), 10.00 (1H, s), 10.46 (1H, s).

(1*R*,2*S*)-1-Acetoxy-8-benzyloxy-2-(*tert*-butyloxycarbonylamino)-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole-6,9-dicarboxaldehyde (32b) Similarly, **31b** (116 mg, 0.222 mmol) in CH_2Cl_2 (5 ml) was formylated with the reagent prepared from DMF (0.3 ml, 4 mmol) and $(COCl)_2$ (0.10 ml, 1.2 mmol) in CH_2Cl_2 (10 ml) at room temperature for 1 h to afford **32b** (89 mg, 81%) as a colorless glass after PTLC [hexane–EtOAc (5:3)]. HRMS Calcd for $C_{27}H_{28}N_2O_7$: 492.1895. Found: 492.1885. $[\alpha]_D^{24}$ +57.2° (c=0.732, $CHCl_3$). MS m/z: 492 (M^+, 2), 418 (2), 392 (3), 363 (3), 286 (4), 242 (9), 226 (3), 91 (100), 59 (12), 57 (9), 43 (24). IR ($CHCl_3$) cm^{-1}: 1746, 1715, 1696, 1662. ^{1}H-NMR δ: 1.47 (9H, s), 2.16 (3H, s), 4.07 (1H, dd, J=15, 9 Hz), 4.56—4.87 (2H, m), 5.20 (2H, s), 5.64 (1H, br d, J=6 Hz, NH), 6.52 (1H, d, J=4 Hz), 7.26 (1H, s), 7.30—7.50 (5H, m), 7.43 (1H, s), 9.91 (1H, s), 10.27 (1H, s).

(1*S*,2*S*)-8-Benzyloxy-2-(*tert*-butyloxycarbonylamino)-2,3-dihydro-1-hydroxy-1*H*-pyrrolo[1,2-*a*]indole-6,9-dicarboxaldehyde (33a) A mixture of **32a** (21 mg, 0.043 mmol) and K_2CO_3 (11 mg, 0.080 mmol) in MeOH (4 ml) was stirred at room temperature for 1 h. Saturated NH_4Cl–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [hexane–EtOAc (2:1)] afforded **33a** (19 mg, 99%) as a colorless glass. HRMS Calcd for $C_{25}H_{26}N_2O_6$: 450.1789. Found: 450.1784. $[\alpha]_D^{25}$ +195° (c=0.71, $CHCl_3$). MS m/z: 450 (M^+, 9), 394 (7), 347 (4), 303 (13), 285 (5), 91 (100), 59 (39), 57 (45). IR ($CHCl_3$) cm^{-1}: 1704 (sh), 1690, 1628. ^{1}H-NMR δ: 1.45 (9H, s), 4.42 (2H, d, J=3 Hz), 4.71—5.00 (1H, m), 5.29 (2H, s), 5.56 (1H, d, J=6 Hz), 5.70 (1H, br d, J=4 Hz, NH), 7.27—7.47 (5H, m), 7.36 (1H, s), 7.49 (1H, s), 10.00 (1H, s), 10.30 (1H, s).

(1*R*,2*S*)-8-Benzyloxy-2-(*tert*-butyloxycarbonylamino)-2,3-dihydro-1-hydroxy-1*H*-pyrrolo[1,2-*a*]indole-6,9-dicarboxaldehyde (33b) Similar treatment of **32b** (17 mg, 0.035 mmol) and K_2CO_3 (6 mg, 0.04 mmol) in MeOH (3 ml) afforded **33b** (14 mg, 90%) as a colorless glass after PTLC [hexane–EtOAc (2:1)]. HRMS Calcd for $C_{25}H_{26}N_2O_6$: 450.1789. Found: 450.1806. $[\alpha]_D^{24}$ −1.4° (c=0.52, $CHCl_3$). MS m/z: 450 (M^+, 1), 394 (6), 376 (3), 350 (2), 333 (2), 303 (3), 285 (3), 242 (4), 91 (100), 59 (15), 57 (13). IR ($CHCl_3$) cm^{-1}: 1712, 1692, 1653. ^{1}H-NMR δ: 1.47 (9H, s), 4.17 (1H, dd, J=9, 6 Hz), 4.40—4.86 (2H, m), 5.28 (2H, s), 5.35—5.61 (1H+NH, m), 7.28—7.56 (7H, m), 9.97 (1H, s), 10.29 (1H, s).

(1*S*,2*S*)-8-Benzyloxy-2-(*tert*-butyloxycarbonylamino)-1-chloro-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole-6,9-dicarboxaldehyde (34a) A mixture of a CH_2Cl_2 solution (3 ml) of **33a** (24 mg, 0.053 mmol) and $SOCl_2$ (0.1 ml, 1 mmol) was stirred at room temperature for 4 h. Saturated $NaHCO_3$–H_2O was added at 0 °C and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [hexane–EtOAc (2:1)] afforded **34a** (21 mg, 84%) as a colorless syrup. HRMS Calcd for $C_{25}H_{25}ClN_2O_5$: 470.1421, 468.1450. Found: 470.1399, 468.1451. $[\alpha]_D^{24}$ +179° (c=0.85, $CHCl_3$). MS m/z: 470, 468 (M^+; 2, 4), 441, 439 (1, 3), 379, 377 (1, 3), 321 (4), 286 (6), 226 (11), 91 (100), 57 (32). IR ($CHCl_3$) cm^{-1}: 1715, 1693, 1662. ^{1}H-NMR (400 MHz) δ: 1.51 (9H, s), 3.93 (1H, dd, J=10, 9 Hz), 4.61 (1H, br dd, J=10, 8 Hz), 5.11—5.23 (1H, m), 5.33 (2H, s), 5.45 (1H, br d, J=9 Hz, NH), 5.84 (1H, d, J=5.5 Hz), 7.37 (1H, s), 7.34—7.50 (5H, m), 7.52 (1H, s), 10.02 (1H, s), 10.49 (1H, s).

(1*R*,2*S*)-8-Benzyloxy-2-(*tert*-butyloxycarbonylamino)-1-chloro-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole-6,9-dicarboxaldehyde (34b) and (3a*S*,10b*S*)-9-Benzyloxy-2,3,3a,10b-tetrahydro-2-oxo-4*H*-oxazolo[5′,4′:3,4]-pyrrolo[1,2-*a*]indole-7,10-dicarboxaldehyde (35) Similarly, **33b** (21 mg, 0.047 mmol) was chlorinated with $SOCl_2$ (0.02 ml, 0.3 mmol) in CH_2Cl_2 (5 ml) for 1.5 h to furnish **34b** (7 mg, 32%) as a less polar material and **35** (9 mg, 52%) as a more polar material after PTLC twice [hexane–EtOAc (5:3) and CH_2Cl_2–MeOH (19:1)]. **34b**: Colorless glass, $[\alpha]_D^{21.5}$ −138° (c=0.493, $CHCl_3$). MS m/z: 376 (M^+−Cl−*tert*-Bu, 5), 347 (7), 285 (9), 91 (100). IR ($CHCl_3$) cm^{-1}: 1714, 1694, 1660. ^{1}H-NMR (400 MHz) δ: 1.44 (9H, s), 4.22 (1H, br d, J=12 Hz), 4.66 (1H, dd, J=12, 5.5 Hz), 4.98—5.06 (1H, m), 5.25 (1H, d, J=11 Hz), 5.29 (1H, d, J=11 Hz), 5.24—5.34 (1H, br s, NH), 5.54 (1H, br s), 7.31 (1H, d, J=0.5 Hz), 7.34—7.45 (5H, m), 7.49 (1H, br s), 9.97 (1H, s), 10.38 (1H, s). **35**: Pale yellow needles, mp 280 °C (dec.) (CH_2Cl_2–MeOH). *Anal.* Calcd for $C_{21}H_{16}N_2O_5 \cdot 1/2H_2O$: C, 65.45; H, 4.45; N, 7.27. Found: C, 64.95; H, 4.40; N, 7.30. HRMS Calcd for $C_{21}H_{16}N_2O_5$: 376.1058. Found: 376.1043. MS m/z: 376 (M^+, 5), 347 (9), 285 (8), 91 (100), 65 (9). IR (KBr) cm^{-1}: 1765, 1738, 1693, 1655. ^{1}H-NMR [$CDCl_3$–CD_3OD (5:1)] δ: 4.23—4.60 (2H, m), 5.07—5.36 (1H, m), 5.29 (2H, s), 6.26 (1H, d, J=8 Hz), 7.26—7.53 (5H, m), 7.33 (1H, s), 7.55 (1H, s), 9.97 (1H, s), 10.41 (1H, s).

(1a*S*,8b*S*)-7-Benzyloxy-1-*tert*-butyloxycarbonyl-1,1a,2,8b-tetrahydroazirino[2′,3′:3,4]pyrrolo[1,2-*a*]indole-5,8-dicarboxaldehyde (8) i)

Prepared from **34a**: A mixture of **34a** (20 mg, 0.043 mmol) and *tert*-BuOK (8 mg, 0.07 mmol) in THF (2 ml) was stirred at room temperature for 30 min under an Ar atmosphere. Saturated NH_4Cl–H_2O was added and the whole was extracted with CH_2Cl_2. Work-up as usual and purification by PTLC [hexane–EtOAc (2 : 1)] afforded **8** (8 mg, 43%) as a colorless glass. HRMS Calcd for $C_{25}H_{24}N_2O_5$: 432.1684. Found: 432.1687. $[\alpha]_D^{23.5}$ +114° (c=0.42, $CHCl_3$). MS m/z: 432 (M^+, 3), 376 (3), 359 (3), 347 (3), 332 (12), 285 (5), 241 (17), 91 (100), 57 (67). IR ($CHCl_3$) cm^{-1}: 1714, 1690, 1658. ^{1}H-NMR (400 MHz) δ: 1.11 (9H, s), 4.02 (1H, dd, J=4, 4 Hz), 4.22 (1H, dd, J=12, 4 Hz), 4.46 (1H, d, J=4 Hz), 4,74 (1H, d, J=12 Hz), 5.32 (1H, d, J=10 Hz), 5.35 (1H, d, J=10 Hz), 7.33 (1H, br s), 7.34—7.50 (6H, m), 9.98 (1H, s), 10.50 (1H, s).

ii) Prepared from **34b**: Analogous treatment of **34b** (14 mg, 0.030 mmol) with *tert*-BuOK (4 mg, 0.04 mmol) in THF (2 ml) for 20 min afforded **8** (4 mg, 31%) after PTLC twice [hexane–EtOAc (5 : 3) and CH_2Cl_2–MeOH (19 : 1)]. A by-product, **35** (2 mg, 18%), was produced as pale yellow needles, mp 280 °C (dec.).

(1*S*,2*S*)-2-(*tert*-Butyloxycarbonylamino)-2,3-dihydo-6,9-dimethyl-1*H*-pyrrolo[1,2-*a*]indole-1,8-diol (36) An MeOH solution (8 ml) of **33a** (5 mg, 0.01 mmol) was hydrogenated over 20% $Pd(OH)_2$–C (4 mg) at room temperature for 1 h. The catalyst was filtered off and the filtrate was evaporated *in vacuo*. Purification by PTLC [hexane–EtOAc (2 : 1)] gave **36** (2 mg, 54%) as a colorless glass. HRMS Calcd for $C_{18}H_{24}N_2O_4$: 332.1735. Found: 332.1732. MS m/z: 332 (M^+, 63), 276 (52), 258 (39), 241 (18), 215 (58), 189 (100), 160 (25), 59 (59), 57 (93). IR ($CHCl_3$) cm^{-1}: 1714. ^{1}H-NMR δ: 1.50 (9H, s), 2.35 (3H, s), 2.51 (3H, s), 3.66 (1H, dd, J=10, 8 Hz), 4.35 (1H, dd, J=10, 7.5 Hz), 4.55—4.82 (1H, m), 5.07 (1H, d, J=6 Hz), 5.36—5.65 (1H, br s, NH), 6.21 (1H, s), 6.56 (1H, s).

(1*S*,2*S*)-1-Acetoxy-8-benzyloxy-2-(*tert*-butyloxycarbonylamino)-6-(1,3-dioxan-2-yl)-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole-9-carboxaldehyde (37) In the same manner as described for the preparation of **31a**, a CH_2Cl_2 solution (2 ml) of **32a** (5 mg, 0.01 mmol), 2-ethyl-2-methyl-1,3-dioxane (0.2 ml) and *p*-TsOH · H_2O (1 mg, 0.005 mmol) was stirred at 0 °C for 45 min to afford **37** (3.5 mg, 63%) as a colorless glass after purification by PTLC (CH_2Cl_2). HRMS Calcd for $C_{30}H_{34}N_2O_8$: 550.2313. Found: 550.2314. MS m/z: 550 (M^+, 8), 476 (8), 403 (8), 385 (8), 343 (11), 300 (5), 284 (8), 91 (100), 59 (37), 57 (22), 43 (39). IR ($CHCl_3$) cm^{-1}: 1756, 1716, 1660. ^{1}H-NMR δ: 1.46 (9H, s), 2.13 (3H, s), 3.83—4.66 (6H, m), 4.82—5.08 (1H + NH, m), 5.23 (2H, s), 5.57 (1H, s), 6.63 (1H, d, J=6 Hz), 6.96 (1H, s), 7.14 (1H, s), 7.28—7.55 (5H, m), 10.39 (1H, s).

(1*S*,2*S*)-8-Benzyloxy-2-(*tert*-butyloxycarbonylamino)-6-(1,3-dioxan-2-yl)-2,3-dihydro-1-hydroxy-1*H*-pyrrolo[1,2-*a*]indole-9-carboxaldehyde (38) i) From **33a**: Similarly, **38** (9 mg, 80%) was obtained as a colorless glass by the reaction of **33a** (10 mg, 0.022 mmol), 2-ethyl-2-methyl-1,3-dioxane (0.1 ml) and *p*-TsOH · H_2O (1 mg, 0.005 mmol) in CH_2Cl_2 (2 ml), followed by purification by PTLC [CH_2Cl_2–MeOH (99 : 1)]. HRMS Calcd for $C_{28}H_{32}N_2O_7$: 508.2208. Found: 508.2198. $[\alpha]_D^{24}$ +215° (c=0.645, $CHCl_3$). MS m/z: 508 (M^+, 11), 434 (6), 405 (5), 361 (23), 343 (13), 317 (4), 259 (5), 188 (3), 91 (100), 59 (64), 57 (28). IR ($CHCl_3$) cm^{-1}: 1706, 1626. ^{1}H-NMR δ: 1.42 (9H, s), 1.33—1.59 (1H, m), 1.97—2.57 (1H, m), 3.83—4.53 (6H, m), 4.65—4.98 (1H, m), 5.24 (2H, s), 5.52 (1H, d, J=6 Hz), 5.57 (1H, s), 5.60—5.73 (1H, br s, NH), 5.73—5.90 (1H, br s, OH), 7.00 (1H, s), 7.13 (1H, s), 7.28—7.57 (5H, m), 10.20 (1H, s).

ii) From **37**: Methanolysis of **37** (5 mg, 0.009 mmol) was conducted as described for the preparation of **33a** using K_2CO_3 (4 mg, 0.03 mmol) in MeOH (2 ml) to afford **38** (3 mg, 65%) as a colorless glass.

(1*S*,2*S*)-2-(*tert*-Butyloxycarbonylamino)-6-(1,3-dioxan-2-yl)-2,3-dihydo-1,8-dihydroxy-1*H*-pyrrolo[1,2-*a*]indole-9-carboxaldehyde (39) An EtOAc solution (8 ml) of **38** (12 mg, 0.024 mmol) was hydrogenated over 20% $Pd(OH)_2$–C (2 mg) at room temperature for 7 h. The catalyst was filtered off and the filtrate was evaporated *in vacuo*. Purification by PTLC [hexane–EtOAc (3 : 2)] gave **39** (9 mg, 91%) as a colorless glass. HRMS Calcd for $C_{21}H_{26}N_2O_7$: 418.1738. Found: 418.1724. $[\alpha]_D^{21.5}$ +20.9° (c=0.51, $CHCl_3$). MS m/z: 418 (M^+, 28), 362 (19), 344 (23), 276 (21), 189 (15), 87 (65), 59 (89), 57 (63), 41 (100). IR ($CHCl_3$) cm^{-1}: 1713, 1622. ^{1}H-NMR δ: 1.44 (9H, s), 1.83—2.49 (1H, m), 3.63—4.44 (6H, m), 4.49—4.94 (1H, m), 5.20—5.69 (1H + NH, m), 5.42 (1H, s), 6.68 (1H, s), 6.75 (1H, s), 9.45 (1H, s), 10.47 (1H, s, OH).

(1*S*,2*S*)-1,8-Diacetoxy-9-acetoxymethyl-2-(*tert*-butyloxycarbonylamino)-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole-6-carboxaldehyde (9a) A solution of **39** (10 mg, 0.024 mmol) and $NaBH_4$ (6 mg, 0.2 mmol) in THF (1 ml) and MeOH (1 ml) was stirred at 0 °C for 45 min under an Ar atmosphere. Saturated NH_4Cl–H_2O was added at 0 °C and the whole was extracted with 10% MeOH-containing CH_2Cl_2. The extract was worked up as usual to give the residue (10 mg). This was acetylated as described for the preparation of **30a** using Ac_2O (0.1 ml) and pyridine (0.3 ml) to afford the crude triacetate (11 mg). A solution of this and AcOH (1 ml) in DME (1 ml) and H_2O (1 ml) was stirred at room temperature for 1.5 h. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [hexane–EtOAc (2 : 1)] furnished **9a** (7 mg, 60%) as a colorless syrup. HRMS Calcd for $C_{24}H_{28}N_2O_9$: 488.1793. Found: 488.1794. $[\alpha]_D^{21.5}$ −136° (c=0.567, $CHCl_3$). MS m/z: 488 (M^+, 9), 386 (19), 355 (7), 330 (13), 270 (94), 228 (13), 57 (54), 43 (100). IR ($CHCl_3$) cm^{-1}: 1748, 1716, 1695. ^{1}H-NMR (400 HHz) δ: 1.50 (9H, s), 1.99 (3H, s), 2.14 (3H, s), 2.40 (3H, s), 3.96 (1H, dd, J=10, 8 Hz), 4.59 (1H, dd, J=10, 10 Hz), 5.00—5.11 (1H, m), 5.11—5.19 (1H, br s, NH), 5.26 (1H, d, J=12 Hz), 5.44 (1H, d, J=12 Hz), 6.32 (1H, d, J=5 Hz), 7.40 (1H, d, J=1 Hz), 7.72 (1H, br s), 10.01 (1H, s).

(1*S*,2*S*)-1,8-Diacetoxy-2-(*tert*-butyloxycarbonylamino)-6-(1,3-dioxan-2-yl)-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole-9-carboxaldehyde (40) As described for the acetylation of **30a**, **39** (10 mg, 0.024 mmol) was treated with Ac_2O (0.1 ml) and pyridine (0.3 ml) to give **40** (9 mg, 75%) after purification by PTLC [hexane–EtOAc (1 : 1)]. HRMS Calcd for $C_{25}H_{30}N_2O_9$: 502.1949. Found: 502.1949. MS m/z: 502 (M^+, 7), 460 (31), 404 (13), 342 (12), 284 (9), 87 (37), 57 (44), 43 (100). IR ($CHCl_3$) cm^{-1}: 1756, 1716, 1674. ^{1}H-NMR δ: 1.47 (9H, s), 2.11 (3H, s), 2.45 (3H, s), 3.60—4.59 (6H, m), 4.84—5.30 (1H + NH, m), 5.59 (1H, s), 6.64 (1H, d, J=6 Hz), 7.13 (1H, s), 7.38 (1H, s), 10.00 (1H, s).

(1*S*,2*S*)-1,8-Diacetoxy-2-(*tert*-butyloxycarbonylamino)-6-(1,3-dioxan-2-yl)-9-(ethylaminocarbonyloxymethyl)-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]-indole (41) As described for the reduction of **39**, a mixture of **40** (8 mg, 0.02 mmol) in THF (2 ml) and MeOH (1 ml) was treated with $NaBH_4$ (3 mg, 0.08 mmol) at 0 °C to give the residue (8 mg). A solution of this, ethyl isocyanate (20 μl, 0.25 mmol) and Et_3N (0.05 ml, 0.04 mmol) in CH_2Cl_2 (2 ml) was stirred at room temperature for 14 h. The solvent was evaporated off *in vacuo* and the residue was purified by PTLC [hexane–EtOAc (1 : 1)] to afford **41** (6 mg, 66%) as a colorless glass. HRMS Calcd for $C_{28}H_{37}N_3O_{10}$: 575.2477. Found: 575.2472. MS m/z: 575 (M^+, 2), 516 (1), 444 (10), 328 (14), 87 (8), 71 (33), 60 (46), 45 (77), 43 (100). IR ($CHCl_3$) cm^{-1}: 1748, 1720 (sh). ^{1}H-NMR δ: 1.21 (3H, t, J=7.5 Hz), 1.48 (9H, s), 1.99 (3H, s), 2.09 (3H, s), 3.12—3.50 (2H, m), 3.67—4.60 (6H, m), 4.74—5.20 (1H + NH, m), 5.36 (2H, s), 5.57 (1H, s), 6.23 (1H, d, J=6 Hz), 7.18 (1H, s), 7.27 (1H, s).

(1*S*,2*S*)-1,8-Diacetoxy-2-(*tert*-butyloxycarbonylamino)-9-(ethylamino-carbonyloxymethyl)-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole-6-carboxaldehyde (9b) As described for the formation of **9a**, **41** (5 mg, 0.009 mmol) was treated with AcOH (1 ml) in DME (1 ml) and H_2O (1 ml) at room temperature for 2.5 h to give **9b** (4 mg, 89%) as a colorless glass after PTLC [hexane–EtOAc (1 : 1)]. HRMS Calcd for $C_{25}H_{31}N_3O_9$: 517.2058. Found: 517.2042. MS m/z: 517 (M^+, 1), 446 (2), 386 (15), 330 (6), 270 (49), 71 (37), 60 (28), 56 (66), 45 (55), 43 (100). IR ($CHCl_3$) cm^{-1}: 1750, 1715, 1694. ^{1}H-NMR δ: 1.24 (3H, t, J=7.5 Hz), 1.50 (9H, s), 2.00 (3H, s), 2.11 (3H, s), 3.20—3.52 (2H, m), 3.73—4.07 (1H, m), 4.38—4.70 (1H, m), 4.87—5.22 (2H, m), 5.22—5.57 (1H, m), 5.37 (2H, s), 6.27 (1H, d, J=5 Hz), 7.57 (1H, s), 7.64 (1H, s), 10.01 (1H, s).

(3a*S*,10b*S*)-9-Benzyloxy-2,3,3a,10b-tetrahydro-2-oxo-4*H*-oxazolo-[5′,4′ : 3,4]pyrrolo[1,2-*a*]indole-7-carboxaldehyde (42) A CH_2Cl_2 solution (4 ml) of **30a** (21 mg, 0.045 mmol) and CF_3COOH (0.4 ml) was stirred at room temperature for 1.5 h. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [CH_2Cl_2–MeOH (19 : 1)] afforded **42** (10 mg, 63%) as pale yellow needles, mp 221—223 °C (CH_2Cl_2–MeOH). *Anal.* Calcd for $C_{20}H_{16}N_2O_4 \cdot 1/2H_2O$: C, 67.22; H, 4.80; N, 7.84. Found: C, 67.18; H, 5.04; N, 7.76. HRMS Calcd for $C_{20}H_{16}N_2O_4$: 348.1109. Found: 348.1104. MS m/z: 348 (M^+, 14), 319 (1), 257 (14), 213 (3), 91 (100), 65 (8). IR ($CHCl_3$) cm^{-1}: 1750, 1728, 1678. ^{1}H-NMR δ: 4.20—4.52 (2H, m), 4.99—5.35 (1H, m), 5.26 (2H, s), 6.02 (1H, d, J=8 Hz), 6.84 (1H, s), 7.16 (1H, s), 7.27—7.58 (6H, m), 9.96 (1H, s).

(3a*S*,10b*S*)-9-Benzyloxy-2,3,3a,10b-tetrahydro-3-[(4-methylphenyl)-sulfonyl]-2-oxo-4*H*-oxazolo[5′,4′ : 3,4]pyrrolo[1,2-*a*]indole-7-carboxaldehyde (43) NaH (60%, 2 mg, 0.05 mmol) was added to a solution of **42** (7 mg, 0.02 mmol) in THF (2 ml) and DMF (0.2 ml) and the solution was stirred at room temperature for 5 min. *p*-TsCl (6 mg, 0.03 mmol) was added at 0 °C, and the mixture was further stirred at the same temperature for 10 min. Saturated NH_4Cl–H_2O was added and the

whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [hexane–EtOAc (2:1)] afforded **43** (9 mg, 89%) as a colorless glass. HRMS Calcd for $C_{27}H_{22}N_2O_6S$: 502.1197. Found: 502.1204. MS *m/z*: 502 (M^+, 14), 411 (14), 212 (3), 91 (100). IR ($CHCl_3$) cm^{-1}: 1790, 1685. ^{1}H-NMR δ: 2.43 (3H, s), 4.64 (2H, d, J=4.5 Hz), 5.23 (2H, s), 5.40—5.66 (1H, m), 5.90 (1H, d, J=8 Hz), 6.82 (1H, s), 7.16 (1H, s), 7.28—7.57 (8H, m), 7.99 (2H, $\underline{A}_2B_2$, J=9 Hz), 9.98 (1H, s).

(3a*S*,10b*S*)-9-Benzyloxy-7-(1,3-dioxan-2-yl)-2,3,3a,10b-tetrahydro-2-oxo-4*H*-oxazolo[5′,4′:3,4]pyrrolo[1,2-*a*]indole (44) In a similar manner to that described for preparation of **31a**, **42** (8 mg, 0.02 mmol) was treated with 2-ethyl-2-methyl-1,3-dioxane (0.1 ml) and *p*-TsOH·H_2O (1 mg, 0.005 mmol) in CH_2Cl_2 (2 ml) at 0 °C for 1 h to give **44** (8 mg, 86%) as a colorless glass after PTLC [CH_2Cl_2–MeOH (19:1)]. HRMS Calcd for $C_{23}H_{22}N_2O_5$: 406.1527. Found: 406.1528. MS *m/z*: 406 (M^+, 35), 362 (6), 315 (60), 91 (100), 87 (22). IR ($CHCl_3$) cm^{-1}: 1760. ^{1}H-NMR δ: 1.30—1.57 (1H, m), 1.97—2.57 (1H, m), 3.79—4.43 (6H, m), 4.80—5.07 (1H, m), 5.20 (2H, s), 5.54 (1H, s), 5.90 (1H, d, J=8 Hz), 6.41 (1H, br s, NH), 6.70 (1H, s), 6.76 (1H, s), 7.03 (1H, s), 7.23—7.58 (5H, m).

(3a*S*,10b*S*)-9-Benzyloxy-10-(dimethylamino)methyl-7-(1,3-dioxan-2-yl)-2,3,3a,10b-tetrahydro-2-oxo-4*H*-oxazolo[5′,4′:3,4]pyrrolo[1,2-*a*]-indole (45) A CH_2Cl_2 solution (2 ml) of **44** (7 mg, 0.02 mmol) and *N*,*N*-dimethylmethyleneammonium iodide (21 mg, 0.11 mmol) was stirred at room temperature for 4 h under an Ar atmosphere. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [CH_2Cl_2–MeOH (19:1)] afforded **45** (6 mg, 75%) as a colorless glass. HRMS Calcd for $C_{26}H_{29}N_3O_5$: 463.2105. Found: 463.2123. MS *m/z*: 463 (M^+, 19), 418 (75), 372 (13), 329 (48), 271 (11), 91 (69), 87 (100). IR ($CHCl_3$) cm^{-1}: 1765. ^{1}H-NMR δ: 1.32—1.60 (1H, m), 2.07—2.59 (1H, m), 2.37 (6H, s), 3.27—3.93 (1H, br s, NH), 3.80—4.45 (8H, m), 4.75—5.04 (1H, m), 5.15 (2H, s), 5.57 (1H, s), 6.57 (1H, d, J=7.5 Hz), 6.86 (1H, s), 7.07 (1H, s), 7.27—7.58 (5H, m).

(3a*S*,10b*S*)-9-Benzyloxy-7-(1,3-dioxan-2-yl)-2,3,3a,10b-tetrahydro-10-(methoxy)methyl-2-oxo-4*H*-oxazolo[5′,4′:3,4]pyrrolo[1,2-*a*]indole (46) An MeOH solution (1 ml) of **45** (3 mg, 0.006 mmol) and MeI (0.15 ml, 6.3 mmol) was stirred at room temperature for 30 min under an Ar atmosphere. The solvent was evaporated *in vacuo*, and the residue was dissolved in MeOH (1 ml) containing NaOMe (6 mg, 0.1 mmol). The mixture was refluxed for 3 h and then allowed to cool. Saturated NaCl–H_2O was added and the whole was extracted with 10% MeOH-containing CH_2Cl_2. Usual work-up and purification by PTLC [3% MeOH–CH_2Cl_2] afforded **46** (1.5 mg, 51%) as a colorless glass. HRMS Calcd for $C_{25}H_{26}N_2O_6$: 450.1789. Found: 450.1792. MS *m/z*: 450 (M^+, 23), 420 (4), 392 (8), 359 (67), 328 (30), 301 (17), 270 (38), 91 (100), 87 (24). IR ($CHCl_3$) cm^{-1}: 1760. ^{1}H-NMR δ: 3.31 (3H, s), 3.81—4.40 (7H, m), 4.80 (2H, s), 5.16 (2H, s), 5.54 (1H, s), 6.08 (1H, d, J=8 Hz), 6.76 (1H, s), 7.01 (1H, s), 7.22—7.67 (5H, m).

(1*S*,2*S*)-8-Benzyloxy-2,3-dihydro-1-hydroxy-2-[(4-methylphenyl)-sulfonyl]amino-1*H*-pyrrolo[1,2-*a*]indole-6-carboxaldehyde (47) A mixture of **43** (8 mg, 0.02 mmol) and K_2CO_3 (14 mg, 0.10 mmol) in CH_2Cl_2 (1 ml) and MeOH (1 ml) was stirred at room temperature for 50 min. The same work-up as in the case of **33a** and PTLC [hexane–EtOAc (2:1)] gave **47** (7 mg, 92%) as a colorless glass. HRMS Calcd for $C_{26}H_{24}N_2O_5S$: 476.1404. Found: 476.1403. MS *m/z*: 476 (M^+, 16), 385 (12), 230 (7), 213 (9), 155 (7), 91 (100), 65 (13). IR ($CHCl_3$) cm^{-1}: 1678. ^{1}H-NMR δ: 2.43 (3H, s), 3.70—4.00 (1H, m), 4.13—4.59 (2H, m), 4.83 (1H, d, J=5 Hz), 5.17 (2H, s), 5.71—6.03 (1H, br s, NH), 6.60 (1H, s), 7.02 (1H, s), 7.18 (1H, s), 7.23—7.57 (7H, m), 7.82 (2H, $\underline{A}_2B_2$, J=8 Hz), 9.77 (1H, s).

(1*S*,2*S*)-1-Acetoxy-2-acetylamino-8-benzyloxy-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole-6,9-dicarboxaldehyde (48) CF_3COOH (0.2 ml, 2.6 mmol) was added to a CH_2Cl_2 solution (2 ml) of **32a** (10 mg, 0.020 mmol) at 0 °C under an Ar atmosphere, and the mixture was stirred at room temperature for 1.5 h. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2, and then worked up as usual to leave the residue (8 mg). This was acetylated with Ac_2O (0.1 ml) and pyridine (0.3 ml) and worked up as in the case of **30a**. Purification by PTLC [CH_2Cl_2–MeOH (99:1)] gave **48** (6 mg, 68%) as a colorless glass. HRMS Calcd for $C_{24}H_{22}N_2O_6$: 434.1476. Found: 434.1477. MS *m/z*: 434 (M^+, 6), 405 (4), 344 (4), 343 (2), 284 (7), 242 (12), 91 (100), 43 (49). IR ($CHCl_3$) cm^{-1}: 1760, 1695, 1666. ^{1}H-NMR δ: 2.03 (3H, s), 2.17 (3H, s), 4.10 (1H, dd, J=11, 6 Hz), 4.65 (1H, dd, J=11, 7.5 Hz), 5.08—5.43 (1H, m), 5.27 (2H, s), 6.07 (1H, br d, J=6 Hz, NH), 6.67 (1H, d, J=6 Hz), 7.29—7.57 (5H, m), 7.33 (1H, s), 7.48 (1H, s), 9.99 (1H, s), 10.44 (1H, s).

(1*S*,2*S*)-1-Acetoxy-8-benzyloxy-2,3-dihydro-2-(trifluoroacetyl)amino-1*H*-pyrrolo[1,2-*a*]indole-6,9-dicarboxaldehyde (49) A CH_2Cl_2 solution (3 ml) of **32a** (10 mg, 0.020 mmol), CF_3COOH (0.3 ml, 4 mmol) and Ac_2O (0.1 ml, 1 mmol) was stirred at room temperature for 3 h. Saturated $NaHCO_3$–H_2O was added at 0 °C and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [hexane–EtOAc (3:2)] afforded **49** (5 mg, 50%) as a colorless glass. HRMS Calcd for $C_{24}H_{19}F_3N_2O_6$: 488.1194. Found: 488.1195. MS *m/z*: 488 (M^+, 4), 459 (3), 338 (4), 226 (3), 91 (100), 43 (17). IR ($CHCl_3$) cm^{-1}: 1772, 1740, 1695, 1668. ^{1}H-NMR δ: 2.17 (3H, s), 4.26 (1H, dd, J=12, 6 Hz), 4.69 (1H, dd, J=12, 7.5 Hz), 5.10—5.48 (1H, m), 5.23 (2H, s), 6.70 (1H, d, J=7 Hz), 7.03—7.20 (1H, br s, NH), 7.30 (1H, s), 7.33—7.47 (5H, m), 7.50 (1H, s), 9.97 (1H, s), 10.37 (1H, s).

(1*S*,2*S*)-8-Benzyloxy-2,3-dihydro-1-hydroxy-2-(trifluoroacetyl)amino-1*H*-pyrrolo[1,2-*a*]indole-6,9-dicarboxaldehyde (50) In the same manner as described for the preparation of **33a**, **49** (4 mg, 0.008 mmol) in MeOH (3 ml) was treated with K_2CO_3 (20 mg, 0.14 mmol) at room temperature for 30 min to afford **50** (3 mg, 82%) as a colorless glass after PTLC [hexane–EtOAc (5:3)]. HRMS Calcd for $C_{22}H_{17}F_3N_2O_5$: 446.1088. Found: 446.1082. MS *m/z*: 446 (M^+, 8), 417 (2), 355 (4), 91 (100), 65 (9). IR ($CHCl_3$) cm^{-1}: 1732, 1696, 1636. ^{1}H-NMR δ: 4.34—4.73 (2H, m), 4.99—5.25 (1H, m), 5.30 (2H, s), 5.69 (1H, d, J=6.5 Hz), 7.30—7.54 (6H, m), 7.49 (1H, s), 7.49—7.71 (1H, br s, NH), 9.98 (1H, s), 10.31 (1H, s).

(1*S*,2*S*)-8-Benzyloxy-1-chloro-2,3-dihydro-2-(trifluoroacetyl)amino-1*H*-pyrrolo[1,2-*a*]indole-6,9-dicarboxaldehyde (51) In the same manner as described for the preparation of **34a**, **50** (5 mg, 0.01 mmol) was chlorinated with $SOCl_2$ (0.2 ml) in CH_2Cl_2 (2 ml) at room temperature for 6 h to afford **51** (3 mg, 58%) as a colorless glass after PTLC [hexane–EtOAc (5:3)]. HRMS Calcd for $C_{22}H_{16}ClF_3N_2O_4$: 466.0720, 464.0750. Found: 466.0699, 464.0767. MS *m/z*: 466, 464 (M^+; 1, 2), 437, 435 (1, 2), 428 (2), 401, 399 (1, 1), 375, 373 (1, 1), 337 (2), 226 (4), 91 (100), 65 (7). IR ($CHCl_3$) cm^{-1}: 1738, 1697, 1668. ^{1}H-NMR δ: 4.06 (1H, dd, J=10.5, 9 Hz), 4.75 (1H, dd, J=10.5, 7.5 Hz), 5.23—5.53 (1H, m), 5.30 (2H, s), 5.90 (1H, d, J=6 Hz), 7.31—7.57 (5H, m), 7.36 (1H, s), 7.50 (1H, s), 10.00 (1H, s), 10.47 (1H, s).

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References

1) Part 12: M. Sakagami, H. Muratake, M. Natsume, *Chem. Pharm. Bull.*, **42**, 1393 (1994).
2) I. Uchida, S. Takase, H. Kayakiri, S. Kiyoto, M. Hashimoto, T. Tada, S. Koda, Y. Morimoto, *J. Am. Chem. Soc.*, **109**, 4108 (1987).
3) H. Terano, S. Takase, J. Hosoda, M. Kohsaka, *J. Antibiot.*, **42**, 145 (1989).
4) T. Fukuyama, S. Goto, *Tetrahedron Lett.*, **30**, 6491 (1989).
5) *a*) J. Woo, S. Th. Sigurdsson, P. B. Hopkins, *J. Am. Chem. Soc.*, **115**, 1199 (1993); *b*) R. M. Williams, S. R. Rajski, *Tetrahedron Lett.*, **34**, 7023 (1993).
6) H. Huang, T. K. Pratum, P. B. Hopkins, *J. Am. Chem. Soc.*, **116**, 2703 (1994).
7) M. Fuji, H. Muratake, M. Natsume, *Chem. Pharm. Bull.*, **40**, 2344 (1992).
8) I. Utsunomiya, M. Fuji, T. Sato, M. Natsume, *Chem. Pharm. Bull.*, **41**, 854 (1993).
9) M. Fuji, H. Muratake, M. Natsume, *Chem. Pharm. Bull.*, **40**, 2338 (1992).
10) J. Rokach, P. Hamel, M. Kakushima, G. M. Smith, *Tetrahedron Lett.*, **22**, 4901 (1981).
11) I. Belsky, *J. Chem. Soc., Chem. Commun.*, **1977**, 237.
12) P. Garner, J. M. Park, *J. Org. Chem.*, **52**, 2361 (1987).
13) A. P. Kozikowski, H. Ishida, *Heterocycles*, **14**, 55 (1980).