Preparation of Alkyl-Substituted Indoles in the Benzene Portion. Part 15.[1] Asymmetric Synthesis of (+)-Duocarmycin SA Using Novel Procedure for Preparation of Hydroxyindoles

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An asymmetric total synthesis of natural (+)-duocarmycin SA (1) starting from L-malic acid (7) was achieved as shown in Chart 5, establishing firmly the absolute configuration of 1. In order to find suitable reaction conditions for the key step, *i.e.*, the formation of an alkoxyindole derivative, model compounds 9 and 40 were synthesized and two acetalization conditions using i) 2-ethyl-2-methyl-1,3-dioxane and boron trifluoride etherate, and ii) 1,3-bis(trimethylsilyloxy)propane and trimethylsilyl triflate were found to be effective. The former conditions were successfully applied to the total synthesis and 49b was prepared from 48 in 54% yield. Further elaborations including i) Curtius rearrangement of 53b to 56, and ii) cleavage of the primary benzyloxy group in the presence of the secondary one in its close vicinity (56→57) led to the relay compound 62, whose conversion to 1 has already been accomplished.

Key words asymmetric total synthesis; duocarmycin SA; potent antitumor substance; alkoxyindole formation reaction; absolute configuration establishment

Duocarmycin SA (**1**), isolated from *Streptomyces* species found in soil collected at Kyoto in 1990, is an exceptionally potent antitumor antibiotic,[2] and exerts its biological effects through reversible, sequence-selective alkylation of AT-rich regions of DNA.[3] The chemical structure of **1** was elucidated by spectroscopic means[4] and later confirmed by two total syntheses[5,6] (Chart 1). However, the absolute configuration of its asymmetric centers remained undetermined, and has been assumed to be as shown by analogy with the absolute structures of CC-1065[7] and pyrindamycin A[8] (=duocarmycin C_2),[9] which were established by X-ray crystallographic analyses. To confirm this, we have executed an asymmetric total synthesis of **1** starting from L-malic acid, and unambiguously defined the absolute configuration of duocarmycin SA (**1**).[10] Here we report our studies relating to this subject in detail.

Synthetic Plan Some time ago, we reported a novel preparative procedure for obtaining 4-, 5-, 6-, and 7-alkoxyindoles starting from *N*-arylsulfonylpyrrole derivatives.[11] However, the 7-alkoxyindole synthesis met difficulties due to the vicinity of the reaction center to the protecting group, *N*-arylsulfonyl, because facile acetalization of the ketone group adjacent to the pyrrole group was essential to the hydroxyindole formation reaction. Thus, an acid-catalyzed cyclization reaction of **2** in the presence of ethylene glycol afforded **3** in a poor yield of 31%. However, if a pyrrole derivative **4** is selected as a key compound for the synthesis of **1**, the methoxycarbonyl group (E) not only satisfies a requirement for the structure of **1**, but also substitutes for the above arylsulfonyl group of **2**→**3**, stabilizing the pyrrole nucleus. The remoteness of the E group from the ketone function has the advantage that the desired 7-alkoxyindole synthesis should proceed readily without steric hindrance.

To test these presumptions, a simple model compound **13** was synthesized from methyl 5-formyl-2-pyrrolecarboxylate[12] (**11**) and methyl vinyl ketone using **12** according to the literature procedure,[13] and **13** was subjected to our previous alkoxyindole formation conditions, *i.e.*, refluxing of a 1,2-dichloroethane solution of **13** with 1,3-propanediol in the presence of sulfuric acid.[11] The expected indole **14** was obtained in 81% yield, demonstrating that compound **4** is in fact a suitable substrate for conversion to the 7-alkoxyindole derivative **5**.

In the structure of **4**, the second ketone group must be placed in a 1,4-relationship to the first one for the indole synthesis. Therefore an asymmetric carbon side chain with a carbonyl function at the terminal is necessary, and

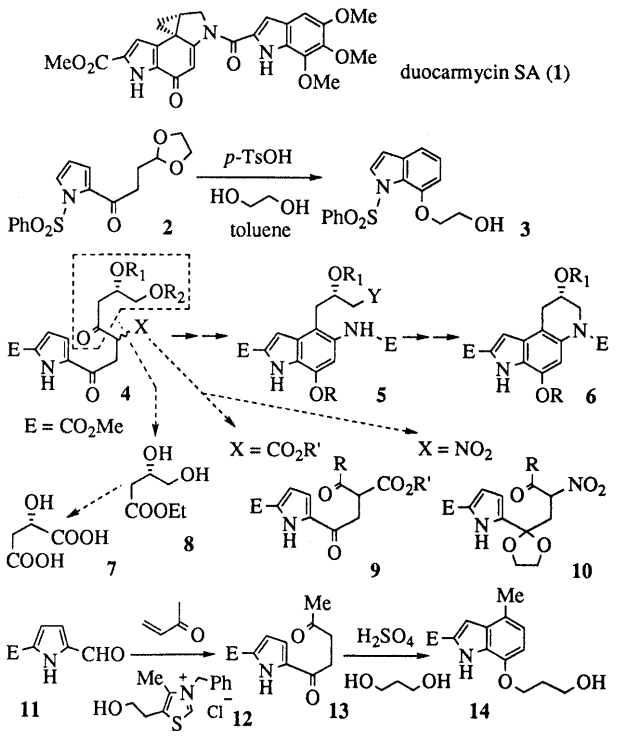

Chart 1

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L-malic acid **7** is an ideal compound for this purpose, since the dihydroxy compound **8** is readily obtainable from **7** in two steps.[14] Substituents X are amine equivalents such as carboxylate and nitro groups, which can be used later to generate the methyl carbamate function in the indole derivative **5**. Then, as in the structure of **6**, construction of the piperidine ring carrying the asymmetric center is next investigated by selective deprotection of the primary alcohol in **5** and activation of this group ($OR_2 \rightarrow OH \rightarrow Y$) to connect with the carbamate nitrogen atom.

Prior to the synthesis using **4** as a key intermediate, model compounds **9** and **10** bearing simple alkyl groups as R were synthesized, and their suitability for acid-catalyzed alkoxyindole formation was studied.

Model Study Using Carboxylate Derivatives 9 Friedel–Crafts acetylation of methyl 2-pyrrolecarboxylate was carried out with acetic anhydride in the presence of boron trifluoride etherate in dichloroethane, and the 5-acetyl derivative **16** was obtained in 45% yield, together with the 4-acetyl isomer **15** in 45% yield (Chart 2).[15] This acetyl compound **16** was converted to its bromoacetal **17** in 97% yield by Nagata's procedure,[16] and acid-catalyzed acetal exchange reaction of **17** afforded the α-bromoketone **18** in 98% yield. This was condensed with methyl and benzyl acetoacetates in the presence of potassium *tert*-butoxide in tetrahydrofuran (THF) to afford the model substrates **9a** and **9b** in 96% and 98% yields, respectively.

Taking into consideration the presence of important hydroxyl functions in **4**, the reaction conditions should be moderate enough to leave the asymmetric center intact during the alkoxyindole formation reaction (Table 1). Therefore, the reaction conditions successfully applied to the pindolol synthesis[17] were tested for **9a** by refluxing a dichloromethane solution with 1,3-propanediol (30 eq) in the presence of sulfuric acid (3 eq) (run 1). However, the reaction proceeded very slowly and required a long refluxing time (30 h); nevertheless, the intermediary monoacetal **20** (23% yield) and diacetal **21** (22% yield) still remained, and the expected indole derivative **19a** was obtained in only 47% yield. In contrast to the ready formation of **14** from **13** in refluxing 1,2-dichloroethane, the use of a low-boiling solvent was insufficient to promote either acetalization of the less reactive ketone group in **20** to form **21** or the pivotal acid-catalyzed cyclization reaction of **21** to **19a**.

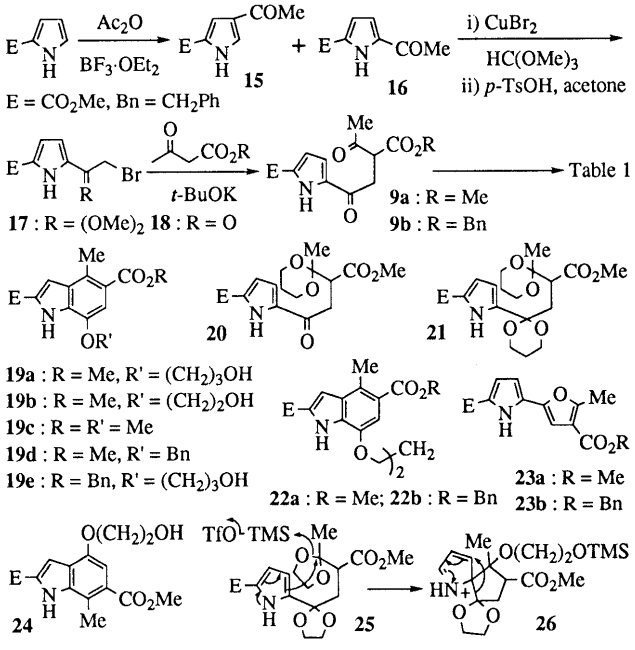


Chart 2

To achieve complete activation of both the ketone group in **20** and the acetal oxygen adjacent to the methyl group in **21**, introduction of boron trifluoride etherate was tried: **9a** in dichloromethane was treated with this reagent in the presence of 2-ethyl-2-methyl-1,3-dioxane at room temperature for 4 h for the purpose of bisacetalization of **9a**, followed by facile nucleophilic interaction of the pyrrole nucleus to the activated acetal oxygen mentioned above (run 2). As expected, Lewis acid-catalyzed acetalization constituted a clean alkoxyindole formation reaction, and **19a** was produced in 86% yield. The only by-product was **22a**, isolated in 3% yield.

Ideally, a benzyl ether **6** ($R = Bn$, $R_1 = H$) would be a suitable target of this study, because this compound had previously been obtained by optical resolution of the racemate and utilized to complete the total synthesis of natural duocarmycin SA (**1**).[1] With this in mind, we tried to extend the above reaction using boron trifluoride etherate to the preparation of the benzyloxyindole derivative **19d**. A dichloromethane solution of **9a** was similarly treated with either 2,2-dimethoxypropane or 2,2-dibenzyloxypropane[18] in the presence of boron trifluoride etherate at room temperature for about one day (run 5 or 6). Whereas the methoxyindole derivative **19c** was obtained in 63% yield, no substantial formation of **19d** was recognized, and **9a** was recovered in 76% yield. Overall, 2,2-dialkoxypropanes seemed to be inferior to the cyclic acetal for our purpose.

The acetalization conditions reported by Noyori and co-workers[19] were applied to our case. A dichloromethane solution of **9a** and 1,3-bis(trimethylsilyloxy)propane was treated with trimethylsilyl (TMS) triflate at room temperature for 9 h (run 3). A 1 : 1 mixture of acetic acid and water was added to this and the mixture was further stirred for 30 min for hydrolysis of the terminal O–TMS bond to liberate the product **19a**. Clean alkoxyindole formation was attained, and **19a** was produced in 86% yield, along with a by-product **23a** in 7% yield. When this reaction on **9a** was performed with 1,2-bis(trimethylsilyloxy)ethane in the presence of TMS triflate, a by-product **24** was obtained in addition to the normal product **19b** in 94% yield (run 4). The reason for the formation of **24** only in this case is unclear, but the reaction mechanism for **24** might involve a spiro derivative **26** obtained by nucleophilic attack of pyrrole on the acetal, as shown by the arrows in **25**. A similar reaction of **9a** was attempted with benzyloxytrimethylsilane and TMS triflate (run 7). However, the major product was **23a**, obtained in 75% yield, and the expected benzyl ether **19d** was isolated in only 5% yield.

In conclusion, both acetal exchange reaction with boron trifluoride etherate and Noyori's acetalization reaction were applicable to our alkoxyindole formation reaction.

Table 1. Indole Formation Reaction of **9** to Form **19**

Run	Material	Reagent (mol eq)	Time (h)	Product	Yield (%)	Other product Yield (%)
1	**9a**	$HO(CH_2)_3OH$ (30), H_2SO_4 (3)	30[a]	**19a**	47	**20**, 23; **21**, 22
2	**9a**	 (50), $BF_3 \cdot OEt_2$ (4)	4	**19a**	86	**22a**, 3
3	**9a**	$TMSO(CH_2)_3OTMS$ (10), TMSOTf (0.2)	9	**19a**	86[b]	**23a**, 7
4	**9a**	$TMSO(CH_2)_2OTMS$ (10), TMSOTf (0.2)	14	**19b**	94[b]	**24**, 3
5	**9a**	$(MeO)_2CMe_2$ (50), $BF_3 \cdot OEt_2$ (4)	19	**19c**	63	—
6	**9a**	$(BnO)_2CMe_2$ (50), $BF_3 \cdot OEt_2$ (4)	21	—	—	**9a**, 76
7	**9a**	BnOTMS (10), TMSOTf (0.2)	13	**19d**	5	**23a**, 75
8	**9b**	(50), $BF_3 \cdot OEt_2$ (4)	4	**19e**	84	**22b**, 2
9	**9b**	$TMSO(CH_2)_3OTMS$ (5), TMSOTf (0.2)	10	**19e**	85[b]	**23b**, 3

a) In CH_2Cl_2 under reflux. *b*) Isolated after treatment with HOAc–H_2O.

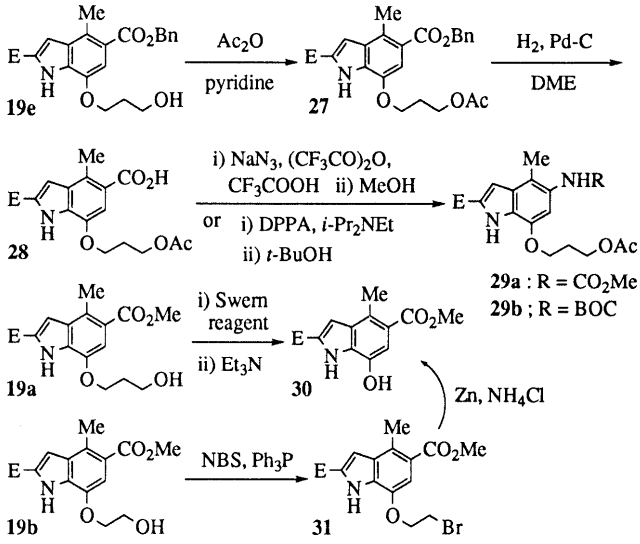


Chart 3

Therefore, these two procedures were applied to the benzyl ester **9b**, and **19e** was obtained in 84% and 85% yields, respectively, as shown in Table 1 (runs 8 and 9). The benzyl ester **19e** was used as a model compound to study the transformation of the ester group to the carbamate required for the generation of **5**. The terminal hydroxy group was protected by the acetyl group in 97% yield (Chart 3). The acetate **27** was submitted to catalytic hydrogenation over palladium–carbon in dimethoxyethane (DME) to afford the carboxylic acid **28** in 98% yield. Schmidt reaction on **28** was tried according to the literature with trifluoroacetic acid (TFA), trifluoroacetic anhydride, and sodium azide in dichloromethane at $-20\,^{\circ}C$ for 20 min.[20] A crude product obtained here was then heated in methanol under reflux to afford the methyl carbamate **29a** in a surprising yield of 92%. Although the yield of this reaction was satisfactory, more moderate reaction conditions were desirable for the total synthesis, since an acid-labile benzyloxy group is present. Curtius rearrangement of **28** was next carried out by refluxing a toluene solution of **28** with diphenylphosphoryl azide[21] (DPPA) and diisopropylethylamine (Hünig base), followed by addition of *tert*-butanol. *tert*-Butyl carbamate **29b** was obtained in a modest yield of 45%, suggesting that the transformation of the carboxylate group to the cabamate group is a crucial step for the total synthesis later on.

Removal of the side chain from **19a** was effected as reported previously by oxidation with Swern reagent, followed by treatment with triethylamine.[11] The hydroxyindole **30** was obtained in 82% yield. A new procedure was developed for transformation of the hydroxyethyl derivative **19b** to **30**. This was attained first by bromination of **19b** with *N*-bromosuccinimide (NBS) in the presence of triphenylphosphine in dichloromethane to give the bromoethyl derivative **31** in 96% yield, followed by treatment of **31** with zinc dust and ammonium chloride in a mixture of 2-propanol and water (14 : 1) under reflux for 30 min. The hydroxyindole **30** was successfully obtained in 91% yield.

Model Study Using Nitro Derivatives 10 Model studies relating to the carboxylate **9** gave us clues for derivatization to the carbamate **5**, but a more direct approach to **5** by way of nitro derivatives is also a possibility. We carried out a model study to investigate this. 5-Formylpyrrole-2-carboxylate[12] **11** was reacted with Grignard reagent derived from vinyl bromide, and the product **32**, obtained in 92% yield, was oxidized to the enone **33** with manganese(IV) oxide in 86% yield (Chart 4). Conjugate addition of nitrous acid[22] to the enone **33** was effected with sodium nitrite and acetic acid in THF at room temperature, and a crude product was treated with 1,2-bis(trimethylsilyloxy)ethane in the presence of TMS triflate to afford the nitro acetal **34** in 51% yield. Condensation of butanal with **34** was carried out with the aid of diisopropylamine in dimethyl sulfoxide[23] (DMSO) to afford **35** in 90% yield, and subsequent oxidation of **35** with pyridinium chlorochromate (PCC) readily gave the requisite compound **10** (R = Pr). However, this α-nitro ketone derivative was in equilibrium with various kinds of tautomers **36**, *i.e.*, (*E* and *Z*)-nitro enol forms and *aci*-nitro ketone forms, which were not well characterized. Therefore, crude **10** was directly submitted to the alkoxyindole formation reaction by treatment with 2-ethyl-2-methyl-1,3-dioxolane in the presence of boron

trifluoride etherate in dichloromethane. The expected indole cyclization did not occur; instead the enone acetal **37** was isolated in 72% yield. Presumably, acetal formation of the side chain ketone group was very much retarded due to the special character of the above α-nitro ketone, and during the reaction period, intramolecular migration of the acetal group in **10** might take place from the ketone group adjacent to the pyrrole to another ketone in the side chain[11] in the presence of boron trifluoride etherate. Then the nitro group would be situated at the β-position to the ketone group and might be readily split off to form **37**. The ketone group in **37** was stabilized by conjugation with both the pyrrole group and the double bond, and therefore resisted further acetalization.

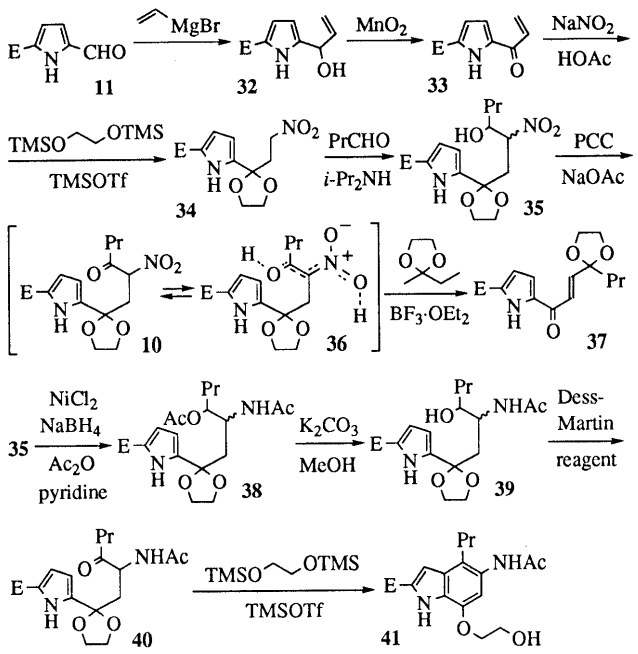


Chart 4

As the nitro ketone **10** was such an unmanageable compound, the nitro group in **35** was reduced beforehand to an amino function with a reagent generated from nickel(II) chloride and sodium borohydride.[24] The product was isolated as the *N*,*O*-diacetate **38** in 75% yield. The *O*-acetyl group was cleaved with potassium carbonate in 93% yield, and the alcohol **39** was oxidized to the acetamino ketone **40** using Dess–Martin periodinane reagent[25] in 89% yield for the alkoxyindole formation reaction. This was attempted by treating **40** with 1,2-bis(trimethylsilyloxy)ethane and TMS triflate in dichloromethane at room temperature. The reaction proceeded very slowly, and required 68 h for completion. In addition to the sluggish nature of this reaction, the yield of the expected compound **41** was only 25%. Therefore the route *via* the nitro compound **10** was abandoned.

Total Synthesis of (+)-Duocarmycin SA Based on the above model studies, our first goal was the indole derivatives **49** (Chart 5). The diol **8** derived from L-malic acid[14] was converted to its dibenzyl ether **42** with benzyl 2,2,2-trichloroacetimidate in the presence of a catalytic amount of trifluoromethanesulfonic acid in 52% yield.[26] The ester group of **42** was partially reduced with diisobutylaluminum hydride (DIBAL) to afford the aldehyde **44** in 87% yield, accompanied by the over-

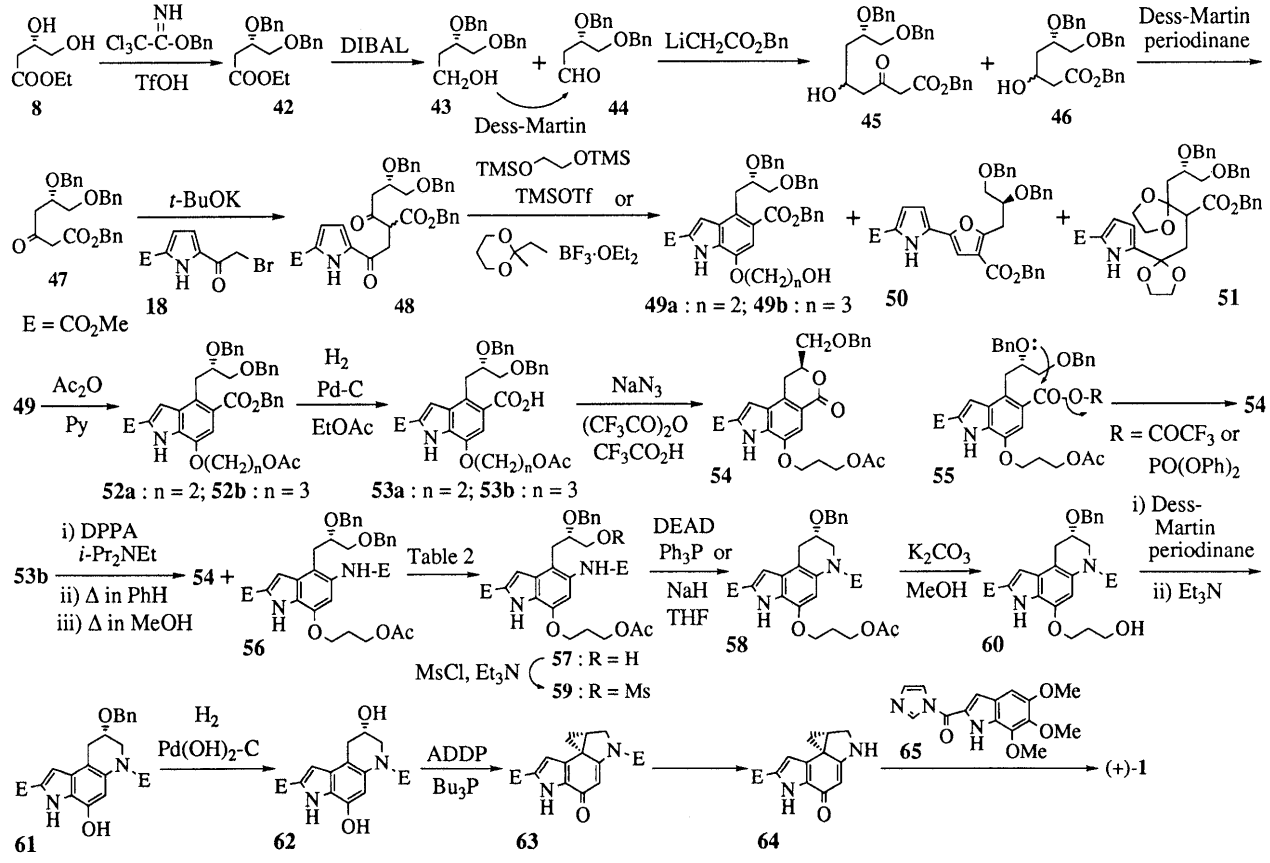


Chart 5

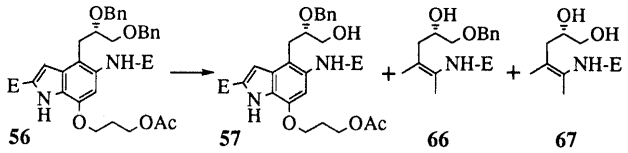
reduction product **43** (7% yield), which was oxidized back to **44** using Dess–Martin periodinane reagent in 75% yield. The aldehyde **44** was then condensed with a lithium compound obtained by reaction of benzyl acetate with lithium diisopropylamide (LDA), and **46** was produced in 78% yield, along with a by-product **45** in 10% yield. Again **46** was oxidized with Dess–Martin reagent to **47** (86% yield),[27] which was coupled with the α-bromoketone **18** using potassium *tert*-butoxide to obtain **48** in 86% yield with small recoveries of **47** (12%) and **18**.

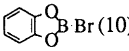
With the necessary substrate in hand with ease, the alkoxyindole formation reaction was examined by applying the two procedures already discussed in the model study. First **48** was treated with 25 eq of 1,2-bis(trimethylsilyloxy)ethane and 2 eq of TMS triflate in dichloromethane at room temperature (26 °C) for 48 h, followed by hydrolysis of the TMS ether bond with 50% acetic acid–water. The reaction proceeded very slowly and required a long period of stirring, yet did not reach completion. The diacetal **51** was formed in 19% yield, and the objective **49a** was isolated in 41% yield, together with a by-product **50** in 15% yield. Next, another alkoxyindole formation reaction was tried by treating **48** with 50 eq of 2-ethyl-2-methyl-1,3-dioxane in the presence of 6 eq of boron trifluoride etherate in dichloromethane at room temperature (20 °C) for 44 h. The reaction was not clean, and the mixture showed many spots of by-products on thin layer chromatography (TLC). Separation afforded **49b** and **50** in 54% and 10% yields, respectively. Among many trials of different reaction conditions, this gave the highest yield of the requisite indole derivatives **49**.

The hydroxyalkyl side chain in **49a** and **49b** was conveniently used as a protecting group of the phenol function, and acetylation afforded **52a** and **52b**, each in 97% yield. Among the three benzyl protecting groups, the benzyl ester was cleaved almost selectively by catalytic hydrogenation of **52a** and **52b** over 10% palladium–charcoal in ethyl acetate at room temperature. Carboxylic acids **53a** and **53b** were obtained in 74% and 75% yields, respectively, accompanied by trace amounts (*ca.* 4% yield each) of the debenzyl products of **53a** and **53b** at the primary alcohol. For conversion of the carboxylic acid function to the carbamate group as in **56**, **53b** was first submitted to the Schmidt reaction conditions.[20] Thus, a dichloromethane suspension of **53b** was treated with sodium azide in the presence of trifluoroacetic anhydride and TFA at −20 °C for 15 min. Judging from TLC examination, a clean reaction took place to afford a single product, but the compound obtained in 88% yield was a lactone derivative **54** rather than an isocyanate.

Next, the Curtius rearrangement using DPPA[21] was investigated. Several unsuccessful experiments soon revealed that the main obstacle hampering this reaction was a very slow reaction rate of the rearrangement of an acid azide into an isocyanate. Therefore the following series of operations was devised for this reaction. A benzene solution of **53b**, DPPA, and Hünig base was refluxed for 18 h until **53b** was no longer detected by TLC. Two spots of the acid azide and the isocyanate were visible, showing that a considerable amount of the acid azide remained unrearranged. Volatile compounds were removed from the reaction mixture *in vacuo* for the purpose of elimination of the Hünig base, fresh benzene was added again, and the mixture was refluxed for 8 h. Then the crude product was washed with sodium bicarbonate to free it from acidic contaminants derived from DPPA, and a mixture containing the isocyanate as a major component was heated in methanol for 3 h to give finally the expected carbamate **56** in 69% yield, accompanied by the lactone **54** in 7% yield. Formation of **54**, both in this case and in the Schmidt reaction, was explained by a facile intramolecular participation of the secondary benzyloxy group to the activated forms of the carboxylic acid as shown in **55**.

Table 2. Debenzylation of **56**



Entry	Reagent (mol eq)	Temperature (°C)	Time (h)	Yield %			
				57	**66**	**67**	**56**
1	EtSH (100) $BF_3 \cdot OEt_2$ (6)	20	15	19	23	17	36
2	BBr_3 (1.7)	−80——55	2	61	3	16	14
3	 (10)	−80——65	1	Trace	88	Trace	—

The next task was to construct the piperidine ring corresponding to the initial plan, **5**→**6**, by connection of the carbamate nitrogen with the primary alcohol carbon in the structure of **57**. For this goal, it was essential to achieve selective deprotection of the benzyl group from the benzylated primary alcohol in **56** in the presence of the benzylated secondary alcohol in close proximity. Three reaction conditions for debenzylation were applied to **56** (Table 2). Fujita's procedure,[28] treatment of **56** with boron trifluoride etherate in the presence of ethanethiol in dichloromethane, resulted in a non-chemoselective deprotection of the benzyl group, affording two mono-debenzylated compounds **57** and **66** in 19% and 23% yields, as well as the bis-debenzylated compound **67** in 17% yield, along with the recovery of **56** in 36% yield (entry 1). Treatment with boron tribromide in dichloromethane at low temperature gave a good result and the required compound **57** was obtained in 61% yield, accompanied by **66** in *ca.* 3% and **67** in 16% yield along with recovered **56** in 14% yield (entry 2). *B*-Bromocatecholborane in dichloromethane[29] afforded an excellent selectivity for production of a single compound in a high yield, but unfortunately this was the undesired product **66**, obtained in 88% yield (entry 3).

Cyclization of **57** to the piperidine derivative **58** was readily effected in 90% yield under Mitsunobu conditions[30] by treating **57** with diethyl azodicarboxylate (DEAD) in the presence of triphenylphosphine in THF. Methanolysis of **58** with potassium carbonate afforded the deacetyl compound **60** in 98% yield. Of course, the conventional two-step procedure for the cyclization to **58**

was studied. The alcohol **57** was activated as its mesylate **59** by treatment with mesyl chloride and triethylamine in dichloromethane in 96% yield, and **59** was treated with sodium hydride in THF for the ring closure. Partial cleavage of the *O*-acetyl bond was observed; therefore the crude mixture was further treated with potassium carbonate in methanol to afford **60** in 92% yield. Oxidation of **60** with Dess–Martin periodinane reagent, followed by warming with triethylamine in dichloromethane for a short period provided the indolol **61** in 86% yield. Removal of the benzyl group from **61** was carried out by medium-pressure hydrogenation (5 atm) over Pearlman's catalyst (20% palladium hydroxide on carbon) in methanol at room temperature (20 °C) to afford (*S*)-**62** in 96% yield. This product (*S*)-**62** possessed the optical rotation value, $[\alpha]_D^{22}$ −4.1° (*c*=0.31, methanol), which coincided well with that, $[\alpha]_D^{21}$ −4.1° (*c*=0.59, methanol), of the corresponding compound (−)-**62** obtained by the optical resolution of racemic **62**.[1] To confirm the identity further, (*S*)-**62** was converted to (7b*R*)-**63**, $[\alpha]_D^{22}$ +184° (*c*=0.228, 10%-methanol-containing dichloromethane), according to the previous report,[6,18] and compared with (+)-**63**,[1] $[\alpha]_D^{21}$ +181° (*c*=0.606, 10%-methanol-containing dichloromethane) (^{1}H-NMR, IR, and MS spectra), establishing that the assignment of the absolute configurations of the resolved compounds (−)-**62** and (+)-**62** had been correct, and therefore, the absolute structure of natural duocarmycin SA was rigorously proven to be **1**, since (+)-**63** had already been transformed into natural duocarmycin SA (**1**) by way of (+)-**64**.[1]

In conclusion, our synthetic effort starting from model studies using compounds **9** and **40** culminated in the accomplishment of an asymmetric total synthesis of duocarmycin SA. Its asymmetric center was introduced from the chirality of L-malic acid. Two reaction conditions for the synthesis of 7-hydroxyindole derivatives were developed, and one of these was successfully utilized in the total synthesis. Benzyl protecting groups were used at the primary and the secondary alcohols, as well as at the ester group. Successive deprotection of the three benzyl protecting groups was smoothly carried out as expected. Among these deprotections, a cleavage of the primary benzyloxy group was devised while the secondary benzyloxy group was present in close vicinity. The present study provided a decisive proof of the absolute structure of **1**.

Experimental

Melting points were determined on a Yanagimoto micro-melting point apparatus without correction. MS and high-resolution MS (HR-MS) 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 in $CDCl_3$ unless otherwise specified, with tetramethylsilane as an internal reference. Column chromatography was conducted on silica gel (Fuji Davison BW 200) or on aluminum oxide (Merck, activity grade II—III) 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.

Methyl 5-(1,4-Dioxopentyl)-1*H*-pyrrole-2-carboxylate (13) Methyl vinyl ketone (0.65 ml, 7.8 mmol) was added to a slurry of **11** (100 mg, 0.654 mmol), **12** (44 mg, 0.16 mmol), Et_3N (0.27 ml, 1.9 mmol), and NaOAc (15.5 mg, 0.19 mmol) in MeOH (5 ml), and the mixture was refluxed under an Ar atmosphere for 16 h. After the mixture had cooled, it was taken up in CH_2Cl_2. The organic layer was worked up as usual and the residue was purified by PTLC [benzene–EtOAc (9 : 1)] to afford **13** (88 mg, 60%) and dimethyl 1*H*-pyrrole-2,5-dicarboxylate[31] (9.5 mg, 8%), mp 128—130 °C (lit. mp 128—130 °C) (EtOH–H_2O). **13**: Colorless scales, mp 109.5—111.5 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{11}H_{13}NO_4$: C, 59.18; H, 5.87; N, 6.28. Found: C, 59.19; H, 5.90; N, 6.31. HR-MS Calcd for $C_{11}H_{13}NO_4$: 223.0844. Found: 223.0860. MS *m/z*: 223 (M^+, 32), 180 (19), 152 (49), 120 (100), 43 (46). ^{1}H-NMR δ: 2.21 (3H, s), 2.75—2.99 (2H, m), 2.99—3.23 (2H, m), 3.87 (3H, s), 6.89 (2H, d, *J*=2.5 Hz, changed to s with D_2O), 9.83 (1H, br s, NH).

Methyl 7-(3-Hydroxypropyl)oxy-4-methyl-1*H*-indole-2-carboxylate (14) A mixture of **13** (20 mg, 0.090 mmol), 1,3-propanediol (207 mg, 2.72 mmol), and 95% H_2SO_4 (15 μl, 0.28 mmol) in 1,2-dichloroethane (5 ml) was refluxed using a Dean–Stark water separator for 14.5 h. The mixture was cooled in an ice bath and saturated $NaHCO_3$–H_2O was added. The whole was extracted with CH_2Cl_2, and the extract was worked up as usual. Purification by PTLC (1% MeOH–CH_2Cl_2) afforded **14** (19 mg, 81%) as colorless needles, mp 115.5—116.5 °C (benzene). *Anal.* Calcd for $C_{14}H_{17}NO_4$: C, 63.86; H, 6.51; N, 5.32. Found: C, 63.98; H, 6.53; N, 5.33. HR-MS Calcd for $C_{14}H_{17}NO_4$: 263.1157. Found: 263.1151. MS *m/z*: 263 (M^+, 68), 205 (19), 173 (100), 145 (30), 31 (36). IR (KBr) cm^{-1}: 1688. ^{1}H-NMR δ: 2.08 (2H, tt, *J*=6, 6 Hz), *ca.* 2.27 (1H, br s, OH), 2.46 (3H, s), 3.91 (3H, s), 3.91 (2H, t, *J*=6 Hz), 4.23 (2H, t, *J*=6 Hz), 6.63 (1H, d, *J*=7.5 Hz), 6.79 (1H, d, *J*=7.5 Hz), 7.21 (1H, d, *J*=2.5 Hz, changed to s with D_2O), 9.54 (1H, br s, NH).

Methyl 4-Acetyl- and 5-Acetyl-1*H*-pyrrole-2-carboxylates (15, 16) $BF_3 \cdot OEt_2$ (2.96 ml, 24.1 mmol) was added to a cooled (0 °C) solution of Ac_2O (3.02 ml, 32 mmol) in 1,2-dichloroethane (20 ml) and the mixture was stirred at that temperature for 10 min. Methyl 1*H*-pyrrole-2-carboxylate (2.003 g, 16.02 mmol) was added portionwise, and stirring was continued at 0 °C for 30 min and at 20 °C for 2 h. The mixture was poured into H_2O and the whole was extracted with CH_2Cl_2. The organic layer was washed with saturated $NaHCO_3$–H_2O and worked up as usual. The residue was separated by SiO_2 (50 g) column chromatography (CH_2Cl_2) to afford **15** (1.209 g, 45%) and **16** (1.202 g, 45%) in order of decreasing polarity. **15**: Colorless prisms, mp 112—112.5 °C (lit.[15] mp 110—111 °C) (CH_2Cl_2–hexane). HR-MS Calcd for $C_8H_9NO_3$: 167.0582. Found: 167.0592. MS *m/z*: 167 (M^+, 29), 152 (39), 136 (9), 120 (100), 43 (14). IR (KBr) cm^{-1}: 1709, 1640. ^{1}H-NMR δ: 2.43 (3H, s), 3.87 (3H, s), 7.27 (1H, dd, *J*=2.5, 1.5 Hz, changed to d, *J*=1.5 Hz with D_2O), 7.55 (1H, dd, *J*=3.5, 1.5 Hz, changed to d, *J*=1.5 Hz with D_2O), 10.08 (1H, br s, NH). **16**: Colorless needles, mp 112—113 °C (lit.[15] mp 109—110 °C) (CH_2Cl_2–hexane). *Anal.* Calcd for $C_8H_9NO_3$: C, 57.48; H, 5.43; N, 8.38. Found: C, 57.36; H, 5.44; N, 8.34. HR-MS Calcd for $C_8H_9NO_3$: 167.0582. Found: 167.0580. MS *m/z*: 167 (M^+, 54), 152 (28), 136 (18), 120 (100), 43 (8). IR (KBr) cm^{-1}: 1718, 1660. ^{1}H-NMR δ: 2.46 (3H, s), 3.88 (3H, s), 6.77—6.95 (2H, m), 10.13 (1H, br s, NH).

Methyl 5-(2-Bromo-1,1-dimethoxyethyl)-1*H*-pyrrole-2-carboxylate (17) $CuBr_2$ (748 mg, 3.35 mmol) was added to a MeOH solution (9 ml) of **16** (266 mg, 1.59 mmol) and $HC(OMe)_3$ (1.50 ml, 13.7 mmol) and the mixture was stirred at 50—55 °C for 1 h. After the mixture had cooled, 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 (5 : 1)] afforded **17** (452 mg, 97%) as a colorless syrup. HR-MS Calcd for $C_{10}H_{14}{}^{81}BrNO_4$ and $C_{10}H_{14}{}^{79}BrNO_4$: 293.0086 and 291.0106. Found: 293.0044 and 291.0113. MS *m/z*: 293 (1) and 291 (1) (M^+), 262 (21) and 260 (21), 230 (26) and 228 (26), 198 (100), 166 (83), 120 (24), 118 (29). IR ($CHCl_3$) cm^{-1}: 1704. ^{1}H-NMR δ: 3.19 (6H, s), 3.65 (2H, s), 3.84 (3H, s), 6.19 (1H, dd, *J*=4, 2.5 Hz), 6.90 (1H, dd, *J*=4, 2.5 Hz), 9.79 (1H, br s, NH).

Methyl 5-Bromoacetyl-1*H*-pyrrole-2-carboxylate (18) An acetone solution (6 ml) of **17** (384 mg, 1.32 mmol) and *p*-TsOH·H_2O (10 mg, 0.053 mmol) was stirred at 20 °C for 2 h. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up gave a crystalline residue, which was recrystallized from CH_2Cl_2–hexane to afford **18** (317 mg, 98%) as colorless needles, mp 137—138.5 °C. *Anal.* Calcd for $C_8H_8BrNO_3$: C, 39.05; H, 3.28; N, 5.69. Found: C, 38.79; H, 3.28; N, 5.73. HR-MS Calcd for $C_8H_8{}^{81}BrNO_3$ and $C_8H_8{}^{79}BrNO_3$: 246.9668 and 244.9688. Found: 246.9645 and 244.9674. MS *m/z*: 247 (20) and 245 (21) (M^+), 216 (5) and 214 (5), 152 (100), 120 (96), 106 (36). IR (KBr) cm^{-1}: 1718, 1655. ^{1}H-NMR δ: 3.90 (3H, s), 4.24 (2H, s),

6.87 (1H, dd, $J=4$, 2.5 Hz, changed to d, $J=4$ Hz with D_2O), 6.94 (1H, dd, $J=4$, 2.5 Hz, changed to d, $J=4$ Hz with D_2O), 10.09 (1H, br s, NH).

Methyl α-Acetyl-5-(methoxycarbonyl)-γ-oxo-1*H*-pyrrole-2-butyrate (9a) *tert*-BuOK (164 mg, 1.46 mmol) was added to a cooled (0 °C) THF solution (5 ml) of methyl acetoacetate (170 mg, 1.46 mmol) under an Ar atmosphere, and the mixture was stirred at that temperature for 20 min. The above bromide **18** (120 mg, 0.488 mmol) was added portionwise and stirring was continued at 0 °C for 20 min. Saturated NH_4Cl–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up followed by purification by PTLC [hexane–EtOAc (5 : 2)] afforded **9a** (132 mg, 96%) as colorless needles, mp 89—90 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{13}H_{15}NO_6$: C, 55.51; H, 5.38; N, 4.98. Found: C, 55.51; H, 5.39; N, 5.09. HR-MS Calcd for $C_{13}H_{15}NO_6$: 281.0898. Found: 281.0887. MS *m/z*: 281 (M^+, 15), 239 (22), 152 (54), 120 (100), 87 (32), 43 (94). IR (KBr) cm^{-1}: 1723, 1662, 1643. ^{1}H-NMR δ: 2.38 (3H, s), 3.30 (1H, dd, $J=18$, 6.5 Hz), 3.57 (1H, dd, $J=18$, 7.5 Hz), 3.75 (3H, s), 3.87 (3H, s), 4.22 (1H, dd, $J=7.5$, 6.5 Hz),), 6.86 (1H, dd, $J=4$, 2.5 Hz, changed to d, $J=4$ Hz with D_2O), 6.94 (1H, dd, $J=4$, 2.5 Hz, changed to d, $J=4$ Hz with D_2O), 10.02 (1H, br s, NH).

Benzyl α-Acetyl-5-(methoxycarbonyl)-γ-oxo-1*H*-pyrrole-2-butyrate (9b) Similarly, **18** (152 mg, 0.618 mmol) was allowed to react with benzyl acetoacetate (356 mg, 1.85 mmol) in the presence of *tert*-BuOK (208 mg, 1.86 mmol) in THF (6 ml) to afford **9b** (217 mg, 98%) after purification by PTLC [hexane–EtOAc (3 : 1)]. Colorless prisms, mp 119—120 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{19}H_{19}NO_6$: C, 63.86; H, 5.36; N, 3.92. Found: C, 63.58; H, 5.43; N, 3.90. HR-MS Calcd for $C_{19}H_{19}NO_6$: 357.1211. Found: 357.1192. MS *m/z*: 357 (M^+, 5), 223 (5), 180 (4), 167 (5), 152 (19), 120 (30), 91 (100), 65 (9), 43 (20). IR (KBr) cm^{-1}: 1734, 1707, 1656. ^{1}H-NMR δ: 2.31 (3H, s), 3.31 (1H, dd, $J=17.5$, 6.5 Hz), 3.56 (1H, dd, $J=17.5$, 7.5 Hz), 3.84 (3H, s), 4.28 (1H, dd, $J=7.5$, 6.5 Hz), 5.14 (2H, s), 6.77—6.97 [2H, m, changed to 6.83 (1H, d, $J=4$ Hz) and 6.90 (1H, d, $J=4$ Hz) with D_2O], 7.17—7.43 (5H, m), 10.36 (1H, br s, NH).

Dimethyl 7-[(3-Hydroxypropyl)oxy]-4-methyl-1*H*-indole-2,5-dicarboxylate (19a) (i) Procedure of Table 1, Entry 1: A CH_2Cl_2 solution (3 ml) of **9a** (32 mg, 0.11 mmol), 1,3-propanediol (262 mg, 3.45 mmol), and 95% H_2SO_4 (18 μl, 0.32 mmol) was refluxed for 30 h. After the mixture had cooled, saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [benzene–EtOAc (2 : 1)] afforded **19a** (17 mg, 47%), together with methyl 2-[5-(methoxycarbonyl)-1*H*-pyrrol-2-yl]-α-(2-methyl-1,3-dioxan-2-yl)-1,3-dioxane-2-propanoate (**21**) (10 mg, 22%) and methyl α-(2-methyl-1,3-dioxan-2-yl)-5-(methoxycarbonyl)-γ-oxo-1*H*-pyrrole-2-butyrate (**20**) (9 mg, 23%) in order of decreasing polarity. **19a**: Colorless needles, mp 147.5—149.5 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{16}H_{19}NO_6$: C, 59.80; H, 5.96; N, 4.36. Found: C, 59.54; H, 5.97; N, 4.36. HR-MS Calcd for $C_{16}H_{19}NO_6$: 321.1211. Found: 321.1225. MS *m/z*: 321 (M^+, 96), 290 (20), 263 (20), 231 (100), 31 (53). IR (KBr) cm^{-1}: 1700, 1687. ^{1}H-NMR δ: 2.11 (2H, tt, $J=6$, 6 Hz), *ca.* 2.20 (1H, br s, OH), 2.72 (3H, s), 3.88 (3H, s), 3.91 (3H, s), 3.95 (2H, t, $J=6$ Hz), 4.28 (2H, t, $J=6$ Hz), 7.26—7.37 (1H, m), 7.29 (1H, s), 9.63 (1H, br s, NH). **20**: Colorless glass. HR-MS Calcd for $C_{16}H_{21}NO_7$: 339.1317. Found: 339.1298. MS *m/z*: 339 (M^+, 1), 324 (2), 308 (1), 210 (6), 152 (6), 120 (18), 101 (100), 73 (13), 43 (42). IR ($CHCl_3$) cm^{-1}: 1730, 1667. ^{1}H-NMR δ: 1.47 (3H, s), 1.54—1.88 (2H, m), 3.13 (1H, dd, $J=17$, 4 Hz), 3.42 (1H, dd, $J=17$, 9 Hz), 3.61—4.17 (5H, m), 3.71 (3H, s), 3.87 (3H, s), 6.79—7.00 (2H, m), 9.82 (1H, br s, NH). **21**: Colorless glass. HR-MS Calcd for $C_{19}H_{27}NO_8$: 397.1735. Found: 397.1732. MS *m/z*: 397 (M^+, 0.4), 382 (1), 366 (1), 210 (100), 178 (27), 120 (26), 101 (100), 73 (10), 43 (45). IR ($CHCl_3$) cm^{-1}: 1728, 1700. ^{1}H-NMR δ: *ca.* 1.09—1.31 (1H, m), 1.31 (3H, s), *ca.* 1.45—2.25 (3H, m), 1.93 (1H, dd, $J=14$, 2 Hz), 2.33 (1H, dd, $J=14$, 11 Hz), 3.53 (3H, s), 3.53—4.24 (9H, m), 3.84 (3H, s), 6.20 (1H, dd, $J=3.5$, 2.5 Hz, changed to d, $J=3.5$ Hz with D_2O), 6.86 (1H, dd, $J=3.5$, 2.5 Hz, changed to d, $J=3.5$ Hz with D_2O), 9.08 (1H, br s, NH).

(ii) Procedure of Table 1, Entry 2: $BF_3 \cdot OEt_2$ (81 μl, 0.66 mmol) was added to a cooled (0 °C) CH_2Cl_2 solution (1 ml) of **9a** (46 mg, 0.16 mmol) and 2-ethyl-2-methyl-1,3-dioxane (1.068 g, 8.22 mmol), and the mixture was stirred at 25 °C for 4 h. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [benzene–EtOAc (2 : 1)] afforded **19a** (45 mg, 86%) and 1,3-bis[[2,5-di(methoxycarbonyl)-4-methyl-1*H*-indol-7-yl]oxy]propane (**22a**) (1.5 mg, 3%) in order of decreasing polarity. **22a**: Colorless needles, mp 215—217 °C (CH_2Cl_2–hexane). HR-MS Calcd for $C_{29}H_{30}N_2O_{10}$: 566.1898. Found: 566.1890. MS *m/z*: 566 (M^+, 75), 535 (23), 304 (54), 272 (100), 245 (45), 213 (42), 170 (47), 59 (21). IR ($CHCl_3$) cm^{-1}: 1710. ^{1}H-NMR δ: 2.44 (2H, quintet, $J=5.5$ Hz), 2.74 (6H, s), 3.88 (6H, s), 3.93 (6H, s), 4.41 (4H, t, $J=5.5$ Hz), 7.29—7.42 (4H, m), 9.17 (2H, br s, NH).

(iii) Procedure of Table 1, Entry 3: TMSOTf (6 μl, 0.03 mmol) was added to a cooled (0 °C) CH_2Cl_2 solution (2 ml) of **9a** (45 mg, 0.16 mmol) and 1,3-bis(trimethylsilyloxy)propane (0.43 ml, 1.6 mmol), and the mixture was stirred at 22 °C for 9 h. HOAc–H_2O (1 : 1) (0.4 ml) was added and stirring was continued at 22 °C for 30 min. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up afforded a crystalline residue, which was recrystallized from CH_2Cl_2–hexane, followed by PTLC (2% MeOH–CH_2Cl_2) separation of the material from the mother liquor to afford **19a** (44 mg, 86%) and methyl 5-[4-(methoxycarbonyl)-5-methylfuran-2-yl]-1*H*-pyrrole-2-carboxylate (**23a**) (3 mg, 7%) in order of decreasing polarity. **23a**: Colorless needles, mp 179.5—180.5 °C (MeOH–CH_2Cl_2). *Anal.* Calcd for $C_{13}H_{13}NO_5$: C, 59.31; H, 4.98; N, 5.32. Found: C, 59.07; H, 5.04; N, 5.36. HR-MS Calcd for $C_{13}H_{13}NO_5$: 263.0793. Found: 263.0795. MS *m/z*: 263 (M^+, 100), 231 (97), 216 (22), 203 (23), 43 (42). IR (KBr) cm^{-1}: 1719, 1683. ^{1}H-NMR δ: 2.61 (3H, s), 3.82 (3H, s), 3.87 (3H, s), 6.42 (1H, dd, $J=4$, 2.5 Hz), 6.79 (1H, s), 6.90 (1H, dd, $J=4$, 2.5 Hz), 9.54 (1H, br s, NH).

Dimethyl 7-(2-Hydroxyethoxy)-4-methyl-1*H*-indole-2,5-dicarboxylate (19b) Similar treatment of **9a** (40 mg, 0.14 mmol) with 1,2-bis(trimethylsilyloxy)ethane (0.35 ml, 1.4 mmol) and TMSOTf (6 μl, 0.03 mmol) in CH_2Cl_2 (1.5 ml) at 27 °C for 14 h afforded a crystalline residue, which was recrystallized from MeOH–CH_2Cl_2, followed by PTLC (2% MeOH–CH_2Cl_2) separation of the material from the mother liquor to afford **19b** (41 mg, 94%) and dimethyl 4-(2-hydroxyethoxy)-7-methyl-1*H*-indole-2,6-dicarboxylate (**24**) (1.5 mg, 3%) in order of decreasing polarity. **19b**: Colorless needles, mp 215—216 °C (MeOH–CH_2Cl_2). *Anal.* Calcd for $C_{15}H_{17}NO_6$: C, 58.62; H, 5.58; N, 4.56. Found: C, 58.20; H, 5.57; N, 4.54. HR-MS Calcd for $C_{15}H_{17}NO_6$: 307.1055. Found: 307.1053. MS *m/z*: 307 (M^+, 100), 276 (22), 263 (15), 231 (92), 45 (27). IR (KBr) cm^{-1}: 1722, 1697. ^{1}H-NMR (DMSO-d_6) δ: 2.66 (3H, s), *ca.* 3.68—3.89 (2H, m), 3.81 (3H, s), 3.89 (3H, s), 3.99—4.20 (2H, m), 4.87 (1H, br s, OH), 7.19 (1H, s), 7.37 (1H, s), 12.00 (1H, br s, NH). **24**: Colorless needles, mp 224—225 °C (MeOH–CH_2Cl_2). *Anal.* Calcd for $C_{15}H_{17}NO_6$: C, 58.62; H, 5.58; N, 4.56. Found: C, 58.22; H, 5.53; N, 4.32. HR-MS Calcd for $C_{15}H_{17}NO_6$: 307.1055. Found: 307.1058. MS *m/z*: 307 (M^+, 100), 275 (31), 263 (25), 231 (92), 45 (34). IR (KBr) cm^{-1}: 1716, 1700. ^{1}H-NMR (DMSO-d_6) δ: 2.72 (3H, s), *ca.* 3.68—3.99 (2H, m), 3.94 (3H, s), 3.99 (3H, s), 4.05—4,28 (2H, m), 4.94 (1H, t, $J=5.5$ Hz, OH), 6.97 (1H, s), 7.28 (1H, s), 12.05 (1H, br s, NH).

Dimethyl 7-Methoxy-4-methyl-1*H*-indole-2,5-dicarboxylate (19c) Similarly, **9a** (50 mg, 0.18 mmol) was stirred with 2,2-dimethoxypropane (1.09 ml, 8.88 mmol) and $BF_3 \cdot OEt_2$ (88 μl, 0.72 mmol) in CH_2Cl_2 (2 ml) at 0 °C for 1.5 h and at 25 °C for 19 h to afford **19c** (31 mg, 63%) after purification by PTLC [hexane–CH_2Cl_2 (1 : 3)]. Colorless needles, mp 208—209 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{14}H_{15}NO_5$: C, 60.64; H, 5.45; N, 5.05. Found: C, 60.47; H, 5.51; N, 5.08. HR-MS Calcd for $C_{14}H_{15}NO_5$: 277.0949. Found: 277.0948. MS *m/z*: 277 (M^+, 100), 245 (70), 230 (14), 216 (39). IR (KBr) cm^{-1}: 1709, 1688. ^{1}H-NMR δ: 2.74 (3H, s), 3.88 (3H, s), 3.91 (3H, s), 3.92 (3H, s), 7.29 (3H, s), 7.34 (1H, d, $J=2$ Hz), 9.21 (1H, br s, NH).

Dimethyl 7-Benzyloxy-4-methyl-1*H*-indole-2,5-dicarboxylate (19d) Similarly, **9a** (47 mg, 0.17 mmol) was allowed to react with benzyl trimethylsilyl ether (0.33 ml, 1.7 mmol) and TMSOTf (7 μl, 0.04 mmol) in CH_2Cl_2 (2.5 ml) at 27 °C for 3 h. To remove $PhCH_2OH$, the crude reaction mixture was acetylated with Ac_2O (0.4 ml) and pyridine (0.5 ml) in CH_2Cl_2 (1 ml). Purification by PTLC [hexane–EtOAc (14 : 1)] afforded **19d** (3 mg, 5%) and **23a** (33 mg, 75%) in order of increasing polarity. **19d**: Colorless prisms, mp 193—194 °C (CH_2Cl_2–hexane). HR-MS Calcd for $C_{20}H_{19}NO_5$: 353.1262. Found: 353.1265. MS *m/z*: 353 (M^+, 15), 322 (3), 262 (8), 230 (11), 170 (9), 91 (100), 65 (6). IR (KBr) cm^{-1}: 1702. ^{1}H-NMR δ: 2.77 (3H, s), 3.90 (3H, s), 3.94 (3H, s), 5.20 (2H, s), 7.28—7.59 (6H, m), 7.36 (1H, d, $J=2.5$ Hz), 9.21 (1H, br s, NH).

5-Benzyl 2-Methyl 7-(3-Hydroxypropyloxy)-4-methyl-1*H*-indole-2,5-dicarboxylate (19e) (i) Table 1, Entry 8: In the same manner as described for the procedure of Table 1, entry 2, **9b** (62 mg, 0.17 mmol) was treated with 2-ethyl-2-methyl-1,3-dioxane (1.127 g, 8.669 mmol) and $BF_3 \cdot OEt_2$ (85 μl, 0.69 mmol) in CH_2Cl_2 (1.5 ml) at 0 °C for 30 min and 26 °C for 4 h to afford **19e** (58 mg, 84%) and 1,3-bis[[5-(benzyloxycarbonyl)-2-

(methoxycarbonyl)-4-methyl-1*H*-indol-7-yl]oxy]propane (**22b**) (1.5 mg, 2%) after purification by PTLC [hexane–EtOAc (2 : 1)]. **19e**: Colorless needles, mp 122—123 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{22}H_{23}NO_6$: C, 66.48; H, 5.83; N, 3.53. Found: C, 66.30; H, 5.91; N, 3.61. HR-MS Calcd for $C_{22}H_{23}NO_6$: 397.1524. Found: 397.1511. MS *m/z*: 397 (M^+, 39), 306 (56), 248 (31), 216 (43), 172 (14), 91 (100), 65 (11), 31 (21). IR (KBr) cm^{-1}: 1691, 1680. ^{1}H-NMR δ: 2.00 (1H, br s, OH), 2.09 (2H, tt, J=6, 6 Hz), 2.74 (3H, s), 3.79—4.07 (2H, m), 3.93 (3H, s), 4.27 (2H, t, J=6 Hz), 5.34 (2H, s), 7.23—7.57 (6H, m), 7.30 (1H, d, J=2.5 Hz), 9.59 (1H, br s, NH). **22b**: Colorless needles, mp 170—172 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{41}H_{38}N_2O_{10}$: C, 68.51; H, 5.33; N, 3.90. Found: C, 68.06; H, 5.35; N, 3.85. HR-MS Calcd for $C_{41}H_{38}N_2O_{10}$: 718.2524. Found: 718.2530. MS *m/z*: 718 (M^+, 10), 610 (3), 519 (6), 288 (9), 245 (10), 213 (5), 91 (100). IR ($CHCl_3$) cm^{-1}: 1711. ^{1}H-NMR δ: *ca.* 2.24—2.58 (2H, m), 2.76 (6H, s), 3.93 (6H, s), 4.39 (4H, t, J=6 Hz), 5.36 (4H, s), 7.24—7.57 (14H, m), 9.19 (2H, br s, NH).

(ii) Table 1, Entry 9: In the same manner as described for the procedure of Table 1, entry 3, **9b** (300 mg, 0.840 mmol) was treated with 1,3-bis(trimethylsilyloxy)propane (1.11 ml, 4.19 mmol) and TMSOTf (41 μl, 0.21 mmol) in CH_2Cl_2 (6 ml) to afford **19e** (283 mg, 85%) and methyl 5-[4-(benzyloxycarbonyl)-5-methylfuran-2-yl]-1*H*-pyrrole-2-carboxylate (**23b**) (9 mg, 3%) after purification by PTLC [benzene–EtOAc (5 : 1)]. **23b**: Colorless needles, mp 175—176 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{19}H_{17}NO_5$: C, 67.25; H, 5.05; N, 4.13. Found: C, 66.99; H, 5.14; N, 4.22. HR-MS Calcd for $C_{19}H_{17}NO_5$: 339.1106. Found: 339.1109. MS *m/z*: 339 (M^+, 66), 248 (24), 216 (100), 200 (12), 144 (11), 120 (14), 91 (80), 65 (13). IR (KBr) cm^{-1}: 1711, 1677. ^{1}H-NMR δ: 2.60 (3H, s), 3.83 (3H, s), 5.26 (2H, s), 6.38 (1H, dd, J=4, 3 Hz, changed to d, J=4 Hz with D_2O), 6.74 (1H, s), 6.87 (1H, dd, J=4, 3 Hz, changed to d, J=4 Hz with D_2O), 7.36 (5H, s), 9.34 (1H, br s, NH).

5-Benzyl 2-Methyl 7-(3-Acetoxypropyloxy)-4-methyl-1*H*-indole-2,5-dicarboxylate (27) A CH_2Cl_2 solution (1 ml) of **19e** (28 mg, 0.071 mmol), Ac_2O (0.30 ml, 3.2 mmol), and pyridine (0.50 ml, 6.2 mmol) was stirred at 26 °C for 2 h. Volatile materials were removed *in vacuo* and saturated $NaHCO_3$–H_2O was added to the residue. The whole was extracted with CH_2Cl_2 and usual work-up followed by purification by PTLC [hexane–EtOAc (3 : 1)] afforded **27** (30 mg, 97%) as colorless prisms, mp 118—119 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{24}H_{25}NO_7$: C, 65.59; H, 5.73; N, 3.19. Found: C, 65.23; H, 5.78; N, 3.26. HR-MS Calcd for $C_{24}H_{25}NO_7$: 439.1629. Found: 439.1640. MS *m/z*: 439 (M^+, 7), 408 (1), 348 (1), 332 (1), 248 (2), 216 (4), 101 (100), 91 (33), 73 (10), 43 (34). IR (KBr) cm^{-1}: 1737, 1694. ^{1}H-NMR δ: 2.04 (3H, s), 2.16 (2H, tt, J=6.5, 6.5 Hz), 2.75 (3H, s), 3.94 (3H, s), 4.21 (2H, t, J=6.5 Hz), 4.30 (2H, t, J=6.5 Hz), 5.36 (2H, s), 7.23—7.56 (7H, m), 9.26 (1H, br s, NH).

7-(3-Acetoxypropyloxy)-2-(methoxycarbonyl)-4-methyl-1*H*-indole-5-carboxylic Acid (28) A DME solution (4 ml) of **27** (29 mg, 0.066 mmol) was hydrogenated over 10% Pd on carbon (5 mg) under an H_2 atmosphere (1 atm) at 25 °C for 1 h. The catalyst was filtered off through a Celite bed, and the Celite was washed with 10% MeOH–CH_2Cl_2. The combined organic layer was evaporated to give a crystalline residue. Recrystallization from CH_2Cl_2 afforded **28** (22.5 mg, 99%) as colorless needles, mp 195—196.5 °C. *Anal.* Calcd for $C_{17}H_{19}NO_7$: C, 58.45; H, 5.48; N, 4.01. Found: C, 58.19; H, 5.44; N, 4.14. HR-MS Calcd for $C_{17}H_{19}NO_7$: 349.1160. Found: 349.1148. MS *m/z*: 349 (M^+, 8), 217 (9), 101 (100), 73 (15), 43 (54). IR (KBr) cm^{-1}: 1722, 1709, 1675. ^{1}H-NMR (10% CD_3OD–$CDCl_3$) δ: 2.07 (3H, s), 2.20 (2H, tt, J=6, 6 Hz), 2.77 (3H, s), 3.95 (3H, s), 4.24 (2H, t, J=6 Hz), 4.32 (2H, t, J=6 Hz), 7.36 (2H, s).

Methyl 7-(3-Acetoxypropyloxy)-5-(methoxycarbonyl)amino-4-methyl-1*H*-indole-2-carboxylate (29a) NaN_3 (180 mg, 2.77 mmol) was added to a cooled (−20 °C) CH_2Cl_2 solution (2 ml) of **28** (96 mg, 0.28 mmol), CF_3CO_2H (0.50 ml, 6.5 mmol), and $(CF_3CO)_2O$ (0.50 ml, 3.5 mmol), and the mixture was stirred at that temperature for 20 min. The volatile materials were removed *in vacuo*, and saturated $NaHCO_3$–H_2O was added to the residue. The whole was extracted with CH_2Cl_2 and worked up as usual to give a crude isocyanate (102 mg). This was dissolved in MeOH (8 ml) and the solution was refluxed for 1 h. MeOH was removed *in vacuo* and the resulting residue was purified by PTLC [hexane–CH_2Cl_2 (1 : 5)] to afford **29a** (96 mg, 92%) as colorless needles, mp 154—155 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{18}H_{22}N_2O_7$: C, 57.13; H, 5.86; N, 7.41. Found: C, 57.28; H, 5.91; N, 7.48. HR-MS Calcd for $C_{18}H_{22}N_2O_7$: 378.1426. Found: 378.1421. MS *m/z*: 378 (M^+, 7), 346 (4), 246 (4), 214 (4), 101 (100), 73 (12), 43 (48). IR (KBr) cm^{-1}: 1727, 1700. ^{1}H-NMR δ: 2.05 (3H, s), 2.14 (2H, tt, J=6, 6 Hz), 2.33 (3H, s), 3.77 (3H, s), 3.93 (3H, s), 4.18 (2H, t, J=6 Hz), 4.29 (2H, t, J=6 Hz), 6.44 (1H, br s, NH), 6.99 (1H, br s), 7.17 (1H, d, J=2 Hz, changed to s with D_2O), 9.14 (1H, br s, indole NH). ^{1}H-NMR of crude isocyanate δ: 2.04 (3H, s), 2.17 (2H, tt, J=6.5, 6.5 Hz), 2.40 (3H, s), 3.92 (3H, s), 4.13 (2H, t, J=6.5 Hz), 4.29 (2H, t, J=6.5 Hz), 6.43 (1H, s), 7.13 (1H, d, J=2 Hz), 9.16 (1H, br s, NH).

Methyl 7-(3-Acetoxypropyloxy)-5-(*tert*-butoxycarbonyl)amino-4-methyl-1*H*-indole-2-carboxylate (29b) A toluene solution (3 ml) containing **28** (26 mg, 0.074 mmol), DPPA (32 μl, 0.15 mmol) and iso-Pr_2NEt (52 μl, 0.30 mmol) was refluxed for 15 h. *tert*-BuOH (1.40 ml, 14.9 mmol) and iso-Pr_2NEt (143 μl, 0.823 mmol) were added and the resulting solution was refluxed for 48 h. After the solution had cooled in an ice bath, H_2O was added and the whole was extracted with CH_2Cl_2. The organic layer was successively washed with saturated $CuSO_4$–H_2O and saturated $NaHCO_3$–H_2O, and worked up as usual. Purification by PTLC [hexane–CH_2Cl_2 (1 : 4)] afforded **29b** (14 mg, 45%) as colorless needles, mp 167—168 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{21}H_{28}N_2O_7$: C, 59.99; H, 6.71; N, 6.66. Found: C, 59.77; H, 6.66; N, 6.67. HR-MS Calcd for $C_{21}H_{28}N_2O_7$: 420.1895. Found: 420.1881. MS *m/z*: 420 (M^+, 4), 364 (5), 346 (4), 214 (4), 187 (4), 101 (100), 73 (9), 43 (35). IR (KBr) cm^{-1}: 1723, 1704, 1687. ^{1}H-NMR δ 1.50 (9H, s), 2.04 (3H, s), 2.15 (2H, tt, J=6.5, 6.5 Hz), 2.33 (3H, s), 3.91 (3H, s), 4.18 (2H, t, J=6.5 Hz), 4.28 (2H, t, J=6.5 Hz), 6.21 (1H, br s, NH), 7.06 (1H, s), 7.17 (1H, d, J=2 Hz, changed to s with D_2O), 9.02 (1H, br s, indole NH).

Dimethyl 7-Hydroxy-4-methyl-1*H*-indole-2,5-dicarboxylate (30) from 19a DMSO (93 μl, 1.3 mmol) was added to a cooled (−76 °C) CH_2Cl_2 solution (2 ml) of 10% v/v $(COCl)_2$ in CH_2Cl_2 (0.38 ml, 0.44 mmol) under an Ar atmosphere, and the mixture was stirred for 5 min. A CH_2Cl_2 solution (2 ml) of **19a** (35 mg, 0.11 mmol) was added to this, and stirring was continued at −76—−72 °C for 30 min. Et_3N (0.30 ml, 2.2 mmol) was added dropwise and the resulting mixture was stirred at −72 °C for 5 min and at −20—−10 °C for 40 min. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with EtOAc. Usual work-up gave a residue, which was then treated with Et_3N (0.3 ml, 2 mmol) in CH_2Cl_2 (3 ml) under reflux for 10 min. The same work-up as described in the previous report[11] followed by purification by PTLC (1% MeOH–CH_2Cl_2) afforded **30** (23.5 mg, 82%) as colorless prisms, mp 264—266 °C (dec.) (MeOH–CH_2Cl_2). HR-MS Calcd for $C_{13}H_{13}NO_5$: 263.0793. Found: 263.0791. MS *m/z*: 263 (M^+, 77), 231 (100), 216 (16), 200 (23), 171 (36), 89 (23). IR (KBr) cm^{-1}: 1700, 1663. ^{1}H-NMR (DMSO-d_6) δ: 2.63 (3H, s), 3.78 (3H, s), 3.86 (3H, s), 7.14 (1H, s), 7.30 (1H, s), 9.60 (1H, br s, OH), 11.69 (1H, br s, NH).

Dimethyl 7-(2-Bromoethoxy)-4-methyl-1*H*-indole-2,5-dicarboxylate (31) NBS (38 ml, 0.21 mmol) was added to a cooled (0 °C) CH_2Cl_2 solution (2 ml) of **19a** (26 mg, 0.085 mmol) and Ph_3P (56 mg, 0.21 mmol), and the mixture was stirred at 26 °C for 30 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–CH_2Cl_2 (1 : 4)] afforded **31** (30 mg, 96%) as colorless needles, mp 159—160 °C (CH_2Cl_2–hexane). HR-MS Calcd for $C_{15}H_{16}{}^{81}BrNO_5$ and $C_{15}H_{16}{}^{79}BrNO_5$: 371.0192 and 369.0211. Found: 371.0194 and 369.0198. MS *m/z*: 371 (100) and 369 (98) (M^+), 340 (19) and 338 (21), 339 (22) and 337 (20), 262 (21), 258 (56), 230 (92), 202 (50), 198 (35), 170 (76), 115 (34). IR (KBr) cm^{-1}: 1720, 1697. ^{1}H-NMR δ: 2.75 (3H, s), 3.70 (2H, t, J=6 Hz), 3.90 (3H, s), 3.95 (3H, s), 4.46 (2H, t, J=6 Hz), 7.29 (1H, s), 7.35 (1H, d, J=2 Hz), 9.26 (1H, br s, NH).

Alternative Formation of 30 from 31 A mixture of **31** (20 mg, 0.054 mmol), Zn dust (18 mg, 0.28 matom), and NH_4Cl (3 mg, 0.06 mmol) in iso-PrOH–H_2O (14 : 1) (3 ml) was refluxed for 30 min. After the mixture had cooled, saturated NH_4Cl–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up gave a crystalline residue, which was recrystallized from MeOH–CH_2Cl_2 to afford **30** (13 mg, 91%) as colorless prisms, mp 264—266 °C (dec.).

Methyl 5-(1-Hydroxy-2-propen-1-yl)-1*H*-pyrrole-2-carboxylate (32) A 0.5 M THF solution of vinylmagnesium bromide (3.0 ml, 1.5 mmol) was added dropwise to a cooled (—20 °C) THF solution (3 ml) of **11** (76 mg, 0.50 mmol), and the mixture was stirred at that temperature for 15 min. Saturated NH_4Cl–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [benzene–EtOAc (7 : 2)] afforded **32** (83 mg, 92%) as a colorless syrup. GC-MS *m/z*: 163 ($M^+ - H_2O$, 100), 131 (63), 104 (72), 77 (30), 51 (28). IR ($CHCl_3$) cm^{-1}: 1691. ^{1}H-NMR δ: 3.50 (1H, br s, OH), 3.80 (3H, s), 5.10—5.47 (3H, m), 5.85—6.27 (1H, m), 6.04 (1H, dd, J=4, 2.5 Hz, changed to d, J=4 Hz with D_2O), 6.81 (1H, dd, J=4, 2.5 Hz, changed to d, J=4 Hz with D_2O),

9.95 (1H, br s, NH).

Methyl 5-Acryloyl-1*H*-pyrrole-2-carboxylate (33) A slurry of **32** (40 mg, 0.22 mmol) and MnO_2 (192 mg, 2.21 mmol) in CH_2Cl_2 (4 ml) was stirred at 27 °C for 45 min. The mixture was filtered through a Celite bed and the Celite was washed with CH_2Cl_2. The combined organic layer was evaporated and purification of the residue by PTLC [benzene–EtOAc (29 : 1)] afforded **33** (34 mg, 86%) as colorless scales, mp 95—96 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_9H_9NO_3$: C, 60.33; H, 5.06; N, 7.82. Found: C, 60.24; H, 5.10; N, 7.83. HR-MS Calcd for $C_9H_9NO_3$: 179.0582. Found: 179.0586. MS *m/z*: 179 (M^+, 65), 164 (17), 152 (19), 148 (24), 120 (100), 55 (24), 27 (27). IR (KBr) cm^{-1}: 1720, 1700, 1651. ^{1}H-NMR δ: 3.89 (3H, s), 5.83 (1H, dd, J=10.5, 2 Hz), 6.50 (1H, dd, J=17, 2 Hz), 6.90 (2H, d, J=2 Hz, changed to s with D_2O), 7.00 (1H, dd, J=17, 10.5 Hz), 10.26 (1H, br s, NH).

Methyl 5-[2-(2-Nitroethyl)-1,3-dioxolan-2-yl]-1*H*-pyrrole-2-carboxylate (34) HOAc (0.58 ml, 10 mmol) was added dropwise to a cooled (0 °C) solution of **33** (121 mg, 0.67 mmol) and $NaNO_2$ (700 mg, 10.1 mmol) in THF (8 ml) and the mixture was stirred at 27 °C for 13.5 h. H_2O was added and the solution was carefully adjusted to pH 6—7 with saturated $NaHCO_3$–H_2O. Extraction with CH_2Cl_2 followed by usual work-up gave a residue (159 mg), which was dissolved in CH_2Cl_2 (6 ml), and then 1,2-bis(trimethylsilyloxy)ethane (1.66 ml, 6.77 mmol) and TMSOTf (98 μl, 0.51 mmol) were successively added to this under an Ar atmosphere at 0 °C. The mixture was stirred at that temperature for 30 min and at 27 °C for 23 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–CH_2Cl_2 (2 : 5)] afforded **34** (93 mg, 51%) as a colorless glass. HR-MS Calcd for $C_{11}H_{14}N_2O_6$: 270.0851. Found: 270.0829. MS *m/z*: 270 (M^+, 8), 239 (3), 196 (90), 164 (100), 120 (48). IR ($CHCl_3$) cm^{-1}: 1702, 1557, 1383. ^{1}H-NMR δ: 2.68 (2H, t, J=7 Hz), 3.74—4.16 (4H, m), 3.85 (3H, s), 4.46 (2H, t, J=7 Hz), 6.17 (1H, dd, J=4, 3 Hz), 6.81 (1H, dd, J=4, 3 Hz), 9.42 (1H, br s, NH).

Methyl 5-[2-(3-Hydroxy-2-nitrohex-1-yl)-1,3-dioxolan-2-yl]-1*H*-pyrrole-2-carboxylate (35) iso-Pr_2NH (90 μl, 0.64 mmol) was added to a DMSO solution (3 ml) of **34** (58 mg, 0.21 mmol) and PrCHO (76 μl, 0.86 mmol), and the mixture was stirred at 27 °C for 2.5 h. Citric acid–H_2O (0.1 N) was added and the whole was extracted with EtOAc. The organic layer was washed with H_2O, while keeping the pH of the aqueous layer at 7 with a few drops of saturated $NaHCO_3$–H_2O. Usual work-up and purification by PTLC [hexane–EtOAc (5 : 2)] afforded **35** (66 mg, 90%) as a colorless glass. HR-MS Calcd for $C_{15}H_{22}N_2O_7$: 342.1426. Found: 342.1416. MS *m/z*: 342 (M^+, 2), 270 (3), 239 (2), 222 (2), 196 (100), 164 (87), 120 (42). IR ($CHCl_3$) cm^{-1}: 1702, 1556. ^{1}H-NMR of two diastereomers δ: 0.76—1.07 (3H, m), 1.15—1.65 (4H, m), 2.03, 2.59 (total 1H, br s each, OH), 2.37, 2.45 (total 1H, dd each, J=16, 2.5 Hz), 2.94, 2.95 (total 1H, dd each, J=16, 9.5 Hz), 3.71—4.17 (5H, m), 3.82 (3H, s), 4.56—4.87 (1H, m), 6.17 (1H, dd, J=4, 3 Hz, changed to d, J=4 Hz with D_2O), 6.81 (1H, dd, J=4, 3 Hz, changed to d, J=4 Hz with D_2O), 9.49 (1H, br s, NH).

Methyl 5-[(*E*)-1-Oxo-3-(2-propyl-1,3-dioxolan-2-yl)-2-propenyl]-1*H*-pyrrole-2-carboxylate (37) PCC (271 mg, 1.26 mmol) was added to a slurry of **35** (43 mg, 0.13 mmol) and NaOAc (21 mg, 0.26 mmol) in CH_2Cl_2 (8 ml), and the mixture was stirred at 27 °C for 13 h. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. The organic layer was successively washed with saturated $CuSO_4$–H_2O and saturated $NaHCO_3$–H_2O, and worked up as usual to give a residue (48 mg). This was dissolved in CH_2Cl_2 (1.5 ml), and then 2-ethyl-2-methyl-1,3-dioxolane (732 mg, 0.31 mmol) and $BF_3 \cdot OEt_2$ (62 μl, 0.50 mmol) were successively added at 0 °C, and the mixture was stirred at that temperature for 30 min and at 27 °C for 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 [benzene–EtOAc (9 : 1)] afforded crude **37** (33 mg), which was further purified by PTLC [hexane–EtOAc (6 : 1)] to give **37** (26.5 mg, 72%) as a colorless glass. HR-MS Calcd for $C_{15}H_{19}NO_5$: 293.1262. Found: 293.1266. MS *m/z*: 293 (M^+, 3), 250 (100), 218 (10), 190 (12), 174 (42), 146 (26), 120 (26), 115 (34), 43 (22). IR ($CHCl_3$) cm^{-1}: 1721, 1662, 1623. ^{1}H-NMR δ: 0.90 (3H, t, J=6.5 Hz), 1.20—1.97 (4H, m), 3.75—4.14 (4H, m), 3.89 (3H, s), 6.81—7.02 (4H, m), 10.11 (1H, br s, NH).

Methyl 5-[2-(2-Acetamido-3-acetoxy-1-hexyl)-1,3-dioxolan-2-yl]-1*H*-pyrrole-2-carboxylate (38) $NaBH_4$ (39 mg, 1.0 mmol) was added to a cooled (0 °C) MeOH suspension (4 ml) of **35** (58 mg, 0.17 mmol) and $NiCl_2 \cdot 6H_2O$ (81 mg, 0.34 mmol), and the mixture was stirred at 0 °C for 10 min and at 26 °C for 1 h. Saturated NH_4Cl–H_2O and saturated $NaHCO_3$–H_2O were added and the whole was thoroughly extracted with 10% MeOH–CH_2Cl_2. Usual work-up gave a residue (53 mg), which was dissolved in CH_2Cl_2 (2 ml) and this solution was stirred with Ac_2O (0.5 ml, 5 mmol) and pyridine 0.8 ml, 10 mmol) at 25 °C for 14 h. The volatile materials were removed *in vacuo*, and saturated $NaHCO_3$–H_2O was added. The whole was extracted with CH_2Cl_2 and worked up as usual. Purification by PTLC [benzene–EtOAc (1 : 1)] afforded **38** (50.5 mg, 75%) as a colorless glass. HR-MS Calcd for $C_{19}H_{28}N_2O_7$: 396.1895. Found: 396.1901. MS *m/z*: 396 (M^+, 2), 365 (1), 281 (1), 222 (1), 196 (100), 164 (36), 120 (13), 43 (28). IR ($CHCl_3$) cm^{-1}: 1730 (sh), 1702, 1666. ^{1}H-NMR of two diastereomers (*ca.* 1 : 1) δ: 0.84 (3H, dif. t, J=7 Hz), 1.01—1.64 (4H, m), *ca.* 1.77—2.17 (2H, m), 1.88, 1.94, 2.02, 2.06 (total 6H, s each), 3.68—4.13 (4H, m), 3.84 (3H, s), 4.13—4.53 (1H, m), 4.79—5.05 (1H, m), 5.63, 5.87 (total 1H, d each, J=9.5, 8.5 Hz, NH), 6.14 (1H, dd, J=3.5, 2.5 Hz, changed to d, J=3.5 Hz with D_2O), 6.81 (1H, dd, J=3.5, 2.5 Hz, changed to d, J=3.5 Hz with D_2O), 9.76—10.13 (1H, br s, pyrrole NH).

Methyl 5-[2-(2-Acetamido-3-hydroxy-1-hexyl)-1,3-dioxolan-2-yl]-1*H*-pyrrole-2-carboxylate (39) A MeOH solution (3 ml) of **38** (50.5 mg, 0.13 mmol) and K_2CO_3 (30 mg, 0.22 mmol) was stirred at 23 °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 [benzene–EtOAc (1 : 1)] afforded **39** (42 mg, 93%) as a colorless glass. HR-MS Calcd for $C_{17}H_{26}N_2O_6$: 354.1789. Found: 354.1813. MS *m/z*: 354 (M^+, 2), 282 (7), 238 (5), 223 (5), 196 (100), 164 (55), 152 (12), 120 (25), 43 (17). IR ($CHCl_3$) cm^{-1}: 1701, 1655. ^{1}H-NMR of two diastereomers δ: 0.72—1.04 (3H, m), 1.12—1.60 (4H, m), 1.88, 1.91 (total 3H, s each), *ca.* 2.29—2.70, *ca.* 3.25—3.84 (total 1H, br s each, OH), 3.46—4.19 (6H, m), 3.84 (3H, s), 6.06—6.37 (1H, m, NH), 6.15 (1H, dd, J=3.5, 2.5 Hz, changed to d, J=3.5 Hz with D_2O), 6.81 (1H, dd, J=3.5, 2.5 Hz, changed to d, J=3.5 Hz with D_2O), 10.07, 10.26 (total 1H, br s each, NH).

Methyl 5-[2-(2-Acetamido-3-oxo-1-hexyl)-1,3-dioxolan-2-yl]-1*H*-pyrrole-2-carboxylate (40) A CH_2Cl_2 solution (3 ml) of **39** (17.5 mg, 0.049 mmol) and Dess–Martin reagent (126 mg, 0.297 mmol) was refluxed for 2.5 h. After it had cooled, saturated $Na_2S_2O_3$–H_2O and saturated $NaHCO_3$–H_2O were added and the whole was extracted with EtOAc. Usual work-up and purification by PTLC [benzene–EtOAc (2 : 3)] afforded **40** (15.5 mg, 89%) as a colorless glass. HR-MS Calcd for $C_{17}H_{24}N_2O_6$: 352.1633. Found: 352.1635. MS *m/z*: 352 (M^+, 2), 281 (1), 262 (1), 222 (3), 196 (100), 164 (53), 120 (19), 71 (5), 43 (15). IR ($CHCl_3$) cm^{-1}: 1704, 1663. ^{1}H-NMR δ: 0.90 (3H, t, J=7 Hz), 1.36—1.81 (2H, m), 1.94 (3H, s), 2.18—2.68 (4H, m), 3.65—4.14 (4H, m), 3.83 (3H, s), 4.66 (1H, ddd, J=12, 9.5, 7.5 Hz), 6.13 (1H, dd, J=3.5, 3 Hz, changed to d, J=3.5 Hz with D_2O), 6.46 (1H, d, J=7.5 Hz, NH), 6.81 (1H, dd, J=3.5, 3 Hz, changed to d, J=3.5 Hz with D_2O), 9.51 (1H, br s, pyrrole NH).

Methyl 5-Acetamido-7-(2-hydroxyethoxy)-4-propyl-1*H*-indole-2-carboxylate (41) TMSOTf (47 μl, 0.24 mmol) was added to a cooled (0 °C) CH_2Cl_2 solution (2 ml) of **40** (8.5 mg, 0.02 mmol) and 1,2-bis(trimethylsilyloxy)ethane (0.12 ml, 0.49 mmol), and the mixture was stirred at 23 °C for 68 h. HOAc–H_2O (1 : 1) (0.5 ml) was added and the mixture was further stirred at 23 °C for 30 min. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with 10% MeOH–CH_2Cl_2. Usual work-up and purification by PTLC (3% MeOH–CH_2Cl_2) afforded **41** (2 mg, 25%) as a colorless powder. HR-MS Calcd for $C_{17}H_{22}N_2O_5$: 334.1527. Found: 334.1518. MS *m/z*: 334 (M^+, 100), 325 (67), 291 (10), 273 (14), 229 (31), 219 (25), 215 (19), 187 (65), 43 (80). IR ($CHCl_3$) cm^{-1}: 1708, 1667. ^{1}H-NMR of major and minor rotamers (400 MHz, 10% CD_3OD–$CDCl_3$) δ: 0.97, 0.90 (total 3H, t each, J=7 Hz), 1.57—1.68 (2H, m), 2.20, 1.87 (total 3H, s each), 2.72—2.81 (2H, m), 3.95, 3.96 (total 3H, s each), *ca.* 3.93—4.03, 4.14—4.19 (total 4H, m), 6.76, 6.48 (total 1H, s each), 7.21, 7.25 (total 1H, s each).

Ethyl (*S*)-3,4-Di(benzyloxy)butyrate (42) TfOH (95 μl, 1.1 mmol) was added dropwise to a cooled (0 °C) solution of **8** (1.060 g, 7.162 mmol) and benzyl 2,2,2-trichloroacetimidate (4.00 ml, 21.5 mmol) in cyclohexane (16 ml) and CH_2Cl_2 (8 ml), and the mixture was stirred at 0 °C for 10 min and at 26 °C for 14 h. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up gave a residue (6.46 g), which was passed through an Al_2O_3 (50 g) column using hexane–CH_2Cl_2 (2 : 3) to remove trichloroacetamide, affording a crude product (3.89 g). This was purified by SiO_2 (100 g) column chromatography using hexane–CH_2Cl_2 (1 : 1) to give **42** (1.226 g, 52%) as a colorless oil. $[\alpha]_D^{25}$ −13.9° (c=2.18, $CHCl_3$). MS *m/z*: 237 (M^+ − Bn, 1), 192 (1), 131 (23), 108 (7), 91 (100), 85 (10), 65 (7). IR (neat) cm^{-1}: 1734. ^{1}H-NMR δ: 1.18

(3H, t, J=7 Hz), 2.58 (2H, d, J=6.5 Hz), 3.47 (1H, dd, J=11, 5.5 Hz), 3.60 (1H, dd, J=11, 5 Hz), 3.90—4.19 (1H, m), 4.08 (2H, q, J=7 Hz), 4.49 (2H, s), 4.61 (2H, s), 7.06—7.44 (10H, m).

(*S*)-3,4-Di(benzyloxy)butanal (44) DIBAL in toluene (1 M, 1.14 ml, 1.14 mmol) was added to a cooled (−76 °C) toluene solution (4 ml) of **42** (268 mg, 0.817 mmol) under an Ar atmosphere, and the mixture was stirred at −76—−63 °C for 1 h. MeOH (2 ml) was added and the mixture was stirred at −63—−61 °C for 10 min. HOAc–H_2O (1 : 4) (4 ml) was added and the mixture was further stirred at 26 °C for 15 min. H_2O was added and the whole was extracted with EtOAc. The organic layer was washed with saturated $NaHCO_3$–H_2O and treated as usual. Purification by PTLC [hexane–EtOAc (6 : 1)] afforded **44** (203 mg, 87%) and (*S*)-3,4-di(benzyloxy)butanol (**43**) (15.5 mg, 7%). **44**: Colorless oil. $[\alpha]_D^{25}$ −23.5° (c=2.03, $CHCl_3$). MS m/z: 193 (M^+ − Bn, 3), 107 (13), 91 (100), 87 (17), 65 (10). IR (neat) cm^{-1}: 1730. ^{1}H-NMR δ: 2.64 (2H, dd, J=6, 2 Hz), 3.49 (1H, dd, J=10, 6 Hz), 3.61 (1H, dd, J=10, 5 Hz), 3.93—4.25 (1H, m), 4.52 (2H, s), 4.52 (1H, d, J=13 Hz), 4.66 (1H, d, J=13 Hz), 7.09—7.46 (10H, m), 9.72 (1H. t, J=2 Hz). **43**: Colorless oil. $[\alpha]_D^{25}$ −31.5° (c=1.31, $CHCl_3$). MS m/z: 195 (M^+ − Bn, 4), 180 (3), 107 (15), 91 (100), 65 (8). ^{1}H-NMR δ: 1.79 (2H, dt, J=6, 6 Hz), 2.29 (1H, br s, OH), 3.38—4.08 (5H, m), 4.50 (1H, d, J=11 Hz), 4.51 (2H, s), 4.70 (1H, d, J=11 Hz), 7.08—7.49 (10H, m).

Dess–Martin Oxidation of 43 A mixture of **43** (75 mg, 0.26 mmol) and Dess–Martin reagent (445 mg, 1.05 mmol) in CH_2Cl_2 (4 ml) was refluxed for 4 h. The same work-up as for the preparation of **40** from **39**, followed by purification using PTLC [hexane–EtOAc (6 : 1)] afforded **44** (56 mg, 75%).

Benzyl (3*RS*,5*S*)-5,6-Di(benzyloxy)-3-hydroxyhexanoate (46) AcOBn (82 μl, 0.57 mmol) was added to a cooled (−74 °C) THF solution (3 ml) of LDA prepared from iso-Pr_2NH (0.12 ml, 0.86 mmol) and 1.66 M BuLi in hexane (0.34 ml, 0.56 mmol) under an Ar atmosphere at −20 °C for 10 min, and the mixture was stirred at −74—−71 °C for 30 min. A THF solution (1.5 ml) of **44** (azeotropically dried with benzene prior to use) (95 mg, 0.33 mmol) was added dropwise to the above, and the mixture was stirred at −71—−66 °C 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 (4 : 1)] afforded **46** (113 mg, 78%) and benzyl (5*RS*,7*S*)-7,8-di(benzyloxy)-5-hydroxy-3-oxooctanoate (**45**) (16 mg, 10%) in order of increasing polarity. **46**: Colorless syrup. MS m/z: 343 (M^+ − Bn, 1), 295 (2), 237 (3), 221 (3), 181 (5), 107 (3), 91 (100), 65 (4). IR (neat) cm^{-1}: 1729. ^{1}H-NMR of two diastereomers δ: 1.69 (2H, dt, J=6.5, 6.5 Hz), 2.28—2.69 (2H, m), 3.14 (1H, br s, OH), 3.34—*ca.* 3.73 (2H, m), 3.64—4.04 (1H, m), *ca.* 4.41—4.65, 4.70 (total 4H, m and d, J=11.5 Hz), 5.08 (2H, s), 7.02—7.54 (15H, m). **45**: Colorless syrup. MS m/z: 368 (M^+ − BnOH, 0.2), 277 (2), 181 (3), 107 (13), 91 (100), 79 (10), 65 (8), 43 (7). IR (neat) cm^{-1}: 1742, 1713. ^{1}H-NMR of two diastereomers δ: 1.53—1.85 (2H, m), 2.38—2.83 (2H, m), 3.35—3.71 (4H, m), 3.46 (1H, s, OH), 3.71—4.40 (2H, m), 4.40—4.72, 4.72 (total 4H, m, d, J=11.5 Hz), 5.13 (2H, s), 7.07—7.49 (15H, m).

Benzyl (*S*)-5,6-Di(benzyloxy)-3-oxohexanoate (47) A mixture of **46** (128 mg, 0.295 mmol) and Dess–Martin reagent (625 mg, 1.47 mmol) in CH_2Cl_2 (6 ml) was refluxed for 5 h. The same work-up as for the preparation of **40**, followed by purification using PTLC [hexane–EtOAc (6 : 1)] afforded **47** (110 mg, 86%) as a colorless syrup. $[\alpha]_D^{25}$ −13.3° (c=1.80, $CHCl_3$). MS m/z: 414 (M^+ − H_2O, 0.3), 341 (0.5), 311 (1), 293 (1), 217 (6), 181 (3), 127 (5), 107 (5), 91 (100), 65 (5). IR (neat) cm^{-1}: 1743, 1719. ^{1}H-NMR δ: 2.68 (1H, dd, J=18, 6.5 Hz), 2.87 (1H, dd, J=18, 6 Hz), 3.31—3.71 (4H, m), 3.88—4.24 (1H, m), 4.38—4.71 (4H, m), 5.11 (2H, s), 7.05—7.48 (15H, m). This compound partially existed as an enol form, whose ^{1}H-NMR signals appeared at δ: 2.47 (2H, d, J=6 Hz), 12.06 (1H, br s, OH).

Benzyl (α*RS*)-α-[(3*S*)-3,4-Di(benzyloxy)-1-oxobutyl]-5-(methoxycarbonyl)-γ-oxo-1*H*-pyrrole-2-butyrate (48) *tert*-BuOK (26 mg, 0.23 mmol) was added to a cooled (0 °C) THF solution (3 ml) of **47** (98 mg, 0.23 mmol) under an Ar atmosphere, and the mixture was stirred at that temperature for 20 min. To this solution, **18** (67 mg, 0.27 mmol) was added portionwise, and the mixture was stirred at 0 °C for 10 min and at 23 °C for 3 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 (7 : 2)] afforded **48** (117 mg, 86%), recovered **18** (18.5 mg, 28% from the used **18**), and recovered **47** (12 mg, 12%) in order of decreasing polarity. **48**: Colorless syrup. HR-MS Calcd for $C_{35}H_{35}NO_8$: 597.2361. Found: 597.2380. MS m/z: 597 (M^+, 0.1), 579 (0.1), 506 (0.1), 489 (1), 476 (1), 471 (1), 398 (1), 383 (1), 342 (2), 306 (2), 292 (3), 216 (4), 152 (4), 120 (7), 91 (100), 79 (5), 65 (4). IR ($CHCl_3$) cm^{-1}: 1740 (sh), 1719, 1663. ^{1}H-NMR of two diastereomers (*ca.* 1 : 1) δ: *ca.* 2.70—3.12 (2H, m), *ca.* 3.12—3.75 (4H, m), 3.84 (3H, s), *ca.* 3.96—4.38 (2H, m), 4.29—4.69 (4H, m), 5.06, 5.08 (total 2H, s each), 6.70—6.98 (2H, m), 6.98—7.46 (15H, m), 9.91 (1H, br s, NH).

5-Benzyl 2-Methyl 4-[(*S*)-2,3-Di(benzyloxy)propyl]-7-(2-hydroxyethoxy)-1*H*-indole-2,5-dicarboxylate (49a) TMSOTf (14 μl, 0.073 mmol) was added to a cooled (0 °C) CH_2Cl_2 solution (3 ml) of **48** (21 mg, 0.035 mmol) and 1,2-bis(trimethylsilyloxy)ethane (0.22 ml, 0.90 mmol) under an Ar atmosphere, and the mixture was stirred at 0 °C for 10 min and at 26 °C for 48 h. HOAc–H_2O (1 : 1) (0.5 ml) was added and the mixture was further stirred at 24 °C for 30 min. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [benzene–EtOAc (4 : 1)] afforded **49a** (9 mg, 41%), benzyl α-[2-[(*S*)-2,3-di(benzyloxy)propyl]-1,3-dioxolan-2-yl]-2-[5-(methoxycarbonyl)-1*H*-pyrrol-2-yl]-1,3-dioxolane-2-propanoate (**51**) (4.5 mg, 19%), and methyl 5-[5-(*S*)-2,3-di(benzyloxy)propyl]-4-(benzyloxycarbonyl)-2-furanyl]-1*H*-pyrrole-2-carboxylate (**50**) (3 mg, 15%). **49a**: Colorless glass. HR-MS Calcd for $C_{37}H_{37}NO_8$: 623.2517. Found: 623.2514. $[\alpha]_D^{25}$ −3.6° (c=1.1, $CHCl_3$). MS m/z: 623 (M^+, 4), 394 (3), 382 (6), 290 (3), 181 (3), 91 (100). IR ($CHCl_3$) cm^{-1}: 1709. ^{1}H-NMR (400 MHz) δ: 3.44—3.58 (4H, m), 3.88 (3H, s), 3.89—3.97 (1H, m), 4.08—4.13 (2H, m), 4.25—4.30 (2H, m), 4.30 (1H, d, J=11.5 Hz), 4.45 (1H, d, J=12 Hz), 4.49 (1H, d, J=11.5 Hz), 4.50 (1H, d, J=12 Hz), 5.29 (2H, s), 7.01—7.06 (2H, m), 7.12—7.16 (3H, m), 7.23—7.38 (9H, m), 7.38—7.42 (3H, m), 10.06 (1H, br s, NH). **50**: Colorless needles, mp 87—89 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{35}H_{33}NO_7$: C, 72.52; H, 5.74; N, 2.42. Found: C, 72.48; H, 5.81; N, 2.69. HR-MS Calcd for $C_{35}H_{33}NO_7$: 579.2255. Found: 579.2266. $[\alpha]_D^{25}$ +6.9° (c=1.0, $CHCl_3$). MS m/z: 579 (M^+, 9), 548 (1), 488 (1), 471 (1), 380 (3), 338 (45), 306 (11), 181 (3), 91 (100), 65 (6). IR (KBr) cm^{-1}: 1713, 1688. ^{1}H-NMR δ: 3.29 (2H, d, J=6.5 Hz), 3.56 (2H, d, J=4.5 Hz), 3.85 (3H, s), *ca.* 3.85—4.16 (1H, m), 4.42 (1H, d, J=11.5 Hz), 4.54 (2H, s), 4.60 (1H, d, J=11.5 Hz), 5.23 (2H, s), 6.39 (1H, dd, J=4, 3 Hz, changed to d, J=4 Hz with D_2O), 6.77 (1H, s), 6.90 (1H, dd, J=4, 3 Hz, changed to d, J=4 Hz with D_2O), 7.03—7.48 (15H, m), 9.37 (1H, br s, indole NH). **51**: Colorless glass. MS m/z: 564 (M^+ − CH_2OBn, 0.4), 430 (4), 327 (16), 196 (55), 164 (17), 115 (7), 91 (100), 65 (4). IR ($CHCl_3$) cm^{-1}: 1727, 1702. ^{1}H-NMR of two diastereomers δ: *ca.* 1.49—3.14 (5H, m), 3.39—4.06 (11H, m), 3.79 (3H, s), 4.41—4.64 (4H, m), 5.07, 5.09 (total 2H, s each), 6.08—6.19 (1H, m), 6.71—6.85 (1H, m), 7.12—7.47 (15H, m), 9.12 (1H, br s, NH).

5-Benzyl 2-Methyl 4-[(*S*)-2,3-Di(benzyloxy)propyl]-7-(3-hydroxypropyloxy)-1*H*-indole-2,5-dicarboxylate (49b) In a similar manner to the procedure of entry 2 in Table 1, **48** (74 mg, 0.12 mmol) was stirred with 2-ethyl-2-methyl-1,3-dioxane (808 mg, 6.22 mmol) and $BF_3 \cdot OEt_2$ (92 μl, 0.75 mmol) in CH_2Cl_2 (3 ml) at 20 °C for 44 h. The same work-up as that of entry 2, followed by separation by PTLC [hexane–EtOAc (1 : 1)] afforded crude **49b** (50 mg) and crude **50** (13.5 mg) in order of decreasing polarity. The former was further purified by PTLC (1% MeOH–CH_2Cl_2) to give **49b** (43 mg, 54%), and the latter was also purified by PTLC [hexane–CH_2Cl_2 (1 : 3)] to afford **50** (7.5 mg, 10%). **49b**: Colorless glass. HR-MS Calcd for $C_{38}H_{39}NO_8$: 637.2673. Found: 637.2674. $[\alpha]_D^{25}$ −4.5° (c=0.72, $CHCl_3$). MS m/z: 637 (M^+, 4), 408 (2), 396 (5), 304 (2), 181 (1), 91 (100), 65 (3), 31 (3). IR ($CHCl_3$) cm^{-1}: 1709. ^{1}H-NMR (400 MHz) δ: 2.13 (2H, tt, J=6, 6 Hz), 3.45—3.59 (4H, m), *ca.* 3.88—3.97 (1H, m), 3.91 (3H, s), 3.94 (2H, t, J=6 Hz), 4.30 (2H, t, J=6 Hz), 4.32 (1H, d, J=12 Hz), 4.46 (1H, d, J=12 Hz), 4.50 (1H, d, J=12 Hz), 4.51 (1H, d, J=12 Hz), 5.30 (2H, s), 7.02—7.07 (2H, m), 7.13—7.18 (3H, m), 7.24—7.44 (12H, m), 9.45 (1H, br s, NH).

5-Benzyl 2-Methyl 7-(2-Acetoxyethoxy)-4-[(*S*)-2,3-di(benzyloxy)propyl]-1*H*-indole-2,5-dicarboxylate (52a) In the same manner as described for the preparation of **27** from **19e**, **49a** (25 mg, 0.040 mmol) was acetylated with Ac_2O (0.30 ml, 3.2 mmol) and pyridine (0.50 ml, 6.2 mmol) in CH_2Cl_2 (1 ml) at 23 °C for 5 h to afford **52a** (26 mg, 97%) as a colorless glass after purification by PTLC [hexane–EtOAc (2 : 1)]. HR-MS Calcd for $C_{39}H_{39}NO_9$: 665.2622. Found: 665.2635. $[\alpha]_D^{26}$ −5.2° (c=1.3, $CHCl_3$). MS m/z: 665 (M^+, 3), 544 (1), 468 (1), 436 (2), 424 (3), 181 (1), 91 (100), 87 (49), 65 (2), 43 (14). IR ($CHCl_3$) cm^{-1}: 1721 (sh), 1707. ^{1}H-NMR δ: 2.10 (3H, s), 3.31—3.75 (4H, m), 3.79—4.08 (1H, m), 3.91 (3H, s), 4.19—4.62 (8H, m), 5.28 (2H, s), 6.91—7.52 (16H, m), 7.43 (1H, d, J=2.5 Hz, changed to s with D_2O), 9.25 (1H, br s, NH).

5-Benzyl 2-Methyl 7-(3-Acetoxypropyloxy)-4-[(*S*)-2,3-di(benzyloxy)propyl]-1*H*-indole-2,5-dicarboxylate (52b) Similarly, **49b** (45 mg, 0.071 mmol) was acetylated with Ac_2O (0.50 ml, 5.3 mmol) and pyridine

(0.80 ml, 9.9 mmol) in CH_2Cl_2 (2 ml) at 16 °C for 5 h to afford **52b** (46.5 mg, 97%) as a colorless glass after purification by PTLC [hexane–EtOAc (2 : 1)]. HR-MS Calcd for $C_{40}H_{41}NO_9$: 679.2779. Found: 679.2806. $[\alpha]_D^{26}$ −4.2° (c=0.73, $CHCl_3$). MS m/z: 679 (M^+, 4), 450 (3), 438 (5), 101 (27), 91 (100), 73 (3), 65 (2), 43 (14). IR ($CHCl_3$) cm^{-1}: 1720 (sh), 1708. ^{1}H-NMR δ: 2.05 (3H, s), 2.18 (2H, tt, J=6, 6 Hz), *ca.* 3.29—3.76 (4H, m), 3.79—4.08 (1H, m), 3.90 (3H, s), 4.22 (2H, t, J=6 Hz), 4.27 (1H, d, J=12 Hz), 4.31 (2H, t, J=6 Hz), 4.46 (2H, s), 4.51 (1H, d, J=12 Hz), 5.28 (2H, s), 6.93—7.52 (16H, m), 7.42 (1H, d, J=2.5 Hz, changed to s with D_2O), 9.25 (1H, br s, NH).

7-(2-Acetoxyethoxy)-4-[(*S*)-2,3-di(benzyloxy)propyl]-2-(methoxycarbonyl)-1*H*-indole-5-carboxylic Acid (53a) In the same manner as described for the preparation of **28** from **27**, **52a** (18 mg, 0.027 mmol) in EtOAc (5 ml) was hydrogenated over 10% Pd–C (4 mg) at 19 °C for 4 h, followed by separation by PTLC (3% MeOH–CH_2Cl_2) to afford recovered **52a** (2 mg, 11%), **53a** (11.5 mg, 74%), and 7-[2-(acetoxy)-ethoxy]-4-[(*S*)-2-(benzyloxy)-3-hydroxypropyl]-2-(methoxycarbonyl)-1*H*-indole-5-carboxylic acid (debenzyl-**53a**) (0.5 mg, *ca.* 4%) in order of increasing polarity. **53a**: Colorless needles, mp 151.5—153.5 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{32}H_{33}NO_9$: C, 66.77; H, 5.78; N, 2.43. Found: C, 66.42; H, 5.77; N, 2.82. HR-MS Calcd for $C_{32}H_{33}NO_9$: 575.2153. Found: 575.2131. $[\alpha]_D^{25}$ −96.9° (c=0.665, $CHCl_3$). MS m/z: 575 (M^+, 3), 378 (2), 334 (7), 91 (50), 87 (100), 43 (22). IR (KBr) cm^{-1}: 1723, 1676. ^{1}H-NMR δ: 2.10 (3H, s), 3.43 (2H, d, J=6.5 Hz), 3.64 (2H, d, J=4.5 Hz), 3.80—4.19 (1H, m), 3.93 (3H, s), 4.19—4.69 (8H, m), 6.78—7.49 (12H, m), 9.33 (1H, br s, NH). Debenzyl-**53a**: Colorless powder: MS m/z: 467 ($M^+ - H_2O$, 4), 407 (1), 346 (3), 286 (2), 200 (2), 91 (19), 87 (100), 65 (3), 43 (23). IR ($CHCl_3$) cm^{-1}: 1712. ^{1}H-NMR (CD_3OD, only selected signals) δ: 2.03 (3H, s), 3.26—3.64 (4H, m), 3.91 (3H, s), 7.13—7.50 (7H, m).

7-(3-Acetoxypropyloxy)-4-[(*S*)-2,3-di(benzyloxy)propyl]-2-(methoxycarbonyl)-1*H*-indole-5-carboxylic Acid (53b) Similarly, **52b** (40 mg, 0.059 mmol) in EtOAc (8 ml) was hydrogenated over 10% Pd–C (10 mg) at 13 °C for 8 h, followed by separation by PTLC (3% MeOH–CH_2Cl_2) to afford recovered **52b** (6 mg, 15%), **53b** (26 mg, 75%), and 7-[3-(acetoxypropyl)oxy]-4-[(*S*)-2-(benzyloxy)-3-hydroxypropyl]-2-(methoxycarbonyl)-1*H*-indole-5-carboxylic acid (debenzyl-**53b**) (1 mg, *ca.* 4%) in order of increasing polarity. **53b**: Colorless needles, mp 140—142 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{33}H_{35}NO_9$: C, 67.22; H, 5.98; N, 2.38. Found: C, 67.25; H, 6.12; N, 2.38. HR-MS Calcd for $C_{33}H_{35}NO_9$: 589.2310. Found: 589.2340. $[\alpha]_D^{22}$ −95.9° (c=1.06, $CHCl_3$). MS m/z: 589 (M^+, 4), 348 (14), 316 (3), 288 (4), 216 (5), 138 (13), 101 (100), 91 (82), 73 (9), 43 (39). IR (KBr) cm^{-1}: 1726, 1711, 1675. ^{1}H-NMR δ: 2.07 (3H, s), 2.19 (2H, tt, J=6.5, 6.5 Hz), 3.42 (2H, d, J=6.5 Hz), 3.63 (2H, d, J=4.5 Hz), 3.80—4.71 (9H, m), 3.94 (3H, s), 6.75—7.49 (12H, m), 9.26 (1H, br s, NH). Debenzyl-**53b**: Colorless powder: $[\alpha]_D^{22}$ −144° (c=1.02, $CHCl_3$). MS m/z: 481 ($M^+ - H_2O$, 5), 360 (6), 318 (4), 200 (4), 101 (100), 91 (32), 73 (11), 43 (45). IR ($CHCl_3$) cm^{-1}: 1724, 1710. ^{1}H-NMR (CD_3OD) δ: 1.75—2.17 (2H, m), 1.91 (3H, s), 3.16—3.70 (4H, m), 3.70—4.27 (5H, m), 3.91 (3H, s), 4.52 (2H, s), 7.01—7.48 (7H, m).

Methyl (*S*)-6-(3-Acetoxypropyloxy)-2-(benzyloxymethyl)-1,2,4,7-tetrahydro-4-oxopyrano[4,3-*e*]indole-8-carboxylate (54) NaN_3 (10 mg, 0.15 mmol) was added to a cooled (−20 °C) CH_2Cl_2 solution (1.5 ml) of **53b** (9 mg, 0.02 mmol), CF_3CO_2H (50 μl, 0.65 mmol), and $(CF_3CO)_2O$ (50 μl, 0.35 mmol), and the mixture was stirred at that temperature for 15 min. The volatile materials were removed at 0 °C *in vacuo*, and saturated $NaHCO_3$–H_2O was added to the residue. The whole was extracted with CH_2Cl_2 and worked up as usual to afford **54** (6.5 mg, 88%) as colorless scales, mp 136.5—137 °C (CH_2Cl_2–hexane), after purification by PTLC [benzene–EtOAc (3 : 1)]. *Anal.* Calcd for $C_{26}H_{27}NO_8$: C, 64.85; H, 5.65; N, 2.91. Found: C, 64.68; H, 5.62; N, 2.91. HR-MS Calcd for $C_{26}H_{27}NO_8$: 481.1735. Found: 481.1722. $[\alpha]_D^{21}$ −63.3° (c=0.263, $CHCl_3$). MS m/z: 481 (M^+, 8), 360 (8), 101 (100), 91 (37), 73 (11), 43 (39). IR (KBr) cm^{-1}: 1745, 1712, 1687. ^{1}H-NMR δ: 2.05 (3H, s), 2.18 (2H, tt, J=6.5, 6.5 Hz), 3.19 (2H, d, J=7.5 Hz), 3.80 (2H, d, J=5 Hz), 3.94 (3H, s), 4.26 (2H, d, J=6 Hz), 4.29 (2H, d, J=6 Hz), 4.55—4.93 (1H, m), 4.63 (2H, s), 7.25 (1H, d, J=2 Hz), 7.34 (5H, s), 7.40 (1H, s), 9.38 (1H, br s, NH).

Methyl 7-(3-Acetoxypropyloxy)-4-[(*S*)-2,3-di(benzyloxy)propyl]-5-[(methoxycarbonyl)amino]-1*H*-indole-2-carboxylate (56) A benzene solution (4 ml) of **53b** (25 mg, 0.042 mmol), DPPA (27 μl, 0.13 mmol), and iso-Pr_2NEt (44 μl, 0.25 mmol) was refluxed for 18 h. The volatile materials were removed *in vacuo* and benzene (4 ml) was added to the residue. The resulting solution was refluxed for 8 h until the more polar spot of the acid azide was no longer detected on SiO_2 TLC [hexane–EtOAc (1 : 1)]. After the mixture had cooled, H_2O was added and the whole was extracted with EtOAc. The organic layer was successively washed with 0.1 N citric acid–H_2O and saturated $NaHCO_3$–H_2O. Usual work-up gave a crude residue (65 mg). A MeOH solution (5 ml) of the residue was refluxed for 3 h and the solvent was evaporated *in vacuo*. Purification of the residue by PTLC [benzene–EtOAc (4 : 1)] afforded **56** (18 mg, 69%) and **54** (1.5 mg, 7%). **56**: Colorless prisms, mp 111—113 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{34}H_{38}N_2O_9$: C, 66.00; H, 6.19; N, 4.53. Found: C, 66.15; H, 6.16; N, 4.51. HR-MS Calcd for $C_{34}H_{38}N_2O_9$: 618.2575. Found: 618.2586. $[\alpha]_D^{22}$ −14.1° (c=0.822, $CHCl_3$). MS m/z: 618 (M^+, 2), 586 (9), 345 (5), 213 (6), 101 (100), 91 (64), 73 (9), 43 (29). IR (KBr) cm^{-1}: 1737, 1700. ^{1}H-NMR (400 MHz) δ: 2.08 (3H, s), 2.20 (2H, tt, J=6, 6 Hz), 3.08 (1H, dd, J=14.5, 7.5 Hz), 3.15 (1H, dd, J=14.5, 4.5 Hz), 3.54 (1H, dd, J=10, 4.5 Hz), 3.57 (1H, dd, J=10, 5 Hz), 3.65 (3H, s), 3.86—3.93 (1H, m), 3.93 (3H, s), 4.24 (2H, t, J=6 Hz), 4.31 (2H, t, J=6 Hz), 4.46 (1H, d, J=11.5 Hz), 4.57 (1H, d, J=12 Hz), 4.60 (1H, d, J=12 Hz), 4.67 (1H, d, J=11.5 Hz), 7.10 (1H, d, J=2.5 Hz), 7.20—7.41 (11H, m), 8.32 (1H, br s, NH), 9.03 (1H, br s, indole NH).

Methyl 7-(3-Acetoxypropyloxy)-4-[(*S*)-2-(benzyloxy)-3-hydroxypropyl]-5-[(methoxycarbonyl)amino]-1*H*-indole-2-carboxylate (57) (Table 2, entry 1) $BF_3 \cdot OEt_2$ (10% v/v) in CH_2Cl_2 (0.15 ml, 0.12 mmol) was added to a cooled (0 °C) CH_2Cl_2 solution (1.5 ml) of **56** (12.5 mg, 0.020 mmol) and EtSH (0.15 ml, 2.0 mmol), and the mixture was stirred at 20 °C 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 PTLC [benzene–EtOAc (2 : 1)] afforded recovered **56** (4.5 mg, 36%), methyl 7-(3-acetoxypropyloxy)-4-[(*S*)-3-(benzyloxy)-2-hydroxypropyl]-5-[(methoxycarbonyl)amino]-1*H*-indole-2-carboxylate (**66**) (2.5 mg, 23%), **57** (2 mg, 19%) and methyl 7-(3-acetoxypropyloxy)-4-[(*S*)-2,3-dihydroxypropyl]-5-[(methoxycarbonyl)amino]-1*H*-indole-2-carboxylate (**67**) (1.5 mg, 17%) in order of increasing polarity. **57**: Colorless glass. HR-MS Calcd for $C_{27}H_{32}N_2O_9$: 528.2106. Found: 528.2089. $[\alpha]_D^{22}$ −26.1° (c=0.346, $CHCl_3$). MS m/z: 528 (M^+, 3), 496 (8), 345 (4), 213 (7), 101 (100), 91 (36), 73 (7), 43 (20). IR ($CHCl_3$) cm^{-1}: 1721. ^{1}H-NMR (400 MHz) δ: 2.05 (1H, br s, OH), 2.08 (3H, s), 2.20 (2H, ddt, J=6, 6, 6 Hz), 3.09 (1H, dd, J=14, 6.5 Hz), 3.15 (1H, dd, J=14, 7 Hz), 3.40—3.48 (1H, m, changed to δ 3.43, dd, J=12.5, 4.5 Hz with D_2O), 3.73 (3H, s), 3.76—3.83 (2H, m, changed to δ 3.76—3.83, 1H, m and δ 3.78, 1H, dd, J=12.5, 3.5 Hz with D_2O), 3.95 (3H, s), 4.21—4.27 (2H, m), 4.31 (2H, t, J=6 Hz), 4.56 (1H, d, J=11.5 Hz), 4.62 (1H, d, J=11.5 Hz), 7.03 (1H, d, J=2 Hz), 7.25 (1H, br s), 7.27—7.37 (5H, m), 8.21 (1H, br s, NH), 9.04 (1H, br s, indole NH). **66**: Colorless glass. HR-MS Calcd for $C_{27}H_{32}N_2O_9$: 528.2106. Found: 528.2132. $[\alpha]_D^{22}$ +8.2° (c=0.38, $CHCl_3$). MS m/z: 528 (M^+, 4), 496 (12), 213 (5), 101 (100), 91 (24), 73 (8), 43 (21). IR ($CHCl_3$) cm^{-1}: 1722. ^{1}H-NMR (400 MHz) δ: 2.07 (3H, s), 2.20 (2H, tt, J=6, 6 Hz), 2.80 (1H, br s, OH), 2.95 (1H, dd, J=14.5, 7.5 Hz), 3.04 (1H, dd, J=14.5, 4 Hz), 3.35 (1H, dd, J=9.5, 8 Hz), 3.61 (1H, dd, J=9.5, 3.5 Hz), 3.75 (3H, s), 3.94 (3H, s), 4.14—4.21 (1H, m), 4.24 (2H, t, J=6 Hz), 4.30 (2H, t, J=6 Hz), 4.52 (1H, d, J=12 Hz), 4.55 (1H, d, J=12 Hz), 7.10 (1H, d, J=2.5 Hz), 7.25 (1H, br s), 7.29—7.39 (5H, m), 8.40 (1H, br s, NH), 9.07 (1H, br s, indole NH). **67**: Colorless glass. HR-MS Calcd for $C_{20}H_{26}N_2O_9$: 438.1637. Found: 438.1652. $[\alpha]_D^{22}$ −4.4° (c=0.37, $CHCl_3$). MS m/z: 438 (M^+, 2), 406 (4), 362 (8), 101 (100), 73 (8), 43 (35). IR ($CHCl_3$) cm^{-1}: 1722. ^{1}H-NMR (400 MHz) δ: *ca.* 1.76—2.84 (2H, br m, OH), 2.07 (3H, s), 2.19 (2H, tt, J=6, 6 Hz), 2.95 (1H, dd, J=14.5, 7.5 Hz), 3.03 (1H, dd, J=14.5, 4.5 Hz), 3.46 (1H, dd, J=11, 7 Hz), 3.76 (1H, dd, J=11, 3.5 Hz), 3.77 (3H, s), 3.94 (3H, s), 4.03—4.11 (1H, m), 4.22 (2H, t, J=6 Hz), 4.30 (2H, t, J=6 Hz), 7.11 (1H, d, J=2 Hz), 7.68 (1H, br s), 8.22 (1H, br s, NH), 9.17 (1H, br s, indole NH).

(Table 2, entry 2) BBr_3 (10% v/v) in CH_2Cl_2 (57 μl, 0.060 mmol) was added to a cooled (−80 °C) CH_2Cl_2 solution (2.5 ml) of **56** (22 mg, 0.036 mmol) under an Ar atmosphere, and the mixture was stirred at −80—−55 °C for 2 h. The same work-up and purification as above afforded **57** (11.5 mg, 61%), **66** (0.5 mg, *ca.* 3%), **67** (2.5 mg, 16%) and recovered **56** (3 mg, 14%).

(Table 2, entry 3) *B*-Bromocatecholborane in CH_2Cl_2 (1 M, 162 μl, 0.162 mmol) was added to a cooled (−80 °C) CH_2Cl_2 solution (2.5 ml) of **56** (10 mg, 0.016 mmol) under an Ar atmosphere, and the mixture was stirred at −80—−65 °C for 1 h. The same work-up and purification as above afforded **66** (7.5 mg, 88%) along with trace amounts (<0.5 mg) of **57** and **67**.

Methyl (*S*)-4-(3-Acetoxypropyloxy)-8-(benzyloxy)-6,7,8,9-tetrahydro-6-(methoxycarbonyl)-3*H*-pyrrolo[3,2-*f*]quinoline-2-carboxylate (58) DEAD (14 μl, 0.089 mmol) was added to a THF solution (2.5 ml) of **57** (15.5 mg, 0.029 mmol) and Ph_3P (23 mg, 0.088 mmol), and the mixture was stirred at 20 °C for 1 h. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [benzene–EtOAc (9 : 1)] afforded **58** (13.5 mg, 90%) as a colorless glass. HR-MS Calcd for $C_{27}H_{30}N_2O_8$: 510.2000. Found: 510.2026. $[\alpha]_D^{22}$ −2.2° (*c*=0.34, $CHCl_3$). MS *m/z*: 510 (M^+, 30), 479 (2), 410 (2), 331 (3), 101 (100), 91 (42), 73 (12), 43 (26). IR ($CHCl_3$) cm^{-1}: 1728, 1704. ^{1}H-NMR (400 MHz) δ: 2.07 (3H, s), 2.20 (2H, tt, *J*=6, 6 Hz), 3.00 (1H, dd, *J*=17, 5.5 Hz), 3.25 (1H, dd, *J*=17, 6 Hz), 3.78 (3H, s), 3.85—3.98 (2H, m), 3.94 (3H, s), 3.99—4.06 (1H, m), 4.21 (2H, t, *J*=6 Hz), 4.31 (2H, t, *J*=6 Hz), 4.65 (1H, d, *J*=12 Hz), 4.74 (1H, d, *J*=12 Hz), 7.08 (1H, br s), 7.12 (1H, d, *J*=2.5 Hz), 7.26—7.39 (5H, m), 9.07 (1H, br s, NH).

Methyl (*S*)-8-(Benzyloxy)-6,7,8,9-tetrahydro-4-(3-hydroxypropyloxy)-6-(methoxycarbonyl)-3*H*-pyrrolo[3,2-*f*]quinoline-2-carboxylate (60) A MeOH solution (2 ml) of **58** (9.5 mg, 0.02 mmol) and K_2CO_3 (20 mg, 0.14 mmol) was stirred at 21 °C 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 [benzene–EtOAc (3 : 4)] afforded **60** (8.5 mg, 98%) as a colorless glass. HR-MS Calcd for $C_{25}H_{28}N_2O_7$: 468.1895. Found: 468.1917. $[\alpha]_D^{22}$ −1.6° (*c*=0.37, $CHCl_3$). MS *m/z*: 468 (M^+, 100), 436 (4), 362 (8), 330 (6), 303 (6), 272 (7), 91 (98), 43 (16). IR ($CHCl_3$) cm^{-1}: 1698. ^{1}H-NMR δ: 2.01 (1H, br s, OH), 2.07 (2H, tt, *J*=6, 6 Hz), 2.94 (1H, dd, *J*=17.5, 5 Hz), 3.26 (1H, dd, *J*=17.5, 6 Hz), 3.69—4.12 (5H, m), 3.76 (3H, s), 3.91 (3H, s), 4.27 (2H, t, *J*=6 Hz), 4.61 (1H, d, *J*=12 Hz), 4.76 (1H, d, *J*=12 Hz), 7.11 (1H, d, *J*=2 Hz, changed to s with D_2O), 7.12 (1H, s), 7.22—7.48 (5H, m), 9.36 (1H, br s, NH).

Methyl 7-(3-Acetoxypropyloxy)-4-[(*S*)-2-(benzyloxy)-3-(methanesulfonyloxy)propyl]-5-[(methoxycarbonyl)amino]-1*H*-indole-2-carboxylate (59) MsCl (10% v/v) in CH_2Cl_2 (85 μl, 0.11 mmol) was added to a cooled (−18 °C) CH_2Cl_2 solution (2 ml) of **57** (14.5 mg, 0.027 mmol) and Et_3N (77 μl, 0.55 mmol), and the mixture was stirred at that temperature for 1 h. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. The organic layer was successively washed with saturated $CuSO_4$–H_2O and saturated $NaHCO_3$–H_2O, and worked up as usual. Purification by PTLC [benzene–EtOAc (2 : 1)] afforded **59** (16 mg, 96%) as colorless prisms, mp 146.5—147.5 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{28}H_{34}N_2O_{11}S$: C, 55.43; H, 5.65; N, 4.62. Found: C, 55.12; H, 5.64; N, 4.51. HR-MS Calcd for $C_{28}H_{34}N_2O_{11}S$: 606.1881. Found: 606.1854. $[\alpha]_D^{22}$ +2.4° (*c*=0.78, $CHCl_3$). MS *m/z*: 606 (M^+, 3), 574 (5), 510 (4), 345 (3), 213 (5), 101 (100), 91 (30), 73 (7), 43 (25). IR (KBr) cm^{-1}: 1737, 1696. ^{1}H-NMR (400 MHz) δ: 2.08 (3H, s), 2.22 (2H, tt, *J*=6, 6 Hz), 3.04 (3H, s), 3.06 (1H, dd, *J*=14.5, 4 Hz), 3.11 (1H, dd, *J*=14.5, 8 Hz), 3.70 (3H, s), 3.95 (3H, s), 3.97—4.04 (1H, m), 4.24 (1H, dd, *J*=10.5, 5.5 Hz), 4.25 (2H, t, *J*=6 Hz), 4.32 (2H, t, *J*=6 Hz), 4.34 (1H, dd, *J*=10.5, 5 Hz), 4.43 (1H, d, *J*=11.5 Hz), 4.63 (1H, d, *J*=11.5 Hz), 7.07 (1H, d, *J*=2.5 Hz), 7.14—7.29 (6H, m), 7.86 (1H, br s, NH), 9.08 (1H, br s, indole NH).

Alternative Formation of 60 from 59 NaH (60%) (5 mg, 0.1 mmol) was added to a cooled (0 °C) THF solution (2.5 ml) of **59** (19 mg, 0.031 mmol), and the mixture was stirred at 0 °C for 10 min and at 20 °C for 1 h. Saturated NH_4Cl–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up gave a residue (19 mg). A MeOH solution (2 ml) of this and K_2CO_3 (20 mg, 0.14 mmol) was stirred at 20 °C for 1 h. The same work-up and purification as above afforded **60** (13.5 mg, 92%).

Methyl (*S*)-8-(Benzyloxy)-6,7,8,9-tetrahydro-4-hydroxy-6-(methoxycarbonyl)-3*H*-pyrrolo[3,2-*f*]quinoline-2-carboxylate (61) A mixture of **60** (12 mg, 0.026 mmol) and Dess–Martin reagent (65 mg, 0.15 mmol) in CH_2Cl_2 (3 ml) was refluxed for 1 h. The same work-up as for the preparation of **40** from **39** gave a crude aldehyde (14 mg). A CH_2Cl_2 solution (2 ml) of this and Et_3N (0.20 ml, 1.4 mmol) was refluxed for 10 min. The same work-up as for the preparation of **30** from **19a** gave a residue, which was purified by PTLC [benzene–EtOAc (2 : 1)] to afford **61** (9 mg, 86%) as a colorless foam. HR-MS Calcd for $C_{22}H_{22}N_2O_6$: 410.1476. Found: 410.1492. $[\alpha]_D^{22}$ −3.7° (*c*=0.23, $CHCl_3$). MS *m/z*: 410 (M^+, 76), 378 (11), 272 (19), 172 (11), 91 (100), 59 (14). IR ($CHCl_3$) cm^{-1}: 1700, 1672. ^{1}H-NMR δ: 2.94 (1H, dd, *J*=17.5, 4.5 Hz), 3.24 (1H, dd, *J*=17.5, 5.5 Hz), *ca.* 3.67—4.14 (3H, m), 3.79 (3H, s), 3.93 (3H, s), 4.62 (1H, d, *J*=11.5 Hz), 4.73 (1H, d, *J*=11.5 Hz), 7.06—7.20 (2H, m), 7.20—7.51 (6H, m including OH), 9.61 (1H, br s, NH). ^{1}H-NMR of the crude aldehyde δ: 2.80—3.11 (1H, m), 2.90 (2H, dt, *J*=1.5, 6 Hz), 3.27 (1H, dd, *J*=17.5, 5.5 Hz), 3.77 (3H, s), 3.77—4.13 (3H, m), 3.92 (3H, s), 4.44 (2H, t, *J*=6 Hz), 4.61 (1H, d, *J*=11.5 Hz), 4.75 (1H, d, *J*=11.5 Hz), 7.08—7.20 (2H, m), 7.20—7.48 (5H, m), 9.23 (1H, br s, NH), 9.90 (1H, t, *J*=1.5 Hz).

Methyl (*S*)-6,7,8,9-Tetrahydro-4,8-dihydroxy-6-(methoxycarbonyl)-3*H*-pyrrolo[3,2-*f*]quinoline-2-carboxylate (62) A MeOH solution (8 ml) of **61** (12 mg, 0.029 mmol) was hydrogenated over 20% $Pd(OH)_2$–C (4 mg) under an H_2 atmosphere (5 atm) at 25 °C for 16 h. The same work-up as for the preparation of **28** from **27**, followed by purification using PTLC [benzene–EtOAc (1 : 1)] afforded **62** (9 mg, 96%) as a colorless powder, whose spectral data were identical with those given in the previous report.[1)]

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References and Notes

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