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Synthetic Approach to Telomerase Inhibitor Dictyodendrin B: Synthesis of the Pyrrolo[2,3-*c*]carbazole Core

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The core structure of the telomerase inhibitor, dictyodendrin B, was synthesized by using the palladium-catalyzed cross-coupling reaction of 3-aryl-1-(2-arylethyl)-4-hydroxy-2,5-bismethoxycarbonylpyrrole triflate with 7-alkoxyindole-3-boronate as the key step.

Key words: telomerase inhibitor; pyrrole alkaloid; dictyodendrin

Telomerase is a specialized reverse transcriptase that serves to maintain the telomere length by adding hexameric repeats (TTAGGG) to the telomeric ends of chromosomes, preventing telomere shortening during cell division.[1,2] Telomerase activity is not usually detectable in human somatic cells. In contrast, more than 85% of human cancer cells have an increased level of telomerase activity, allowing the cell to have an indefinite proliferative capacity. Therefore, telomerase could be an effective and relatively safe molecular target for cancer chemotherapy.[3]

Dictyodendrins A–E (**1**–**5**) are the first telomerase-inhibiting marine natural products isolated from the marine sponge, *Dictyodendrilla verongiformis*, that was collected in southern Japan by Fusetani *et al.* in 2003.[4] These alkaloids completely inhibited telomerase at a concentration of 50 μg/ml. They also demonstrated that the sulfate functions of the molecules were essential for bioactivity, as the desulfated compound was completely inactive. The first total synthesis of dictyodendrin B was achieved by Früstner's group in 2005.[5] They utilized low-valent titanium-mediated reductive cyclization and subsequent photochemical dehydrogenative cyclization to form the core pyrrolo[2,3-*c*]carbazole ring. Thereafter, they extended this strategy to the total syntheses of dictyodendrins C and E.[6]

In our continuing study on the synthesis and biological activities of lamellarin-class marine alkaloids, we have developed an efficient method for the synthesis of differently substituted 3,4-diarylpyrroles by utilizing Hinsberg-type pyrrole synthesis and sequential palladium-catalyzed cross-coupling reactions.[7–9] It is plausible that this strategy could be applicable to the syntheses of the pyrrolocarbazole alkaloids, dictyodendrins, by using 7-alkoxyindole-3-boronate in the second cross-coupling reaction (Scheme 1). Based on this strategy, we prepared the putative precursor to dictyodendrins having the core pyrrolo[2,3-*c*]carbazole system and the all requisite functions. The details of our work are described here.

Results and Discussion

Our strategy for the synthesis of dictyodendrins is shown retrosynthetically in Scheme 1. We envisaged that the core pyrrolo[2,3-*c*]carbazole system of dictyodendrin B (**2**) could be constructed by the intramolecular aldol reaction of keto-aldehyde **6a** or its equivalent and subsequent Baeyer-Villiger oxidation. The two benzoyl moieties could be installed at the 2- and 5-positions of the pyrrole by aryl anion addition to the two ester functions of **8**. Alternatively, the tetracyclic system of dictyodendrin A (**1**) could be constructed by the intramolecular Friedel-Crafts type of acylation of diacid **7**. The two phenylacetic acid units could be installed by the Friedel-Crafts type of alkylation of **9** which could itself be obtained from common intermediate **8** by decarboxylation.

One of the building blocks for the synthesis, 3-aryl-4-hydroxypyrrole triflate **10**, was synthesized from tyramine in five steps with a 31% overall yield according to the procedure used for our previous synthesis of lamellarins D, N and L[8] (Scheme 2).

Other synthons, 7-alkoxyindole-3-boronates **11a–c**, were synthesized as shown in Scheme 3. To optimize the second cross-coupling reaction with triflate **10**, three indole-3-boronates, **11a**–**11c**, differing in the protecting groups of indole nitrogen and the phenolic hydroxy group, were prepared. Among the known methods for the preparation of a 7-hydroxy/alkoxyindole, Baltoli's method[10] is the most convenient by virtue of the accessibility of the desired product. One can easily obtain 7-substituted indoles in a single step by the reaction of nitrobenzenes with vinylmagnesium bromide. The reaction, however, has the limitation that the nitrobenzenes must have a bulky substituent at the *ortho* position; if not, the reaction results in markedly lower yield of the product. In this context, starting 2-nitrophenol was protected as a diphenylmethyl ether, and 7-alkoxyindole **16**[11] was prepared according to Baltoli's protocol. *N*-SEM-protected indole-3-boronate **11a** was

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Abbreviations: BOM, benzyloxymethyl; SEM, 2-trimethylsilylethoxymethyl; Boc, *tert*-butoxycarbonyl

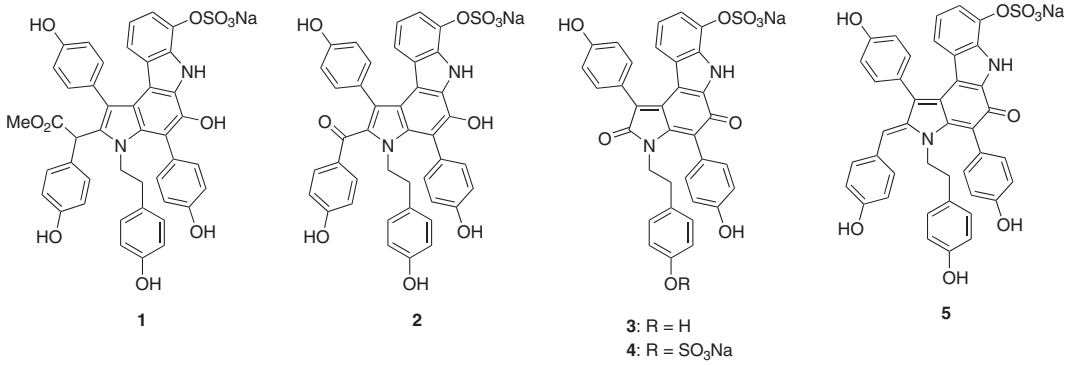
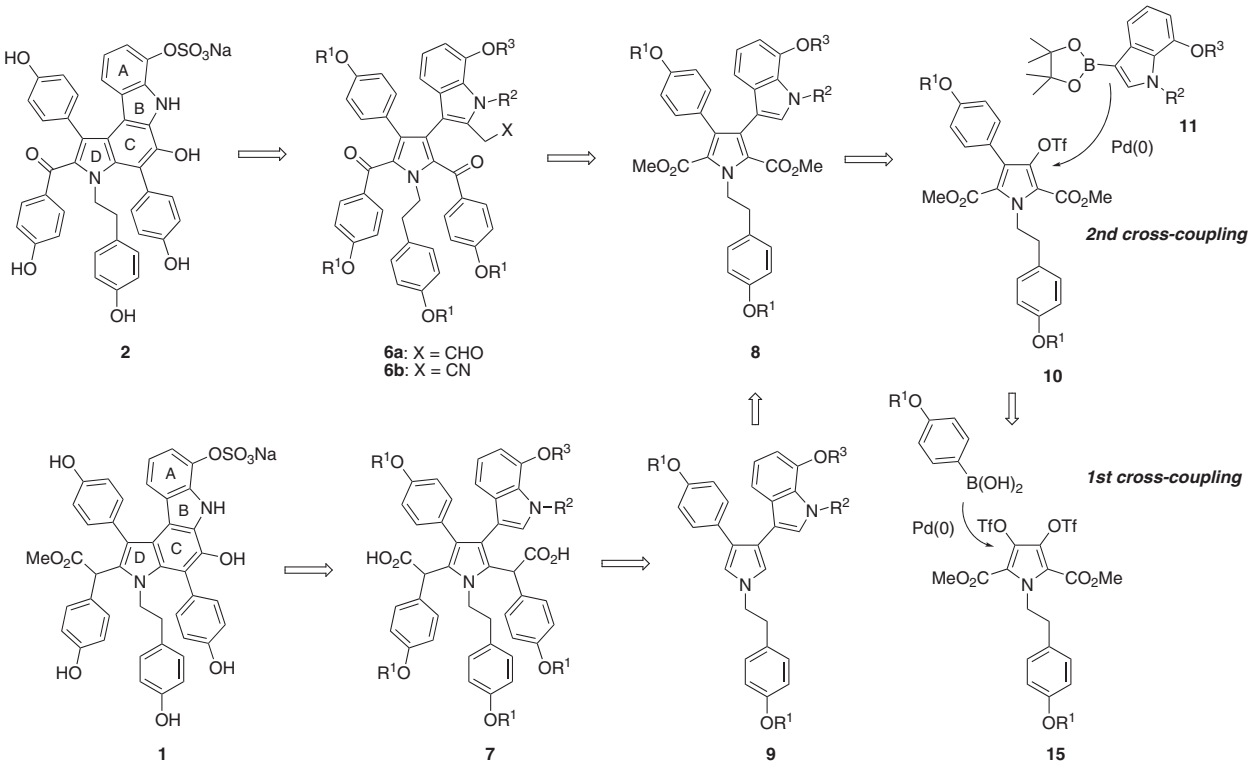
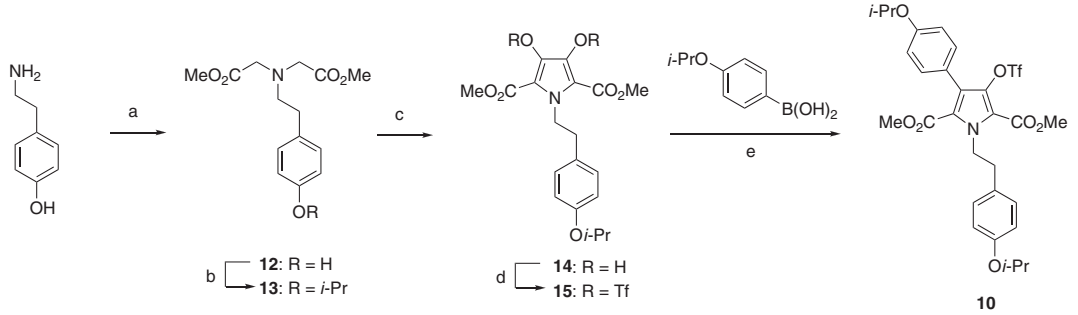


Fig. 1. Dictyodendrins A–E.

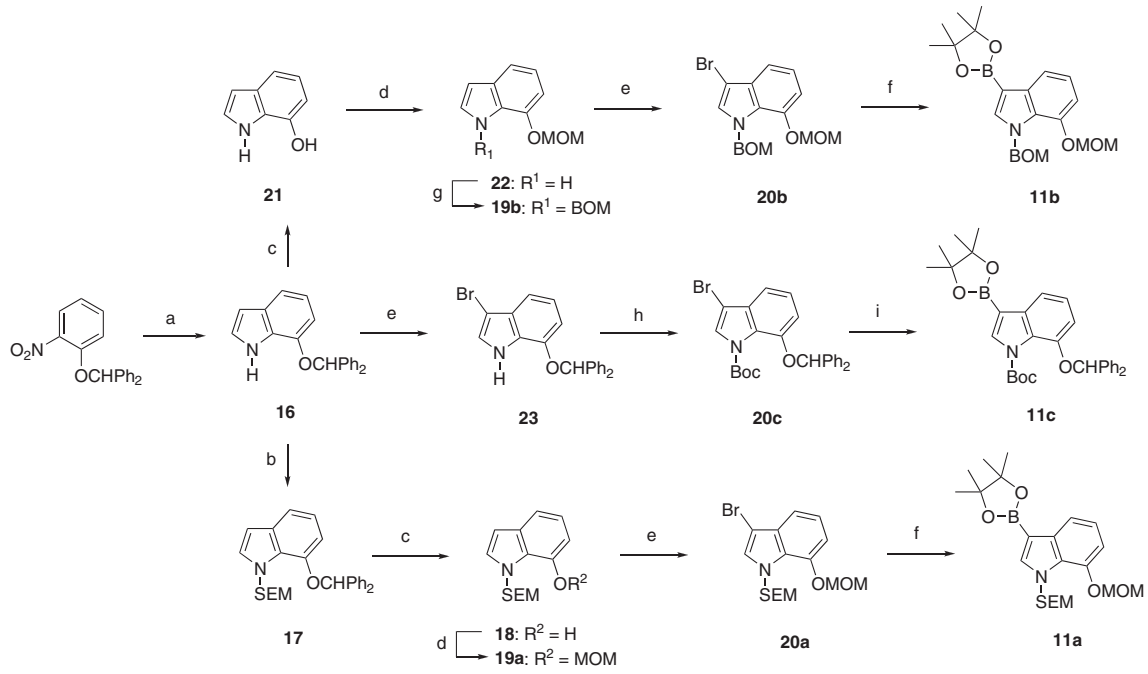


Scheme 1. Retrosynthetic Analysis of Dictyodendrins A and B.



Scheme 2. Synthesis of Key Intermediate Pyrrole Monotriflate **10**.
Reagents and conditions: (a) $BrCH_2CO_2Me$, $NaHCO_3$, CH_3CN, reflux, 66%; (b) 2-bromopropane, K_2CO_3, DMSO, 55 °C, 3 h, 67%; (c) $(CO_2Me)_2$, NaH, THF, reflux, 84%; (d) Tf_2O, pyridine, 0 °C, 98%; (e) 4 mol % $Pd(Ph_3P)_4$, aq. Na_2CO_3, THF, reflux, 85%.

synthesized as follows. The indole nitrogen of **16** was initially protected as an SEM ether by reacting with 2-trimethylsilylethoxymethyl chloride and sodium hydride, and the diphenylmethyl-protecting group was replaced with a methoxymethyl (MOM) ether by hydrogenolysis and subsequent etherification with chloromethyl methyl ether, giving **19a** in 79% for the three steps. Bromination of **19a** with *N*-bromosuccinimide in THF at a low temperature (−78 °C) occurred exclusively at the 3-posision, affording **20a** as the sole product in a 63%



Scheme 3. Syntheses of 7-Alkoxyindole-3-boronates.

Reagents and conditions: (a) CH_2=CHMgBr, THF, −40 °C, 63%; (b) SEM-Cl, NaH, DMF, rt, 94%; (c) H_2, $Pd(OH)_2$-C, EtOAc, 50 °C, 88% for **18**, rt, 92% for **21**; (d) MOM-Cl, K_2CO_3, 18-crown-6, acetone, rt, 95% for **19a**, reflux, 64% for **22**; (e) NBS, THF, −78 °C to rt, 63% for **20a**, 76% for **20b**, 76% for **23**; (f) BuLi, THF, −78 °C, then *i*-PrOBPin, rt, 84% for **11a**, 77% for **11b**; (g) BOM-Cl, NaH, DMF, rt, 99.9%; (h) $(Boc)_2O$, NaH, DMF, rt, 92%; (i) bis(pinacolato)diboron, KOAc, 5 mol % $PdCl_2$(dppf), dppf, DMSO, 80 °C, 85%.

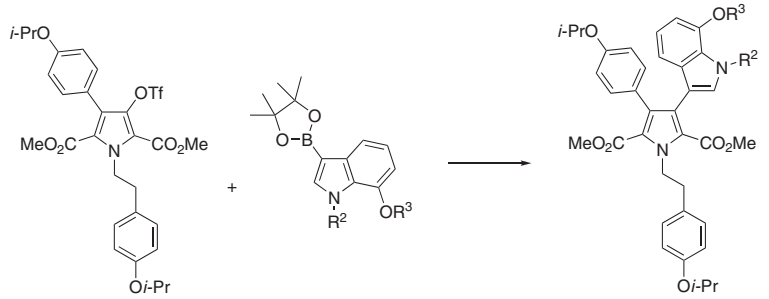
yield. Finally, relatively stable boronate **11a** was obtained by a halogen-lithium exchange reaction with butyllithium and subsequent borylation with 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxabolorane in an 84% yield. Benzyloxymethyl (BOM)-protected **11b** was also synthesized in a 34% overall yield in a similar manner to that for **11a**, except for the order of protection of the indole amino group and phenolic hydroxy group. Preparation of *tert*-butoxycarbonyl (Boc)-protected indole-3-boronate **11c** required a small modification of the sequence. Since bromination of the *N*-Boc derivative of **16** gave a mixture of 3- and 4-bromoindoles, the bromination was performed prior to Boc protection to obtain 3-bromoindole **23** in a 76% yield. This unstable indole was immediately protected as the carbamate, and final borylation was conducted by a palladium-catalyzed cross-coupling reaction with bis(pinacolato)diboron[12] in a 78% yield for the two steps.

With both pyrrole triflate **10** and indole boronates **11a–c** in hand, we next investigated their cross-coupling reactions under a variety of reagents and conditions (Table 1). Among the catalysts tested (runs 1–4), standard tetrakistriphenylphosphine palladium(0) was found to be the most effective (run 4). We next examined the base used for the reaction (runs 4–7) and found a stronger base, potassium phosphate, to be the most effective (run 7). Under optimized conditions using 8–10 mol % of the palladium(0) catalyst and potassium phosphate in refluxing 1,2-dimethoxyethane, the cross-coupling products, **8a–c**, were obtained in moderate to high yields (runs 7–9).

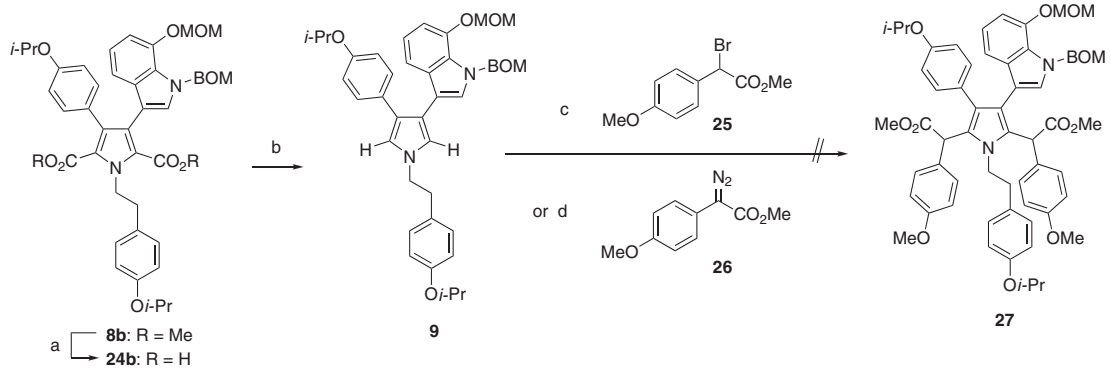
In the total synthesis of the marine pyrrole alkaloid, purpurone, Steglich *et al.*[13] employed acidic alumina-mediated double Friedel-Crafts alkylation of a 3,4-diarylpyrrole with an α-bromophenylacetate and subsequent intramolecular double Friedel-Crafts acylation to construct the core dibenzo[*c,g*]carbazole-5,9-dione system. We first tried to apply this strategy for installation of the two phenylacetate units and construction of the C-ring in dictyodendrin A (Scheme 4). Consequently, pyrrole **9**, which was readily obtained by the alkaline hydrolysis and subsequent decarboxylation[14] of diester **8b**, was reacted with excess (4.0 equiv.) bromide **25** in the presence of a large excess (40 equiv.) of acidic alumina[13] in refluxing chloroform; however, the desired alkylation failed and gave a complex mixture of decomposition products. Installation of the phenylacetate units by a rhodium(III)-catalyzed carbene-insertion reaction[13] was also attempted; however, the reaction only afforded a mixture of monoalkylated products in a low yield.

We next investigated an alternative approach to dictyodendrins *via* diketone **29** (Scheme 5). We had initially planned to introduce the 4-alkoxybenzoyl moieties *via* a Weinreb amide; however, triazine ester[15] **28** prepared for this transformation was found to be unexpectedly stable and did not react with *N,O*-dimethylhydroxylamine. Thus, activated ester **28** was directly reacted with 2.2 equiv. of 4-methoxyphenylmagnesium bromide in ether at −20 °C to obtain diketone **29** in a 76% yield. The reaction did not proceed at a lower temperature (−78 °C), while the reaction at over 0 °C gave a considerable amount of over-addition products. Conversion from diketone **29** to dictyodendrin B required functionalization of the indole 2-position. We first attempted to introduce an aldehyde function, as keto-aldehyde **30** was expected to afford the tetracyclic system by an intramolecular reductive coupling reaction. Despite many trials of electrophilic formylation involving Vilsmeier-Haack[16] and Duff[17] conditions, no corresponding aldehyde could be obtained and, in some cases, five-membered alcohol **32**

Table 1. Palladium-Catalyzed Cross-Coupling Reactions of Pyrrole Triflate **10** with Indole Boronates **11a–c**

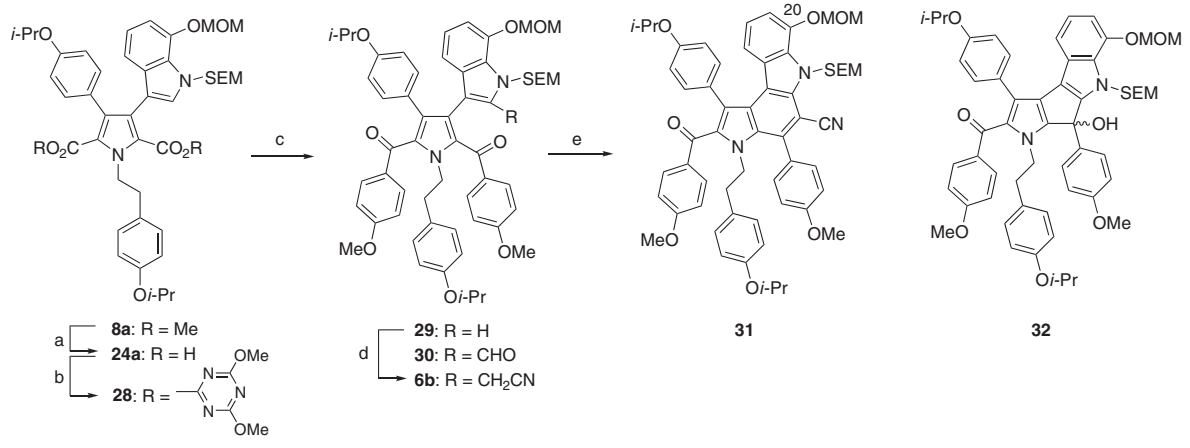


Run	Boronate	Catalyst, additive (mol %)	Base	Solvent	Condition	Product	Yield
1	**11c**	$Pd(OAc)_2$ (5), DPEPhos (20)	CsF	dioxane	80 °C, 8 h	**8c**	11%
2	**11c**	$Pd(OAc)_2$ (3.4), PCy_3 (4.2)	KF	THF-dioxane	70 °C, 7 h	**8c**	10%
3	**11c**	$PdCl_2$(dppf) (18), dppf (10)	K_3PO_4	dioxane	80 °C, 20 h	**8c**	0%
4	**11c**	$Pd(PPh_3)_4$ (15)	Na_2CO_3	DME-H_2O	95 °C, 48 h	**8c**	42%
5	**11c**	$Pd(PPh_3)_4$ (5)	Cs_2CO_3	toluene	80 °C, 24 h	**8c**	30%
6	**11c**	$Pd(PPh_3)_4$ (5)	Tl_2CO_3	toluene	80 °C, 24 h	**8c**	0%
7	**11c**	$Pd(PPh_3)_4$ (10)	K_3PO_4	DME	95 °C, 22 h	**8c**	59%
8	**11b**	$Pd(PPh_3)_4$ (8)	K_3PO_4	DME	95 °C, 19 h	**8b**	84%
9	**11a**	$Pd(PPh_3)_4$ (8)	K_3PO_4	DME	95 °C, 28 h	**8a**	63%



Scheme 4.

Reagents and conditions: (a) 3.0 M NaOH, EtOH, reflux, 4 h, 100%; (b) Cu_2O, quinoline, 180 °C, 10 min, 98%; (c) **25**, acidic Al_2O_3, $CHCl_3$, reflux; (d) **26**, cat. $[Rh(OAc)_2]_2$, CH_2Cl_2, rt.



Scheme 5. Construction of the Core Pyrrolo[2,3-c]carbazole System of Dictyodendrin B.

Reagents and conditions: (a) 3.0 M NaOH, EtOH, reflux, 17 h, 95%; (b) 2-chloro-4,6-dimethoxy-1,3,5-triazine, *N*-methylmorpholine, THF, rt, 20 h, 70%; (c) *p*-$MeOC_6H_4MgBr$, Et_2O, −20 °C, 1.5 h, 76%; (d) EtOC(=S)SCH_2CN, dilauroyl peroxide, $ClCH_2CH_2Cl$, reflux, 7.5 h, 36%; (e) DBU, CH_2Cl_2, rt, 21 h, 79%.

formed through intramolecular attack of the indole to the ketone carbonyl group was produced as the major product. After various examinations, the functionalization was finally effected by free radical addition reactions. Refluxing **29** and dithiocarbonic acid *O*-ethyl *S*-cyanomethyl ester [EtO(C=S)SCH$_2$CN] in 1,2-dichloroethane with slow addition of the radical initiator, dilauroyl peroxide,[18] afforded cyanomethyl derivative **6b** in a 36% yield with 19% recovery of **29**. The low yield of the reaction was probably due to decomposition of the materials, since a considerable amount of highly polar compounds was produced in the reaction; however, the addition of aqueous sodium bicarbonate to neutralize the by-product, lauric acid, did not improve the yield. The use of other radical initiators such as di-*tert*-butyl peroxide and triethylborane/O_2 was also unsuccessful. Finally, the core tetracyclic system was constructed by intramolecular aldol condensation of **6b**, using diazabicyclo[5.4.0]undec-7-ene (DBU) as the base in a 79% yield. Tetracyclic compound **31** had all the requisite functions for conversion to dictyodendrin B (**2**).

In summary, we prepared the putative synthetic precursor of dictyodendrins by using Hinsberg-type pyrrole formation and sequential Suzuki-Miyaura cross-coupling reactions as the key reactions. Conversion of **31** to dictyodendrin B (**2**) requires reduction and Baeyer-Villiger oxidation of the nitrile moiety and regioselective sulfation of the hydroxy group at the 10-positon. Completion of the total synthesis and improvement of the radical addition reaction is currently underway in our laboratory.

Experimental

Melting point (mp) data are uncorrected. Unless stated otherwise, ^{1}H-NMR spectra (400 MHz or 300 MHz) and ^{13}C-NMR spectra (100 MHz) were recorded in $CDCl_3$ on a JEOL JNM-AL400 or a Varian Gemini 300 spectrometers, using tetramethylsilane as an internal standard (Supplemental; see *Biosci. Biotechnol. Biochem.* Web site). Mass spectra (EI amd FAB) were recorded on a JEOL JMS-700N spectrometer, and FT-IR spectra were recorded on a Nicolet Nexus 670 spectrometer. Gravity column chromatography and medium-pressure liquid choromatography (MPLC) were performed by using Kanto Chemical Co. spherical silica gel 60, with particle size 100–210 μm and 40–50 μm, respectively.

Dimethyl N-*[2-(4-hydroxyphenyl)ethyl]iminodiacetate (**12**).* A mixture of tyramine (1.37 g, 10.0 mmol), methyl bromoacetate (2.00 ml, 21.1 mmol) and $NaHCO_3$ (3.52 g, 41.9 mmol) in dry CH_3CN (20 ml) was refluxed for 2.5 h. The mixture was cooled to room temperature, poured into water (200 ml), and extracted with CH_2Cl_2. After drying (Na_2SO_4) and removing the solvent, the oily residue was chromatographed on silica gel eluted with hexane/EtOAc (1:1) to give **12** as a pale yellow oil (1.86 g, 6.61 mmol, 66%). IR ν_{max} (KBr) cm^{-1}: 3413 (OH), 2954, 1755 (C=O), 1726 (C=O), 1514, 1440, 1206, 1012, 830, 773. NMR δ_H (400 MHz): 2.68–2.74 (2H, m, –NCH$_2$C*H*$_2$Ar), 2.89–2.95 (2H, m, –NC*H*$_2$CH$_2$Ar), 3.60 (4H, s, NC*H*$_2$CO$_2$Me × 2), 3.71 (s, 6H, –CO$_2$C*H*$_3$ × 2), 5.27–6.39 (1H, br., O*H*), 6.75 (d, J = 8.4 Hz, 2H, 3″-H), 7.02 (d, J = 8.4 Hz, 2H, 2″-H). NMR δ_C (100 MHz): 34.2 (CH$_2$), 52.2 (CH$_3$ × 2), 55.5 (CH$_2$ × 2), 57.0 (CH$_2$), 115.8 (CH × 2), 130.2 (CH × 2), 131.8 (C), 154.7 (C), 172.4 (C=O × 2). *Anal.* Calcd. for $C_{14}H_{19}NO_5$: C, 59.78; H, 6.81; N, 4.98%. Found: C, 59.83; H, 7.01; N, 4.98%.

Dimethyl N-*[2-(4-isopropoxyphenyl)ethyl]iminodiacetate (**13**).* To a mixture of **12** (1.02 g, 3.63 mmol) and pulverized K_2CO_3 (1.00 g, 7.26 mmol) in dry DMSO (7.0 ml) was added 2-bromopropane (0.510 ml, 5.45 mmol) as a neat liquid. After 3 h at 55 °C, additional 2-bromopropane (0.170 ml, 1.82 mmol) was added, and heating was continued for a further 15 h. After cooling to room temperature, the mixture was then poured into water (50 ml) and extracted three times with ether (50 ml each). The ethereal extracts were combined, successively washed with 10% aqueous NaOH, water and brine, and dried over Na_2SO_4. After removing the solvent, the oily residue was chromatographed on silica gel eluted with hexane/EtOAc (3:1) to give **13** (0.785 g, 2.43 mmol, 67%) as a viscous colorless oil. IR ν_{max} (KBr) cm^{-1}: 2978, 1754 (C=O), 1512, 1241, 1199, 1139 (C–O–C), 956, 830. NMR δ_H (400 MHz): 1.31 (6H, d, J = 6.0 Hz, –CH(C*H*$_3$)$_2$), 2.69–2.76 (2H, m, –NCH$_2$C*H*$_2$Ar), 2.89–2.96 (2H, m, –NC*H*$_2$CH$_2$Ar), 3.60 (4H, s, NC*H*$_2$CO$_2$Me × 2), 3.71 (s, 6H, –CO$_2$C*H*$_3$ × 2), 4.43–4.55 (1H, m, –C*H*(CH$_3$)$_2$), 6.79 (2H, d, J = 8.4 Hz, 3″- and 5″-Hs), 7.08 (2H, d, J = 8.4 Hz, 2″- and 6″-Hs). NMR δ_C: 22.5 (CH$_3$ × 2), 34.3 (CH$_2$), 52.1 (CH$_3$ × 2), 55.6 (CH$_2$ × 2), 57.0 (CH$_2$), 70.4 (CH), 116.4 (CH × 2), 130.2 (CH × 2), 131.9 (C), 156.7 (C), 171.7 (C=O × 2). *Anal.* Calcd. for $C_{17}H_{25}NO_5$: C, 63.14; H, 7.79; N, 4.33%. Found: C, 63.15; H, 7.72; N, 4.34%.

*Dimethyl 3,4-dihydroxy-1-[2-(4-isopropoxyphenyl)ethyl]pyrrole-2,5-dicarboxylate (**14**).* To a refluxing suspension of dimethyl oxalate (4.20 g, 35.6 mmol) and NaH (60% dispersion in mineral oil, 2.85 g, *ca.* 71.3 mmol, prewashed with dry hexane) in dry THF (25 ml) was added dropwise a solution of **13** (5.77 g, 17.9 mmol) in dry THF (45 ml) over a period of 30 min. The mixture was refluxed for an additional 3 h, before being cooled and quenched with acetic acid (4.6 ml). After removing the solvent *in vacuo*, the residue was poured into ice-cooled water, and the pH value was adjusted to 3.0 with 3 M aqueous HCl. The precipitate thus formed was collected by filtration and recrystallized from MeOH to give **14** as white crystals (5.62 g, 14.9 mmol, 84%), mp 138–140 °C. IR ν_{max} (KBr) cm^{-1}: 3344 (OH), 1659 (C=O), 1502, 1462, 1337, 1301, 1255, 1167 (C–O–C), 1105, 981, 954, 771, 665. NMR δ_H (400 MHz): 1.32 (6H, d, J = 6.0Hz, –CH(C*H*$_3$)$_2$), 2.82 (2H, t, J = 7.2 Hz, NCH$_2$C*H*$_2$Ar), 3.92 (6H, s, –CO$_2$C*H*$_3$ × 2), 4.45–4.56 (1H, m, –C*H*(CH$_3$)$_2$), 4.66 (2H, t, J = 7.2 Hz, NC*H*$_2$CH$_2$Ar), 6.80 (2H, d, J = 8.4 Hz, 3″- and 5″-Hs), 6.99 (2H, d, J = 8.4 Hz, 2″- and 6″-Hs), 7.53 (2H, s, OH). NMR δ_C: 22.6 (*C*H$_3$ × 2), 38.0 (CH$_2$), 48.6 (*C*H$_2$), 52.4 (*C*H$_3$ × 2), 70.5 (*C*H), 111.1 (C × 2), 116.5 (CH × 2), 130.4 (CH × 2), 130.7 (C), 139.3 (C × 2), 157.2 (C), 163.2 (C=O × 2). *Anal.* Calcd. for $C_{19}H_{23}NO_7$: C, 60.47; H, 6.14; N, 3.71%. Found: C, 60.53; H, 6.16; N, 3.64%.

*Dimethyl 1-[2-(4-isopropoxyphenyl)ethyl]-3,4-bis(trifluoromethanesulfonyloxy)pyrrole-2,5-dicarboxylate (**15**).* To a solution of **14** (6.04 g, 16.0 mmol) in pyridine (24 ml) was added dropwise trifluoromethanesulfonic anhydride (6.00 ml, 35.7 mmol) as a neat liquid at 0 °C, and the mixture was stirred at 0 °C for 80 min. The reaction mixture was allowed to warm to room temperature, quenched with brine, and extracted twice with ether. The combined ethereal extracts were successively washed with 3 M aqueous HCl, water and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residual solid was recrystallized from *i*-Pr$_2$O to give **15** (9.98 g, 15.6 mmol, 98%) as white crystals, mp 81–82 °C. IR ν_{max} (KBr) cm^{-1}: 2980, 1738 (C=O), 1513, 1433, 1395, 1246 (SO$_2$), 1131 (C–O–C), 982, 812, 604. NMR δ_H (400 MHz): 1.32 (6H, d, J = 6.0Hz, –CH(C*H*$_3$)$_2$), 2.98 (2H, t, J = 7.2 Hz, NCH$_2$C*H*$_2$Ar), 3.88 (6H, s, –CO$_2$C*H*$_3$ × 2), 4.44–4.55 (1H, m, –C*H*(CH$_3$)$_2$), 5.05 (2H, t, J = 7.2 Hz, NC*H*$_2$CH$_2$Ar), 6.77 (2H, d, J = 8.4 Hz, 3″- and 5″-Hs), 6.98 (2H, d, J = 8.4 Hz, 2″- and 6″-Hs). NMR δ_C: 22.4 (CH$_3$ × 2), 37.2 (CH$_2$), 49.2 (CH$_2$), 52.7 (CH$_3$ × 2), 70.3 (CH), 116.5 (CH × 2), 117.3 (C), 117.7 (C × 2), 128.9 (C × 2), 128.9 (CF$_3$), 130.5 (CH × 2), 157.4 (C), 158.6 (C=O × 2). *Anal.* Calcd. for $C_{21}H_{21}F_6NO_{11}S_2$: C, 39.32; H, 3.30; N, 2.18%. Found: C, 39.08; H, 3.11; N, 2.13%.

*Dimethyl 3-(4-isopropoxyphenyl)-1-[2-(4-isopropoxyphenyl)ethyl]-4-(trifluoromethanesulfonyloxy)pyrrole-2,5-dicarboxylate (**10**).* To a degassed solution of **15** (5.85 g, 9.12 mmol) and 4-isopropoxyphenylboronic acid (1.60 g, 9.12 mmol) in THF (160 ml) were successively added a solution of Na_2CO_3 (7.00 g, 66.04 mmol) in water (20 ml) and Pd(PPh$_3$)$_4$ (0.46 g, 0.40 mmol). The mixture was refluxed for 3 h under an Ar atmosphere, before being cooled to room temperature and quenched with water. The mixture was then concentrated *in vacuo*, and

the products were extracted 3 times with CH_2Cl_2, The combined organic extracts were successively washed with water and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was passed through a short column of silica gel eluted with hexane/EtOAc (1:1), and the eluate was concentrated *in vacuo*. The residue was recrystallized from *i*-Pr_2O/hexane to give **10** as white crystals (4.89 g, 7.79 mmol, 85%), mp 106–107 °C. IR ν_{max} (KBr) cm^{-1}: 1726 (C=O), 1612, 1558, 1512, 1422, 1309 (SO_2), 1243 (SO_2), 1137 (C–O–C), 953 (C–O–C), 817, 606. NMR δ_H (400 MHz): 1.31 (6H, d, $J = 6.0$ Hz, –CH(CH_3)$_2$), 1.35 (6H, d, $J = 6.0$ Hz, –C(CH_3)$_2$), 3.02 (2H, t, $J = 7.6$ Hz, NCH_2CH_2Ar), 3.58 (3H, s, $–CO_2CH_3$), 3.91 (3H, s, $–CO_2CH_3$), 4.45–4.56 (1H, m, –CH(CH_3)$_2$), 4.53–4.64 (1H, m, –CH(CH_3)$_2$), 4.93 (2H, t, $J = 7.6$ Hz, NCH_2CH_2Ar), 6.80 (2H, d, $J = 8.4$ Hz, 3‴- and 5‴-Hs), 6.88 (2H, d, $J = 8.4$ Hz, 3″- and 5″-Hs), 7.07 (2H, d, $J = 8.4$ Hz, 2‴- and 6‴-Hs), 7.13 (2H, d, $J = 8.4$ Hz, 2″- and 6″-Hs). NMR δ_C: 22.4 ($CH_3 \times 2$), 22.5 ($CH_3 \times 2$), 37.6 (CH_2), 49.2 (CH_2), 52.1 (CH_3), 52.3 (CH_3), 70.3 (CH), 70.4 (CH), 115.8 (CH × 2), 116.4 (CH × 2), 118.0 (C), 122.3 (C), 123.2 (C), 123.5 (C), 127.5 (C), 128.3 (C), 129.9 (C), 130.5 (CH × 2), 131.9 (CH × 2), 136.5 (CF_3), 157.2 (C), 158.1 (C), 161.4 (C=O × 2). *Anal*. Calcd. for $C_{29}H_{32}F_3NO_9S$: C, 55.50; H, 5.14; N, 2.23%. Found: C, 55.48; H, 5.09; N, 2.23%.

*1-(2-Trimethylsilanylethoxymethyl)-7-diphenylmethyloxy-indole (**17**).* To a stirred slurry of NaH (60% dispersion in mineral oil, 0.63 g, *ca*. 15.7 mmol, prewashed with dry hexane) in dry DMF (13 ml) was added portionwise 7-diphenylmethoxyindole[11] (**16**, 3.91 g, 13.1 mmol) prepared from 1-nitro-2-diphenylmethyloxybenzene and vinylmagnesium bromide in a 63% yield at 0 °C under an Ar atmosphere. After stirring the mixture for 15 min at the same temperature, 2-(trimethylsilyl)-ethoxymethyl chloride (2.43 ml, 13.7 mmol) was added dropwise, and the mixture was allowed to warm to room temperature. After stirring for 3 h, additional NaH (60% dispersion in mineral oil, 0.12 g, *ca*. 1.6 mmol) and 2-(trimethylsilyl)ethoxymethyl chloride (0.20 ml, 1.3 mmol) were added. After 1 h, the reaction was quenched with 10% aqueous NH_4Cl, and the mixture was extracted twice with ether. The combined ethereal extracts were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The oily residue was purified by column chromatography over silica gel eluted with hexane/EtOAc (5:1) to give **17** (5.30 g, 12.3 mmol, 94%) as a pale yellow oil. IR ν_{max} (KBr) cm^{-1}: 1616, 1574, 1493, 1303, 1249 ($SiCH_3$), 1067 (C–O–C), 859, 835, 744, 717, 701. NMR δ_H (400 MHz): −0.06 (9H, s, –Si(CH_3)$_3$), 0.85 (2H, t, $J = 8.4$ Hz, $–CH_2CH_2SiMe_3$), 3.43 (2H, t, $J = 8.4$ Hz, $–CH_2CH_2SiMe_3$), 5,76 (2H, s, NCH_2O), 6.41 (1H, s, –CHPh$_2$), 6.49 (1H, d, $J = 2.8$ Hz, 3-H), 6.57 (1H, d, $J = 8.0$ Hz, 4-H), 6.87 (1H, t, $J = 8.0$ Hz, 5-H), 7.15 (1H, d, $J = 3.6$ Hz, 2-H), 7.17 (1H, d, $J = 8.0$ Hz, 6-H), 7.24–7.30 (2H, m, Ar-*H*s), 7.31–7.38 (4H, m, Ar-*H*s), 7.48–7.52 (4H, m, Ar-*H*s). NMR δ_H: −1.6 (*C*H × 3), 17.7 (CH_2), 64.9 (CH_2), 77.4 (CH_2), 81.8 (*C*H), 102.7 (CH), 105.7 (CH), 113.6 (CH), 120.1(CH), 126.6 (C), 126.7 (CH × 4), 127.5 (CH × 2), 128.4 (CH × 4), 129.0 (CH), 131.3 (C), 141.1 (C × 2), 145.5 (C). EIMS *m/z*: 429 (M^+), 356 ($M^+ - SiMe_3$), 312 ($M^+ - OCH_2CH_2SiMe_3$), 167 (base peak, $CHPh_2$). HREIMS *m/z* calcd. for $C_{27}H_{31}NO_2Si$ (M^+), 429.2124; found, 429.2126.

*7-Hydroxy-1-(2-trimethylsilanylethoxymethyl)-indole (**18**).* A solution of **17** (6.57 g, 15.3 mmol) in EtOAc (50 ml) was hydrogenated over 20% $Pd(OH)_2$ on carbon (0.50 g) at 50 °C for 3 h. The reaction mixture was then filtered through a pad of Celite, and the insoluble material was washed well with hot EtOH. The filtrate was concentrated *in vacuo*, and the residue was chromatographed on silica gel eluted with hexane/EtOAc (4:1) to give **18** (3.52 g, 13.4 mmol, 88%) as white crystals, mp 49–50 °C. IR ν_{max} (KBr) cm^{-1}: 3287 (OH), 1623, 1583, 1484, 1455, 1308, 1245 ($SiCH_3$), 1118, 1060 (C–O–C), 1032, 917, 833. NMR δ_H (400 MHz): −0.06 (9H, s, –Si(CH_3)$_3$), 1.02 (2H, t, $J = 8.4$ Hz, $–CH_2CH_2SiMe_3$), 3.70 (2H, t, $J = 8.4$ Hz, $–CH_2CH_2SiMe_3$), 5,53 (2H, s, NCH_2O), 6.47 (1H, d, $J = 2.8$ Hz, 3-H), 6.78 (1H, d, $J = 8.0$ Hz, 4-H), 7.00 (1H, t, $J = 2.8$ Hz, 2-H), 7.04 (1H, t, $J = 8.0$ Hz, 5-H), 7.19 (1H, d, $J = 8.0$ Hz, 6-H), 7.87 (1H, br. s, –OH). NMR δ_C: −0.6 ($CH_3 \times 3$), 18.5 (CH_2), 67.1 (CH_2), 78.4 (CH_2), 103.6 (CH), 110.2 (CH), 113.9 (CH), 122.6 (CH), 126.9 (C), 128.7 (CH), 133.4 (C), 144.2 (C). *Anal*. Calcd. for $C_{14}H_{21}NO_2Si$: C, 63.84; H, 8.04; N, 5.32%. Found: C, 63.49; H, 8.04; N, 5.15%.

*7-Methoxymethoxy-1-(2-trimethylsilanylethoxymethyl)-indole (**19a**).* To a degassed suspension of K_2CO_3 (5.90 g, 42.7 mmol) and a catalytic amount of 18-crown-6 ether in dry acetone (40 ml) was added **18** (2.81 g, 10.7 mmol) at 0 °C under an Ar atmosphere, and the reaction mixture was stirred at the same temperature for 30 min. Chloromethylmethyl ether (0.90 ml, 11.7 mmol) was then added, and the whole was allowed to warm to room temperature and stirred for 3 h. The mixture was then poured into water and extracted twice with ether. The combined ethereal extracts were successively washed with 1% aqueous NH_3 and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was chromatographed on silica gel eluted with hexane/EtOAc (4:1) to give **19a** (3.15 g, 10.2 mmol, 95%) as white crystals. An analytically pure sample was obtained by recrystallization from hexane, mp 48–49 °C. IR ν_{max} (KBr) cm^{-1}: 1580, 1494, 1306, 1250 ($SiCH_3$), 1153, 1078 (C–O–C), 1046 (C–O–C), 959, 862, 835, 785, 721. NMR δ_H (300 MHz): −0.07 (9H, s, –Si(CH_3)$_3$), 0.85 (2H, t, $J = 8.4$ Hz, $–CH_2CH_2SiMe_3$), 3.50 (2H, t, $J = 8.2$ Hz, $–CH_2CH_2SiMe_3$), 3.54 (3H, s, $–OCH_2OCH_3$), 5.33 (2H, s, $–OCH_2OCH_3$), 5.76 (2H, s, NCH_2O), 6.50 (1H, d, $J = 3.2$ Hz, 3-H), 6.91 (1H, d, $J = 7.8$ Hz, 4-H), 7.01 (1H, t, $J = 7.8$ Hz, 5-H), 7.13 (1H, d, $J = 3.2$ Hz, 2-H), 7.26 (1H, dd, $J = 0.9$, 7.8 Hz, 6-H). NMR δ_C: −0.6 ($CH_3 \times 3$), 18.7 (CH_2), 57.1 (CH_3), 66.2 (CH_2), 78.4 (CH_2), 95.8 (CH_2), 103.0 (CH), 103.9 (CH), 115.7 (CH), 121.4 (CH), 127.0 (C), 130.1 (CH), 132.5 (C), 145.7 (C). *Anal*. Calcd. for $C_{16}H_{25}NO_3Si$: C, 62.50; H, 8.20; N, 4.56%. Found: C, 62.24; H, 8.13; N, 4.30%.

*3-Bromo-7-methoxymethoxy-1-(2-trimethylsilanylethoxymethyl)-indole (**20a**).* A solution of **19a** (2.89 g, 9.40 mmol) in dry THF (50 ml) was cooled to −78 °C, and *N*-bromosuccinimide (1.67 g, 9.40 mmol) was added in one portion. After 1.5 h at −78 °C, the reaction mixture was gradually warmed to room temperature and kept for 1.5 h. The reaction was then quenched with water, and the THF was removed *in vacuo*. The mixture was extracted twice with CH_2Cl_2, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was chromatographed on silica gel eluted with hexane/EtOAc (4:1) to give **20a** (2.27 g, 5.88 mmol, 63%) as white crystals. An analytically pure sample was obtained by recrystallization from hexane/EtOAc, mp 40.0–41.5 °C. IR ν_{max} (KBr) cm^{-1}: 1579, 1498, 1401, 1318, 1248 ($SiCH_3$), 1156 (C–O–C), 1082 (C–O–C), 976, 862, 831, 783, 735. NMR δ_H (300 MHz): −0.06 (9H, s, –Si(CH_3)$_3$), 0.86 (2H, t, $J = 8.2$ Hz, $–CH_2CH_2SiMe_3$), 3.50 (2H, t, $J = 8.2$ Hz, $–CH_2CH_2SiMe_3$), 3.53 (3H, s, $–OCH_2OCH_3$), 5.32 (2H, s, $–OCH_2OCH_3$), 5.72 (2H, s, NCH_2O), 6.97 (1H, dd, $J = 0.9$, 7.8 Hz, 4-H), 7.10 (1H, t, $J = 7.8$ Hz, 5-H), 7.17 (1H, s, 2-H), 7.21 (1H, dd, $J = 1.0$, 7.8 Hz, 6-H). NMR δ_C: −1.9 ($CH_3 \times 3$), 17.4 (CH_2), 55.9 (CH_3), 65.2 (CH_2), 77.2 (CH_2), 91.6 (CH), 94.5 (CH_2), 107.4 (CH), 112.7 (CH), 120.9 (CH), 125.3 (C), 127.6 (CH), 129.8 (C), 144.2 (C). *Anal*. Calcd. for $C_{16}H_{24}BrNO_3Si$: C, 49.74; H, 6.26; N, 3.63%. Found: C, 50.01; H, 6.37; N, 3.36%.

*7-Methoxymethoxy-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(2-trimethylsilanylethoxymethyl)-indole (**11a**).* To a solution of **20a** (1.90 g, 4.92 mmol) in dry THF (50 ml) was added dropwise a 2.31 M hexane solution of BuLi (2.55 ml, 5.90 mmol) at −78 °C under an Ar atmosphere. After 2 h, 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolan (2.00 ml, 9.84 mmol) was added dropwise, and the whole was warmed to room temperature and stirred for 25 h. The reaction was quenched by adding brine, and the mixture was extracted with ether. The extract was washed with brine and the aqueous layer was back-extracted with ether. The organic layers were combined, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was chromatographed on silica gel eluted with hexane/EtOAc (4:1) to give **11a** (1.80 g, 4.15 mmol, 84%) as a colorless oil. IR ν_{max} (KBr) cm^{-1}: 1547, 1379, 1292, 1246 ($SiCH_3$), 1149, 1107 (C–O–C), 1082 (C–O–C), 986, 856, 835, 788, 737, 682. NMR δ_H (400 MHz): −0.06 (9H, s, –Si(CH_3)$_3$), 0.86 (2H, t, $J = 8.4$ Hz, $–CH_2CH_2SiMe_3$), 1.36 (12H, s, –C(CH_3)$_2$ × 2), 3.50 (2H, t, $J = 8.4$ Hz, $–CH_2CH_2SiMe_3$), 3.54 (3H, s, $–OCH_2OCH_3$), 5.31 (2H, s, $–OCH_2OCH_3$), 5.74 (2H, s, NCH_2O), 6.92 (1H, d, $J = 8.0$ Hz, 4-H), 7.07 (1H, t, $J = 8.0$ Hz, 5-H), 7.58 (1H, s, 2-H), 7.69 (1H, d, $J = 8.0$ Hz, 6-H). NMR δ_C: −1.4 ($CH_3 \times 2$), 17.8 (CH_2), 24.9 ($CH_3 \times 4$), 56.2 (CH_3), 65.5 (CH_2), 77.7 (CH_2), 82.9 (*C* × 2), 95.0 (CH_2), 95.0 (CH), 107.3 (CH), 116.5 (CH), 121.2 (CH), 127.0 (C), 135.5 (CH), 138.9 (C), 144.7 (C). *Anal*. Calcd. for $C_{22}H_{36}BNO_5Si$: C, 60.97; H, 8.37; N, 3.23%. Found: C, 61.20; H, 8.16; N, 2.89%.

*7-Hydroxyindole (**21**).* Compound **16** (6.27 g, 20.9 mmol) was hydrogenated over 20% $Pd(OH)_2$ on carbon (320 mg) in EtOAc at room temperature for 1 d. The mixture was filtered through a pad of Celite, and the filtrate was concentrated *in vacuo*. The oily residue was chromatographed on silica gel eluted with EtOAc to give **21** (2.57 g, 13.0 mmol, 92%) as a yellow oil. This unstable compound was used for the next step without further purification. NMR δ_H (400 MHz): 4.20–5.09 (1H, br., –OH), 6.53 (1H, dd, $J = 2.0$, 5.2 Hz, 3-H), 6.58 (1H, d, $J = 7.2$ Hz, 4-H), 6.94 (1H, t, $J = 8.0$ Hz, 5-H), 7.23 (1H, t, $J = 2.8$ Hz, 2-H), 7.24 (1H, t, $J = 8.0$ Hz, 6-H), 8.24–8.64 (1H, br., NH).

*7-Methoxymethoxyindole (**22**).* To a mixture of **21** (1.246 g, 9.358 mmol) and pulverized K_2CO_3 (1.85 g, 13.4 mmol) in dry acetone (35 ml) was added chloromethyl methyl ether (0.61 ml, 8.0 mmol) as a neat liquid, and the whole was heated under reflux for 3 h before being quenched by a 5% NH_4OH solution. After the acetone had been removed *in vacuo*, the residue was extracted three times with EtOAc, and the combined organic extracts were dried over Na_2SO_4. The oily residue was passed through a short column of silica gel eluted with hexane/EtOAc (3;1) to give crude **22** (0.717 g, 4.05 mmol, 64%) as a yellow oil. This unstable indole was used for the next step without further purification. NMR δ_H (400 MHz): 3.57 (3H, s, $-OCH_3$), 5.30 (2H, s, $-OCH_2O-$), 6.54 (1H, dd, $J = 2.1$, 4.0 Hz, 3-H), 6.86 (1H, d, $J = 7.6$, 6-H), 7.00 (1H, t, $J = 7.8$ Hz, 5-H), 7.19 (1H, d, $J = 2.8$ Hz, 2-H), 7.31 (1H, d, $J = 8.0$ Hz, 4-H), 8.72 (1H, br., NH).

*1-Benzyloxymethyl-7-methoxymethoxyindole (**19b**).* To a stirred and cooled (0 °C) slurry of NaH (60% in oil, 704 mg, 17.6 mmol, prewashed with dry hexane) in dry DMF (10 ml) was added a solution of **22** (2.607 g, 14.71 mmol) in DMF (15 ml) under an Ar atmosphere. After 10 min, benzyl chloromethyl ether (2.45 ml, 17.6 mmol) was added as drops, and the mixture was stirred at room temperature for 3 h. The reaction was then quenched by a 10% NH_4Cl solution, and the mixture was extracted three times with ether. The ethereal extracts were combined, washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The oily residue was chromatographed on silica gel eluted with hexane/EtOAc (3:1) to give **19b** (4.371 g, 14.70 mmol, 99.9%) as a pale yellow oil. IR ν_{max} (KBr) cm^{-1}: 1581, 1493, 1306, 1247, 1208, 1150, 1051, 961, 786, 724, 696. NMR δ_H (400 MHz): 3.50 (3H, s, $-OCH_2OCH_3$), 4.46 (2H, s, $-OCH_2Ph$), 5.29 (2H, s, $-OCH_2OCH_3$), 5.86 (2H, s, NCH_2O), 6.53 (1H, d, $J = 3.2$ Hz, 3-H), 6.92 (1H, d, $J = 8.0$ Hz, 4-H), 7.03 (1H, t, $J = 8.0$ Hz, 5-H), 7.15 (1H, d, $J = 3.2$ Hz, 2-H), 7.20–7.39 (6H, m, 4-H and Ar-*H*s). *Anal*. Calcd. for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71%. Found: C, 72.58; H, 6.52; N, 4.56%.

*1-Benzyloxymethyl-3-bromo-7-methoxymethoxyindole (**20b**).* The title compound was synthesized from **19b** in a 76% yield by the same procedure as that for the synthesis of **20a** as white crystals, mp 63.5–64.0 °C. IR ν_{max} (KBr) cm^{-1}: 1581, 1494, 1379, 1313, 1246, 1155, 1086 (C–O–C), 1072 (C–O–C), 971, 921, 778, 732. NMR δ_H (400 MHz): 3.49 (3H, s, $-OCH_2OCH_3$), 4.47 (2H, s, $-OCH_2Ph$), 5.28 (2H, s, $-OCH_2OCH_3$), 5.82 (2H, s, NCH_2O), 6.98 (1H, $J = 8.0$ Hz, 4-H), 7.12 (1H, t, $J = 8.0$ Hz, 5-H), 7.19 (1H, s, 2-H), 7.27–7.37 (5H, m, Ar-*H*s), 7.23 (1H, d, $J = 8.0$ Hz, 6-H). *Anal*. Calcd. for $C_{18}H_{18}BrNO_3$: C, 57.46; H, 4.82; N, 3.72%. Found: C, 57.49; H, 4.89; N, 3.69%.

*1-Benzyloxymethyl-7-methoxymethoxy-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) indole (**11b**).* The title compound was synthesized from **20b** in a 77% yield by the same procedure as that for the synthesis of **11a** as white crystals, mp 77.0–77.5 °C. IR ν_{max} (KBr) cm^{-1}: 1618, 1547, 1493, 1377, 1291, 1242, 1149, 1063 (C–O–C), 989, 852, 787, 738. NMR δ_H (400 MHz): 1.28 (12H, s, $-OC(CH_3)_2-C(CH_3)_2O-$), 3.48 (3H, s, $-OCH_2OCH_3$), 4.46 (2H, s, $-OCH_2Ph$), 5.27 (2H, s, $-OCH_2OCH_3$), 5.84 (2H, s, NCH_2O), 6.92 (1H, d, $J = 8.0$ Hz, 4-H), 7.08 (1H, t, $J = 8.0$ Hz, 5-H), 7.22–7.34 (5H, m, Ar-*H*s), 7.59 (1H, s, 2-H), 7.69 (1H, d, $J = 8.0$ Hz, 6-H). *Anal*. Calcd. for $C_{24}H_{30}BNO_5$: C, 68.10; H, 7.14; N, 3.31%. Found: C, 68.11; H, 7.17; N, 3.32%.

*3-Bromo-7-diphenylmethoxyindole (**23**).* The title compound was synthesized from **16** in a 76% yield by the same procedure as that for the synthesis of **20a** as white crystals, mp 89–91 °C. IR ν_{max} (KBr) cm^{-1}: 3407, 1573, 1318, 1250, 1195, 1068 (C–O–C), 988, 933, 773, 746, 700, 507. NMR δ_H (400 MHz): 6.36 (1H, s, $-CHPh_2$), 6.61 (1H, d, $J = 8.0$ Hz, 4-H), 6.96 (1H, t, $J = 8.0$ Hz, 5-H), 7.14 (1H, d, $J = 8.0$ Hz, 6-H), 7.18 (1H, d, $J = 2.4$ Hz, 2-H), 7.26–7.38 (6H, m, Ar-*H*s), 7.38–7.44 (4H, m, Ar-*H*s), 8.46 or 8.36–8.57 (1H, br., NH). *Anal*. Calcd. for $C_{21}H_{16}BrNO$: C, 66.68; H, 4.26; N, 3.70%. Found: C, 66.70; H, 4.52; N, 3.40%.

1-tert-*Butoxycarbonyl-3-bromo-7-diphenylmethoxyindole (**20c**).* To a stirred and cooled (10 °C) slurry of NaH (60% in mineral oil, 0.49 g, 12.2 mmol, prewashed with dry hexane) in dry DMF (5 ml), was added as drops a solution of **23** (3.55 g, 9.39 mmol) and di-*tert*-butyl dicarbonate (2.46 g, 11.3 mmol) in dry DMF (15 ml) under an Ar atmosphere. The mixture was stirred at room temperature for 5 h and then quenched with a 10% NH_4Cl solution. The mixture was extracted three times with EtOAc, and the combined organic extracts were successively washed with water and brine. After drying (Na_2SO_4) and removing the solvent, the solid residue was recrystallized from *i*-Pr_2O to give **20c** (2.963 g, 6.194 mmol, 66%) as white crystals, mp 154–155 °C. The mother liquid was concentrated, and the residue was chromatographed on silica gel eluted with hexane/EtOAc (9:1) to give more of **20c** (1.167 g, 2.438 mmol, 26%). IR ν_{max} (KBr) cm^{-1}: 1755 (C=O), 1589, 1493, 1332, 1237, 1151 (C–O–C), 998, 703, 594, 582. NMR δ_H (400 MHz): 1.61 (9H, s, $-OC(CH_3)_3$), 6.28 (1H, s, $-CHPh_2$), 6.75 (1H, dd, $J = 2.4$, 7.4 Hz, 4-H), 7.05–7.12 (2H, m, 5-H and 6-H), 7.19–7.25 (2H, m, Ar-*H*s), 7.27–7.34 (4H, m, Ar-*H*s), 7.51 (1H, s, 2-H), 7.26–7.38 (6H, m, Ar-*H*s), 7.38–7.44 (4H, m, Ar-*H*s), 8.46 or 8.36–8.57 (1H, br., NH). *Anal*. Calcd. for $C_{26}H_{24}BrNO_3$: C, 65.28; H, 5.06; N, 2.93%. Found: C, 64.98; H, 4.99; N, 2.77%.

1-tert-*Butoxycarbonyl-7-methoxymethoxy-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) indole (**11c**).* A mixture of **20c** (2.410 g, 5.038 mmol), bispinacolate diboron (1.920 g, 7.557 mmol) and anhydrous K_2CO_3 (1.480 g, 15.11 mmol) in dry DMSO (15 ml) was purged with dry Ar gas for 10 min. $PdCl_2$ (dppf) (210 mg, 5 mol %) was then added, and the mixture was stirred at 80 °C for 20 h under an Ar atmosphere. After cooling to room temperature, the mixture was diluted with toluene and filtered through a pad of Celite. The filtrate was successively washed with water and brine, and the aqueous layers were re-extracted with toluene. The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The oily residue was chromatographed on silica gel eluted with toluene/EtOAc (9:1) to give **11c** (2.249 g, 4.280 mmol, 85%) as white crystals, mp 137–140 °C. IR ν_{max} (KBr) cm^{-1}: 1755 (C=O), 1613, 1580, 1493, 1323, 1228, 1137, 1048 (C–O–C), 1013 (C–O–C), 851, 705, 587. NMR δ_H (400 MHz): 1.35 (12H, s, $C(CH_3)_2 \times 2$), 1.60 (9H, s, $-OC(CH_3)_3$), 6.29 (1H, s, $-CHPh_2$), 6.67 (1H, d, $J = 8.0$ Hz, 4-H), 7.03 (1H, t, $J = 8.0$ Hz, 5-H), 7.12–7.36 (6H, m, Ar-*H*s), 7.54 (1H, d, $J = 8.0$ Hz, 6-H), 7.59–7.65 (4H, m, Ar-*H*s), 7.86 (1H, d, $J = 2.4$ Hz, 2-H). *Anal*. Calcd. for $C_{32}H_{36}BNO_5$: C, 73.15; H, 6.91; N, 2.67%. Found: C, 72.87; H, 6.92; N, 2.53%.

*Dimethyl 3-(4-isopropoxyphenyl)-1-[2-(4-isopropoxyphenyl)ethyl]-4-[7-methoxymethoxy-1-(2-trimethylsilanylethoxymethyl)-indol-3-yl]-pyrrole-2,5-dicarboxylate (**8a**).* A mixture of **10** (2.06 g, 3.28 mmol), **11a** (1.42 g, 3.28 mmol) and K_3PO_4 (4.18 g, 19.7 mmol) in dry DME (50 ml) was purged with dry Ar gas for 5 min. $Pd(PPh_3)_4$ (0.30 g, 0.26 mmol) was then added, and the whole was heated under reflux under an Ar atmosphere for 19 h. The reaction mixture was cooled to room temperature, filtered through a short column of silica gel with the aid of EtOAc, and concentrated *in vacuo*. The residue was roughly separated by chromatography on silica gel eluted with toluene/EtOAc (19:1), and the crude product was then purified by MPLC over silica gel eluted with *i*-Pr_2O/hexane (1:1) to give **8a** (1.63 g, 2.08 mmol, 63%) as a faint greenish amorphous powder. An analytically pure sample was obtained by recrystallization from hexane as white crystals, mp 128.5–129.5 °C. IR ν_{max} (KBr) cm^{-1}: 1722 (C=O), 1711 (C=O), 1615, 1577, 1510, 1438, 1375, 1326, 1291, 1243 ($SiCH_3$), 1211, 1076 (C–O–C), 1040 (C–O–C), 958, 829, 733, 527. NMR δ_H (400 MHz): −0.09 (9H, s, $-Si(CH_3)_3$), 0.76 (2H, t, $J = 8.0$ Hz, $-CH_2CH_2SiMe_3$), 1.28 (6H, d, $J = 6.0$ Hz, $-CH(CH_3)_2$), 1.32 (6H, d, $J = 6.0$ Hz, $-C(CH_3)_2$), 3.12 (2H, t, $J = 8.0$ Hz, NCH_2CH_2Ar), 3.25 (2H, t, $J = 8.0$ Hz, $-CH_2CH_2SiMe_3$), 3.37 (3H, s, $-CO_2CH_3$),

3.55 (3H, s, –OCH_2OCH_3), 3.57 (3H, s, –CO_2CH_3), 4.42–4.49 (1H, m, –$CH(CH_3)_2$), 4.48–4.55 (1H, m, –$CH(CH_3)_2$), 4.90 (2H, t, J = 8.0 Hz, NCH_2CH_2Ar), 5.30 (2H, s, –OCH_2OCH_3), 5.59 (2H, s, NCH_2O), 6.62 (1H, s, 2‴-H), 6.65 (2H, d, J = 8.4 Hz, 3′- and 5′-Hs), 6.81–6.87 (3H, m, 3‴-H, 5‴-H and 6‴-H), 6.89–6.95 (4H, m, 2‴-H, 6‴-H, 4‴-H and 5‴-H), 7.19 (2H, d, J = 8.4 Hz, 2′- and 6′-Hs). *Anal*. Calcd. for $C_{44}H_{56}N_2O_9Si$: C, 67.32; H, 7.19; N, 3.57%. Found: C, 67.13; H, 7.42; N, 3.32%.

*Dimethyl 4-[1-benzyloxymethyl-7-methoxymethoxyindol-3-yl]-3-(4-isopropoxyphenyl)-1-[2-(4-isopropoxyphenyl)ethyl]pyrrole-2,5-dicarboxylate (**8b**).* White crystals, mp 117–118 °C. IR ν_{max} (KBr) cm^{-1}: 1722 (C=O), 1711 (C=O), 1435, 1243, 1209, 1164 (C–O–C), 1105, 1040 (C–O–C), 950, 731. NMR δ_H (400 MHz): 1.18 (6H, d, J = 6.0 Hz, –$CH(CH_3)_2$), 1.31 (6H, d, J = 6.0 Hz, –$C(CH_3)_2$), 3.12 (2H, t, J = 8.0 Hz, NCH_2CH_2Ar), 3.35 (3H, s, –CO_2CH_3), 3.50 (3H, s, –OCH_2OCH_3), 3.58 (3H, s, –CO_2CH_3), 4.09 (2H, s, –OCH_2Ph), 4.26–4.34 (1H, m, –$CH(CH_3)_2$), 4.47–4.50 (1H, m, –$CH(CH_3)_2$), 4.91 (2H, t, J = 8.0 Hz, NCH_2CH_2Ar), 5.27 (2H, s, –OCH_2OCH_3), 5.67 (2H, s, NCH_2O), 6.63 (1H, s, 2′-H), 6.64 (2H, d, J = 8.4 Hz, 3⁗- and 5⁗-Hs), 6.83 (2H, d, J = 8.4 Hz, 3‴- and 5‴-Hs), 6.88 (1H, t, J = 4.4 Hz, 5′-H), 6.95 (2H, d, J = 8.4 Hz, 2‴- and 6‴-Hs), 6.96–7.00 (2H, m, 4′- and 6′-Hs), 7.09–7.14 (2H, m, Ph-*H*s), 7.19 (2H, d, J = 8.4 Hz, 2⁗- and 6⁗-Hs), 7.24–7.32 (3H, m, Ph-*H*s). *Anal*. Calcd. for $C_{46}H_{50}N_2O_9$: C, 71.30; H, 6.50; N, 3.62%. Found: C, 71.00; H, 6.58; N, 3.44%.

*Dimethyl 4-[1-*tert*-butoxycarbonyl-7-diphenylmethoxyindol-3-yl]-3-(4-isopropoxyphenyl)-1-[2-(4-isopropoxyphenyl)ethyl]pyrrole-2,5-dicarboxylate (**8c**).* White crystals, mp 75–76 °C. IR ν_{max} (KBr) cm^{-1}: 1754 (C=O), 1711 (C=O), 1302, 1235, 1152 (C–O–C), 1046 (C–O–C), 957, 704. NMR δ_H (400 MHz): 1.29 (6H, d, J = 6.0 Hz, –$CH(CH_3)_2$), 1.31 (6H, d, J = 6.0 Hz, –$C(CH_3)_2$), 1.52 (9H, s, –$OC(CH_3)_3$), 3.10 (2H, t, J = 7.6 Hz, NCH_2CH_2Ar), 3.31 (3H, s, –CO_2CH_3), 3.57 (3H, s, –CO_2CH_3), 4.41–4.54 (2H, m, –$CH(CH_3)_2$ × 2), 4.89 (2H, t, J = 7.6 Hz, NCH_2CH_2Ar), 6.25 (1H, s, –$CHPh_2$), 6.64 (1H, d, J = 8.0 Hz, 4′-H), 6.69 (2H, d, J = 8.4 Hz, 3″- and 5″-Hs), 6.76 (1H, d, J = 8.0 Hz, 6′-H), 6.82 (2H, d, J = 8.4 Hz, 3⁗- and 5⁗-Hs), 6.88 (1H, s, 2′-H), 6.91 (1H, t, J = 8.0 Hz, 5′-H), 6.92 (2H, d, J = 8.4 Hz, 2⁗- and 6⁗-Hs), 7.17 (2H, d, J = 8.4 Hz, 2″- and 6″-Hs), 7.19–7.25 (2H, m, Ph-*H*s), 7.26–7.33 (4H, m, Ph-*H*s), 7.61–7.67 (4H, m, Ph-*H*s). *Anal*. Calcd. for $C_{54}H_{56}N_2O_9$: C, 73.95; H, 6.44; N, 3.19%. Found: C, 73.72; H, 6.54; N, 3.04%.

*3-(4-Isopropoxyphenyl)-1-[2-(4-isopropoxyphenyl)ethyl]-4-[7-methoxymethoxy-1-(2-trimethylsilanylethoxymethyl)-indol-3-yl]pyrrole-2,5-dicarboxylic acid (**24a**).* A solution of diester **8a** (1.40 g, 1.79 mmol) in a mixture of 3 M aqueous NaOH (30 ml) and EtOH (30 ml) was stirred vigorously at 90 °C for 17 h. The reaction mixture was cooled to room temperature and concentrated *in vacuo*. The residue was diluted with cold water, and the pH was adjusted to 2–3 with 3 M aqueous HCl while cooling in an ice-water bath. The precipitated diacid was extracted twice with EtOAc, and the combined organic layers were washed with brine. After drying (Na_2SO_4) and removing the solvent, the solid residue was chromatographed on silica gel eluted with hexane/EtOAc (1:1) to give **24a** (1.28 g, 1.69 mmol, 95%) as pale yellow crystals. An analytical sample was obtained by recrystallization from EtOH/hexane (1:1) as white crystals, mp 155 °C. IR ν_{max} (KBr) cm^{-1}: 2977 (OH), 1691 (C=O), 1659 (C=O), 1430, 1244 ($SiCH_3$), 1105 (C–O–C), 1078 (C–O–C), 835, 735. NMR δ_H (400 MHz): −0.09 (9H, s, –$Si(CH_3)_3$), 0.76 (2H, t, J = 8.0 Hz, –$CH_2CH_2SiMe_3$), 1.26 (6H, d, J = 6.0 Hz, –$CH(CH_3)_2$), 1.30 (6H, d, J = 6.0 Hz, –$C(CH_3)_2$), 3.09 (2H, t, J = 7.2 Hz, NCH_2CH_2Ar), 3.25 (2H, t, J = 8.0 Hz, –CH_2CH_2 $SiMe_3$), 3.53 (3H, s, –OCH_2OCH_3), 4.39–4.46 (1H, m, –$CH(CH_3)_2$), 4.46–4.53 (1H, m, –$CH(CH_3)_2$), 4.99 (2H, t, J = 7.2 Hz, NCH_2CH_2Ar), 5.28 (2H, s, –OCH_2OCH_3), 5.63 (2H, s, NCH_2O), 6.64 (2H, d, J = 8.4 Hz, 3′- and 5′-Hs), 6.78 (2H, d, J = 8.4 Hz, 3‴- and 5‴-Hs), 6.80 (1H, s, 2⁗-H), 6.88 (1H, dd, J = 2.0, 6.8 Hz, 6⁗-H), 6.93–7.00 (4H, m, 2‴-, 6‴-, 4⁗- and 5⁗-Hs), 7.11 (2H, d, J = 8.4 Hz, 2′- and 6′-Hs). *Anal*. Calcd. for $C_{42}H_{52}N_2O_9Si$: C, 66.64; H, 6.92; N, 3.70%. Found: C, 66.52; H, 7.02; N, 3.47%.

*3-(4-Isopropoxypheyl)-1-[2-(4-isopropoxyphenyl)ethyl]-4-[7-methoxymethoxy-1-(2-trimethylsilanylethoxymethyl)-indol-3-yl]pyrrole-2,5-dicarboxylic acid bis-(4,6-dimethoxy-1,3,5-triazin-2-yl) ester (**28**).* To a solution of diacid **24a** (1.0670 g, 1.4095 mmol), and 2-chloro-4,6-dimethoxy-1,3,5-triazine (0.5688 mg, 3.2397 mmol) in dry THF (15 ml) was added dropwise *N*-methylmorpholine (1.55 ml, 14.1 mmol), and the mixture was stirred at room temperature for 19.5 h. The mixture was then diluted with ether, successively washed with cold 1 M aqueous HCl and 5% aqueous $NaHCO_3$, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was chromatographed on silica gel eluted with hexane/EtOAc (1:1) to give **28** (1.0147 g, 0.9802 mmol, 70%) as a yellow amorphous solid. IR ν_{max} (KBr) cm^{-1}: 2976, 1755 (C=O), 1728 (C=O), 1581, 1469, 1366, 1243 ($SiCH_3$), 1124 (C–O–C), 835, 815. NMR δ_H (400 MHz): −0.11 (9H, s,; –$Si(CH_3)_3$), 0.73 (2H, t, J = 8.0 Hz, –$CH_2CH_2SiMe_3$), 1.20 (6H, d, J = 6.0 Hz, –$CH(CH_3)_2$), 1.32 (6H, d, J = 6.0 Hz, –$C(CH_3)_2$), 3.15–3.31 (4H, m, NCH_2CH_2Ar and –$CH_2CH_2SiMe_3$), 3.52 (3H, s, –OCH_2OCH_3), 3.87 (6H, s, $ArOCH_3$), 3.99 (6H, s, $ArOCH_3$), 4.31–4.39 (1H, m, –$CH(CH_3)_2$), 4.48–4.55 (1H, m, –$CH(CH_3)_2$), 4.98 (2H, t, J = 8.0 Hz, NCH_2CH_2Ar), 5.24 (2H, s, –OCH_2OCH_3), 5.58 (2H, s, NCH_2O), 6.53 (2H, d, J = 8.4 Hz, 3′- and 5′-Hs), 6.76 (1H, t, J = 7.2 Hz, 5⁗-H), 6.79–6.85 (5H, m, 3‴-, 5‴-, 2⁗-, 4⁗- and 6⁗-Hs), 6.98 (2H, d, J = 8.4 Hz, 2‴- and 6‴-Hs), 7.29 (2H, d, J = 8.4 Hz, 3‴- and 6‴-Hs). *Anal*. Calcd. for $C_{52}H_{62}N_8O_{13}Si$: C, 60.33; H, 6.04; N, 10.82%. Found: C, 59.99; H, 6.10; N, 10.54%.

*3-(4-Isopropoxyphenyl)-1-[2-(4-isopropoxyphenyl)ethyl]-2,5-bis-(4-methoxybenzoyl)-4-[7-methoxymethoxy-1-(2-trimethylsilanylethoxymethyl)-indol-3-yl]pyrrole (**29**).* To a solution of activated ester **28** (711.1 mg, 0.6869 mmol) in dry ether (15 ml) was added dropwise a 0.5 M THF solution of 4-methoxyphenylmagnesium bromide (3.00 ml, 1.50 mmol) at −20 °C under an Ar atmosphere, and the whole was stirred at the same temperature for 1.5 h. The reaction was then quenched with 10% aqueous NH_4Cl, and the mixture was extracted twice with ether. The combined ethereal extract was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was chromatographed on silica gel eluted with hexane/EtOAc (5:1) to give **29** (488.4 mg, 0.5211 mmol, 76%) as a pale yellow amorphous powder. IR ν_{max} (KBr) cm^{-1}: 2974, 1598 (C=O), 1510, 1249 ($SiCH_3$), 1163 (C–O–C), 985, 835. NMR δ_H (400 MHz): −0.08 (9H, s, –$Si(CH_3)_3$), 0.76 (2H, t, J = 8.0 Hz, –$CH_2CH_2SiMe_3$), 1.13 (6H, d, J = 6.0 Hz, –$CH(CH_3)_2$), 1.27 (6H, d, J = 6.0 Hz, –$C(CH_3)_2$), 3.02 (2H, t, J = 8.0 Hz, NCH_2CH_2Ar), 3.20 (2H, t, J = 8.0 Hz, –$CH_2CH_2SiMe_3$), 3.46 (3H, s, –OCH_2OCH_3), 3.63 (3H, s, $ArOCH_3$), 3.71 (3H, s, $ArOCH_3$), 4.24–4.32 (1H, m, –$CH(CH_3)_2$), 4.38–4.46 (1H, m, –$CH(CH_3)_2$), 4.58 (2H, t, J = 8.0 Hz, NCH_2CH_2Ar), 5.19 (2H, s, –OCH_2OCH_3), 5.45 (2H, s, NCH_2O), 6.36 (2H, d, J = 8.4 Hz, 3⁗- and 5⁗-Hs), 6.43 (2H, d, J = 8.4 Hz, 3⁗- and 5⁗-Hs), 6.59 (2H, d, J = 8.4 Hz, 3′- and 5′-Hs), 6.66–6.76 (6H, m, 3‴-, 5‴-, 2⁗⁗-, 4⁗⁗-, 5⁗⁗- and 6⁗⁗-Hs), 6.80 (2H, d, J = 8.4 Hz, 2‴- and 6‴-Hs), 7.11 (2H, d, J = 8.4 Hz, 2′- and 6′-Hs), 7.56 (2H, d, J = 8.4 Hz, 2⁗- and 6⁗-Hs), 7.61 (2H, d, J = 8.4 Hz, 2⁗⁗- and 6⁗⁗-Hs). *Anal*. Calcd. for $C_{56}H_{64}N_2O_9Si$: C, 71.77; H, 6.88; N, 2.99%. Found: C, 71.42; H, 6.88; N, 2.74%.

*4-[2-Cyanomethyl-7-methoxymethoxy-1-(2-trimethylsilanylethoxymethyl)-indol-3-yl]-3-(4-isopropoxyphenyl)-1-[2-(4-isopropoxyphenyl)-ethyl]-2,5-bis-(4-methoxybenzoyl) pyrrole (**6b**).* To a refluxing degassed solution of **29** (30.1 mg, 32.1 µmol) and $EtO(C{=}S)SCH_2CN$ (19.4 mg, 120.0 µmol), which had been prepared by the reaction of EtONa, CS_2 and $ClCH_2CN$ in EtOH by a standard procedure, in dry 1,2-dichloroethane (1.0 ml), a solution of dilauroyl peroxide (47.8 mg, 120.0 µmol) in dry 1,2-dichloroethane (0.5 ml) was dropwise added over a period of 5.5 h *via* a syringe pump. The solution was further refluxed for 2 h and concentrated *in vacuo*. The crude product was chromatographed on silica gel eluted with toluene/EtOAc (19:1) to afford **6b** (11.1 mg, 1.14 µmol, 36%) as a yellow amorphous powder. IR ν_{max} (KBr) cm^{-1}: 2974, 2252 (C≡N), 1594 (C=O), 1510, 1251 ($SiCH_3$), 1164 (C–O–C), 1107, 1075, 983, 836, 767. NMR δ_H (400 MHz): −0.08 (9H, s, $Si(CH_3)_3$), 0.68–0.83 (2H, m, –$CH_2CH_2SiMe_3$), 1.13 (3H, d, J = 6.0 Hz, –$CH(CH_3)(CH_3)$), 1.15 (3H, d, J = 6.0 Hz, –$CH(CH_3)(CH_3)$), 1.27 (3H, d, J = 6.0 Hz, –$CH(CH_3)(CH_3)$), 1.28 (3H, d, J = 6.0 Hz, –$CH(CH_3)(CH_3)$), 2.87–

2.97 (1H, m, $NCH_2CH_aH_bAr$), 3.16–3.27 (1H, m, $NCH_2CH_aH_bAr$), 3.17–3.28 (2H, m, $-CH_2CH_2SiMe_3$), 3.33 (1H, d, $J = 17.6$ Hz, $ArCH_aHbCN$), 3.47 (1H, d, $J = 17.6$ Hz, $ArCH_aH_bCN$), 3.47 (3H, s, $-OCH_2OCH_3$), 3.65 (3H, s, $ArOCH_3$), 3.71 (3H, s, $ArOCH_3$), 4.24–4.33 (1H, m, $-CH(CH_3)_2$), 4.40–4.48 (1H, m, $-CH(CH_3)_2$), 4.42–4.51 (1H, m, $NCH_aH_bCH_2Ar$), 4.76–4.85 (1H, m, $NCH_aH_bCH_2Ar$), 5.22 (1H, d, $J = 10.4$ Hz, $-OCH_aH_bOCH_3$), 5.24 (1H, d, $J = 10.4$ Hz, $-OCH_aH_bOCH_3$), 5.60 (1H, d, $J = 11.2$ Hz, NCH_aH_bO), 5.89 (1H, d, $J = 11.2$ Hz, NCH_aH_bO), 6.37 (2H, d, $J = 8.4$ Hz, 3‴″- and 5‴″-Hs), 6.53 (2H, d, $J = 8.4$ Hz, 3‴″- and 5‴″-Hs), 6.60 (2H, d, $J = 8.4$ Hz, 3‴″- and 5‴″-Hs), 6.67 (2H, d, $J = 8.4$ Hz, 2‴″- and 6‴″-Hs), 6.73 (2H, d, $J = 8.4$ Hz, 3‴- and 5‴-Hs), 6.80 (1H, d, $J = 8.0$ Hz, 4′-H), 6.89 (1H, t, $J = 8.0$ Hz, 5′-H), 6.94 (1H, d, $J = 8.0$ Hz, 6′-H), 7.13 (2H, d, $J = 8.4$ Hz, 2‴- and 6‴-Hs), 7.45 (2H, d, $J = 8.4$ Hz, 2‴″- and 6‴″-Hs), 7.61 (2H, d, $J = 8.4$ Hz, 2‴″- and 6‴″-Hs). NMR δ_C: −1.5, 14.0, 17.6, 21.7, 21.8, 22.0, 22.1, 37.9, 47.8, 55.2, 56.3, 64.6, 69.6, 69.7, 74.0, 95.1, 107.9, 111.6, 112.7, 113.1, 114.0, 115.6, 115.8, 116.0, 118.1, 120.6, 125.8, 126.6, 128.7, 130.0, 130.0, 130.6, 130.6, 130.9, 131.0, 131.5, 131.8, 132.4, 133.0, 143.8, 156.3, 156.5, 162.9, 163.2, 188.6, 188. FABMS *m/z*: 975 (M^+), 858 ($M^+ - OCH_2CH_2SiMe_3$), 135 (base peak, $C(O)C_6H_4OCH_3$). HRFABMS *m/z*: calcd. for $C_{58}H_{65}N_3O_9Si$ (M^+), 975.4490; found, 975.4482.

*5-Cyano-1-(4-isopropoxyphenyl)-2-(4-methoxybenzoyl)-7-methoxymethoxy-4-(4-methoxyphenyl)-3-[2-(4-methoxyphenyl)ethyl]-6-(2-trimethylsilanylethoxymethyl)-3,6-dihydro-pyrrolo[2,3-c]carbazole (**31**).* A solution of **6b** (4.2 mg, 4.2 µmol) and DBU (4.0 µl, 26.9 µmol) in dry CH_2Cl_2 (0.5 ml) was stirred at room temperature for 21 h. The mixture was concentrated *in vacuo*, and the product was purified by silica gel TLC (Merck, Silica Gel 60 F_{254}, 0.25 mm layer thickness) developed with toluene/EtOAc (4:1) to afford cyclized product **31** (3.3 mg, 3.4 µmol, 79%) as a pale yellow oil. IR ν_{max} (KBr) cm^{-1}: 2974, 2214 (C≡N), 1599 (C=O), 1512, 1246 ($SiCH_3$), 1168 (C–O–C), 1072, 889, 837. NMR δ_H (400 MHz): −0.13 (9H, s, $-Si(CH_3)_3$), 0.85 (2H, t, $J = 8.0$ Hz, $-CH_2CH_2SiMe_3$), 1.27 (6H, d, $J = 6.0$ Hz, $-CH(CH_3)_2$), 1.32 (6H, d, $J = 6.0$ Hz, $-C(CH_3)_2$), 2.56 (2H, t, $J = 8.0$ Hz, NCH_2CH_2Ar), 3.50 (2H, t, $J = 8.0$ Hz, $-CH_2CH_2SiMe_3$), 3.57 (3H, s, $-OCH_2OCH_3$), 3.78 (3H, s, $ArOCH_3$), 3.90 (3H, s, $ArOCH_3$), 3.85–3.90 (2H, m, NCH_2CH_2Ar), 4.37–4.45 (1H, m, $-CH(CH_3)_2$), 4.49–4.57 (1H, m, $-CH(CH_3)_2$), 5.35 (2H, s, $-OCH_2OCH_3$), 6.07 (1H, d, $J = 8.0$ Hz, 10-H), 6.50 (2H, d, $J = 8.4$ Hz, 3‴″- and 5‴″-Hs), 6.56 (2H, s, NCH_2O), 6.60 (2H, d, $J = 8.4$ Hz, 2‴″- and 6‴″-Hs), 6.67 (1H, t, $J = 8.0$ Hz, 9-H), 6.71 (2H, d, $J = 8.4$ Hz, 3″- and 5″-Hs), 6.76 (2H, d, $J = 8.4$ Hz, 3′- and 5′-Hs), 7.06 (1H, d, $J = 8.0$ Hz, 8-H), 7.10 (2H, d, $J = 8.4$ Hz, 3‴- and 5‴-Hs), 7.21 (2H, d, $J = 8.4$ Hz, 2′- and 6′-Hs), 7.58 (2H, d, $J = 8.4$ Hz, 2‴- and 6‴-Hs), 7.62 (2H, d, $J = 8.4$ Hz, 2″- and 5″-Hs). NMR δ_C: −1.5 ($CH_3 \times 3$), 17.9 (CH_2), 21.8 ($CH_3 \times 2$), 22.0 ($CH_3 \times 2$), 36.8 (CH_2), 47.7 (CH_2), 55.4 (CH_3), 55.4 (CH_3), 56.4 (CH_3), 64.9 (CH_2), 69.7(CH), 70.1 (CH), 74.2 (CH_2), 94.6 (C), 95.4 (CH_2), 111.2 (CH), 113.4 ($CH \times 2$), 114.2 ($CH \times 2$), 115.6 ($CH \times 2$), 116.0 ($CH \times 2$), 117.2 (C), 118.2 (C), 118.9 (CH), 119.9 (C), 120.0 (CH), 124.6 (C), 125.4 (C), 127.5 ($CH \times 2$), 128.6 (C), 129.5 (C), 129.5 (C), 130.1 (C), 130.5 (C), 130.9 (C), 131.5 ($CH \times 2$), 131.8 (C), 132.4 ($CH \times 2$), 132.9 ($CH \times 2$), 135.4 (C), 140.1 (C), 144.1(C), 156.4 (C), 157.3 (C), 160.2 (C), 163.8(C), 190.3 (C=O). FABMS *m/z*: 957 (M^+), 884 ($M^+ - SiMe_3$), 840 ($M^+ - OCH_2CH_2SiMe_3$), 77 (base peak, C_6H_5). HRFABMS *m/z*: calcd. for $C_{58}H_{63}N_3O_8Si$ (M^+), 957.4384; found, 957.4414.

*3-(1-Benzyloxymethyl-7-methoxymethoxyindol-3-yl)-4-(4-isopropoxyphenyl)-1-[2(4-isopropoxyphenyl)ethyl]-1H-pyrrole (**9**).* A mixture of diacid **24b** (1.038 g, 1.390 mmol), obtained from **8b** by the same procedure as that for **8a** to **24a**, and Cu_2O (418 mg, 2.923 mmol) in degassed quinoline (5 ml) was heated at 180 °C for 10 min. The mixture was then cooled to room temperature, diluted with ether, and filtered through a pad of Celite. The filtrate was successively washed with 1 M aqueous HCl and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude product was chromatographed on silica gel eluted with hexane/EtOAc (3:1) to give **9** (0.901 g, 1.368 mmol, 98%) as a brown viscous oil. IR ν_{max} (KBr) cm^{-1}: 2974, 1726, 1494, 1241, 1155, 1107, 1060, 947, 785, 734, 697. NMR δ_H (400 MHz): 1.26 (6H, d, $J = 6.0$ Hz, $-CH(CH_3)_2$), 1.33 (6H, d, $J = 6.0$ Hz, $-C(CH_3)_2$), 3.07 (2H, t, $J = 7.2$ Hz, NCH_2CH_2Ar), 3.52 (3H, s, $-OCH_2OCH_3$), 4.07–4.15 (2H, m, NCH_2CH_2Ar), 4.38 (2H, s, $-OCH_2Ph$), 4.36–4.44 (1H, m, $-CH(CH_3)_2$), 4.48–4.56 (1H, m, $-CH(CH_3)_2$), 5.30 (2H, s, $-OCH_2OCH_3$), 5.74 (2H, s, NCH_2O), 6.71 (2H, d, $J = 8.4$ Hz, 3″- and 5″-Hs), 6.72 (1H, d, $J = 2.4$ Hz, 2- or 5-H), 6.79 (1H, d, $J = 2.4$ Hz, 2- or 5-H), 6.84 (1H, s, 2′-H), 6.84 (2H, d, $J = 8.4$ Hz, 3‴″- and 5‴″-Hs), 6.92 (1H, d, $J = 8.0$ Hz, 4′-H), 7.00 (1H, t, $J = 8.0$ Hz, 5′-H), 7.06 (2H, d, $J = 8.4$ Hz, 2‴″- and 6‴″-Hs), 7.16–7.32 (8H, m, 6′-H, 2″-H, 6″-H and Ph-Hs). FABMS *m/z*: 658 (M^+, base peak), 551 ($M^+ - OCH_2Ph$), 507 ($M^+ - OCH_2CH_2SiMe_3$, −*i*-Pr). HRFABMS *m/z*: calcd. for $C_{42}H_{46}N_2O_5$ (M^+), 658.3407; found, 658.3403.

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References

1) Counter CM, Avilion AA, Lefeuvre CE, Stewart NG, Greider CW, Harley CB, and Bacchetti S, *EMBO J.*, **11**, 1921–1929 (1992).
2) Harley CB, Kim NW, Prowse KR, Weinrich SL, Hirsch KS, West MD, Bacchetti S, Hirte HW, Counter CM, Greider CW, Piatyszek MA, Wright WE, and Shay JW, *Cold Spring Harb. Symp. Quant. Biol.*, **59**, 307–315 (1994).
3) Kelland LR, *IDrugs*, **2**, 550–552 (1999).
4) Warabi K, Matsunaga S, van Soest RWM, and Fusetani N, *J. Org. Chem.*, **68**, 2765–2770 (2003).
5) Fürstner A, Domostoj MM, and Scheiper B, *J. Am. Chem. Soc.*, **127**, 11620–11621 (2005).
6) Fürstner A, Domostoj MM, and Scheiper B, *J. Am. Chem. Soc.*, **128**, 8087–8094 (2006).
7) Iwao M, Takeuchi T, Fujikawa N, Fukuda T, and Ishibashi F, *Tetrahedron Lett.*, **44**, 4443–4446 (2003).
8) Fujikawa N, Ohta T, Yamaguchi T, Fukuda T, Ishibashi F, and Iwao M, *Tetrahedron*, **62**, 594–604 (2006).
9) Yamaguchi T, Fukuda T, Ishibashi F, and Iwao M, *Tetrahedron Lett.*, **47**, 3755–3757 (2006).
10) Bartoli G, Palmieri G, Bosco M, and Dalpozzo R, *Tetrahedron Lett.*, **16**, 2129–2132 (1989).
11) Dobson DR, Gilmore J, and Long DA, *Synlett*, 79–80 (1992).
12) Ishiyama T, Murata M, and Miyaura N, *J. Org. Chem.*, **60**, 7508–7510 (1995).
13) Peschko C and Steglich W, *Tetrahedron Lett.*, **41**, 9477–9481 (2000).
14) Boger DL, Soenen DR, Boyce CW, Hedrick MP, and Jin Q, *J. Org. Chem.*, **65**, 2479–2483 (2000).
15) Blotny G, *Tetrahedron*, **62**, 9507–9522 (2006).
16) Sommers AH, Michaels RJJr, and Weston AW, *J. Am. Chem. Soc.*, **74**, 5546 (1952).
17) Belostotskaya IS, Komissarova NL, Prokof'eva TI, Kurkovskaya LN, and Vol'eva VB, *Russ. J. Org. Chem.*, **41**, 703–706 (2005).
18) Osornio YM, Cruz-Almanza R, Jiménez-Montaño V, and Miranda LD, *Chem. Commun.*, 2316–2317 (2003).