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SYNTHESIS OF LAMELLARINS VIA REGIOSELECTIVE ASSEMBLY OF 1,2-DIARYLATED [1]BENZOPYRANO[3,4-*b*]PYRROL-4(3*H*)-ONE CORE

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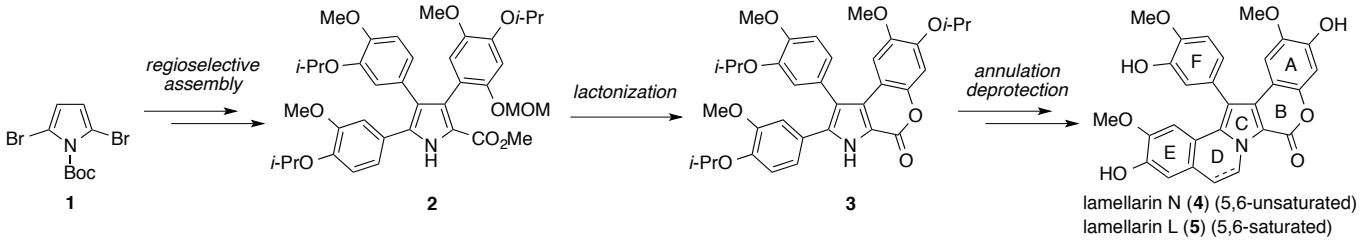
Abstract – A modular synthesis of lamellarins has been developed. The key reactions in this synthesis are the assembly of 1,2-diarylated [1]benzopyrano-[3,4-*b*]pyrrol-4(3*H*)-ones from a preexisting [1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one core and the appropriate arylboronic acids. The obtained 1,2-diarylated [1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-ones could be easily converted into the corresponding lamellarin derivatives by intramolecular annulation between the pyrrole nitrogen and the C2 aromatic ring.

INTRODUCTION

Lamellarins are polycyclic pyrrole alkaloids possessing a unique 14-phenyl-6*H*-[1]benzopyrano-[4´,3´:4,5]pyrrolo[2,1-*a*]isoquinolin-6-one ring system.[1] In rare cases (lamellarins O, P, Q, and R), the compounds possess simple, nonfused 3,4-diarylpyrrole-2-carboxylate structures.[2d,2e] Since the first isolation of lamellarins A–D from the marine prosobranch mollusk *Lamellaria* sp. in 1985, more than 50 lamellarins have been isolated from tunicates, sponges, and prosobranchs.[2] These lamellarins exhibit a wide range of useful biological activities: potent antiproliferative activity against several cancer cell lines,[2g,h,j,k,m,n,3] multi-drug resistance (MDR) reversal activity,[2n,3a] anti-HIV activity,[2j,3c,4] topoisomerase I inhibition,[5] inhibition of mitochondrial function,[6] and protein kinase inhibition.[3i,7] Because of their unique structures and significant biological activities, lamellarins have attracted the attention of synthetic organic and medicinal chemists. Since the first synthesis of lamellarins in 1997, numerous methods for their preparation have been proposed.[8] The methods can be categorized into two groups: one utilizes formation of the pyrrole core as the key step and the other employs regioselective functionalization of the

This paper is dedicated to Professor Dr. Masakatsu Shibasaki on the occasion of his 70th birthday.

preexisting pyrrole core. Compared to the former approaches, the latter syntheses are more effective since a wide range of natural and artificial lamellarins can be obtained easily by simple modification of the aromatic building blocks substituted on the central pyrrole core (C-ring). In fact, the syntheses of lamellarins using such modular approaches have been developed by several groups.[8h,i,j,q,u,w,x] For example, we developed a modular synthesis of lamellarins L (**4**) and N (**5**) via the following sequence: 1) regioselective assembly of 3,4,5-differentially arylated pyrrole-2-carboxylates **2** from 2,5-dibromo-1-(*tert*-butoxycarbonyl)-1*H*-pyrrole **1** and arylboronic acids; 2) lactonization of **2** to construct the B-ring of lamellarins; 3) intramolecular annulation of 1,2-diaryl-[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-ones **3** to construct the D-ring; and 4) deprotection (Scheme 1).[8u]

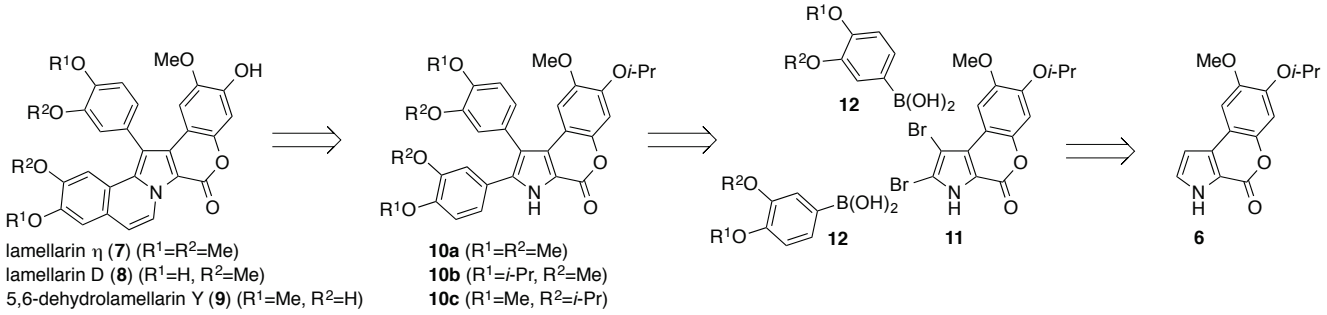


Scheme 1

In most of the modular lamellarin syntheses, the A-ring module is introduced after construction of the E- and F-rings, whereas the synthesis using the other strategy has been rarely reported.[8q] To prepare libraries of biologically active lamellarin analogues for lead discovery and/or optimization in medicinal chemistry, it is essential to develop a synthetic method based upon a new strategy. We focused our attention on compound **3** and expected that another total synthesis of lamellarins would be possible if 1,2-diaryl-[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-ones could be efficiently synthesized by introduction of the E- and F-ring modules into a preexisting [1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one core, which corresponds to the A–C ring system of lamellarins. In this paper, we report the alternative modular synthesis of lamellarins starting from 7-isopropyl-8-methoxy-[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one **6**.

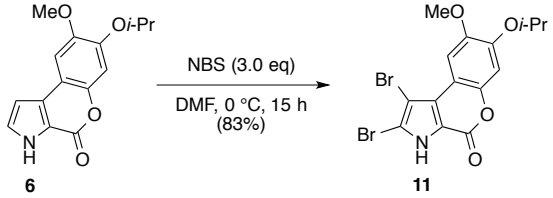
RESULTS AND DISCUSSION

We initially selected lamellarins η (**7**) and D (**8**), and 5,6-dehydrolamellarin Y (**9**), as the targets for this synthetic approach. Lamellarins **7**, **8**, and **9** can be prepared from 1,2-diaryl-[1]benzopyrano[3,4-*b*]-pyrrol-4(3*H*)-ones **10a**, **10b**, and **10c**, as depicted retrosynthetically in Scheme 2. Since the substituents at the C1 and C2 positions of **10a–c** are the same, intermediates **10** may be obtained by the double cross-coupling of 1,2-dibromo-[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-ones **11** with arylboronic acids **12**. Dibromide **11** can be prepared from [1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one **6**, which is easily accessible from *N*-benzenesulfonyl-1*H*-pyrrole.[8p]



Scheme 2

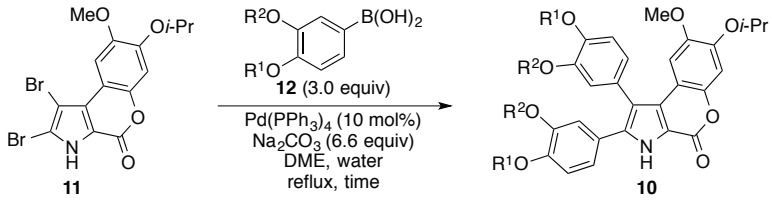
Based on the retrosynthetic analysis, we first synthesized **10a–c**. Dibromide **11** was obtained by the treatment of **6** with *N*-bromosuccinimide (NBS) in DMF (Scheme 3).



Scheme 3

We next investigated the Suzuki–Miyaura cross-coupling of **11** with arylboronic acids **12**. The results are summarized in Table 1. Treatment of **11** with 3.0 equiv of **12a** in the presence of 10 mol% $Pd(PPh_3)_4$ and 6.6 equiv Na_2CO_3 in a 1,2-dimethoxyethane (DME)/water mixture under reflux for 12.5 h furnished **10a** in 78% yield (entry 1). Cross-coupling of **11** with arylboronic acids **12b** and **12c** under similar conditions afforded the corresponding products **10b** and **10c** in identical yields of 72% (entries 2 and 3).

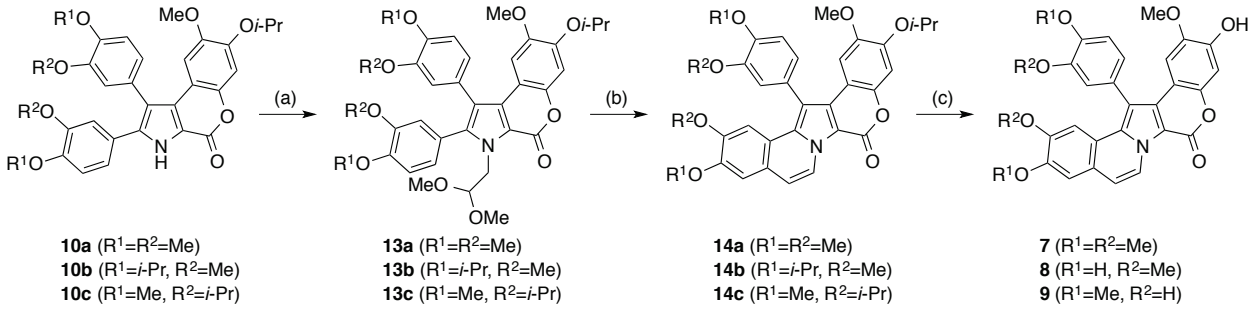
Table 1. Synthesis of 1,2-diarylated [1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-ones **10** via cross-coupling of **11** with arylboronic acids **12**



entry	**12**	R^1	R^2	time (h)	**10**	yield (%)[a]
1	**12a**	Me	Me	12.5	**10a**	78
2	**12b**	*i*-Pr	Me	13	**10b**	72
3	**12c**	Me	*i*-Pr	15	**10c**	72

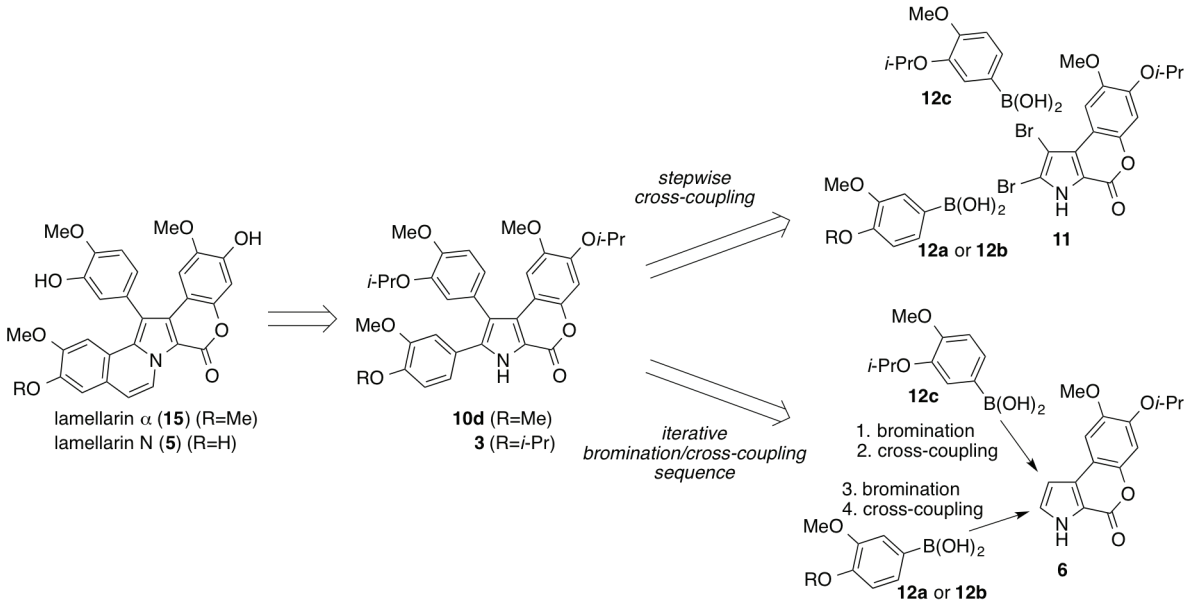
[a] Isolated yield.

We then focused on the conversion of **10a–c** to lamellarins η (**7**) and D (**8**), and 5,6-dehydrolamellarin Y (**9**) (Scheme 4). Treatment of **10a–c** with bromoacetaldehyde dimethyl acetal in the presence of Cs_2CO_3 as a base in DMF gave 2,2-dimethoxyethylated **13a–c** in 72–96% yields. Subsequently, TfOH-mediated cyclization of **13a–c** in CH_2Cl_2 at 0 °C for 2.5 h afforded **14a–c** in good to excellent yields. Final deprotection of the isopropyl groups of **14a–c** using excess BCl_3 afforded the corresponding lamellarins **7**, **8**, and **9** in 87–98% yields.



Scheme 4. *Reagents and conditions*: (a) $BrCH_2CH(OMe)_2$ (6.6 equiv), Cs_2CO_3 (6.6 equiv), DMF, 110 °C, 14–18 h (**13a**: 72%, **13b**: 94%, **13c**: 96%); (b) cat. TfOH, CH_2Cl_2, 0 °C, 2.5 h (**14a**: 99%, **14b**: 87%, **14c**: 99%); (c) BCl_3, CH_2Cl_2, –78 °C, 0.5 h then rt, 3 h (**7**: 87%, **8**: 98%, **9**: 98%).

Encouraged by the successful total synthesis of lamellarins **7**, **8**, and **9**, we attempted the synthesis of other types of lamellarins, α (**15**) and N (**5**). The retrosynthetic analysis of **15** and **5** is depicted in Scheme 5. Both **15** and **5** can be obtained from 1,2-diaryl-[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-ones **10d** and **3** in a similar manner as described above. As opposed to the cases of **10a–c**, the C1 and C2 aryl

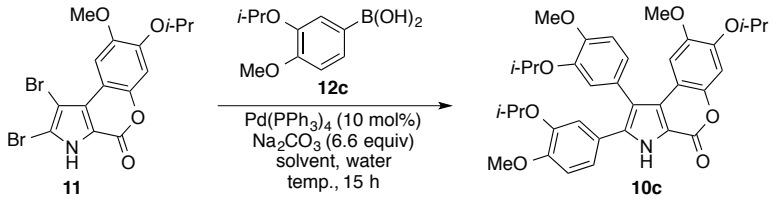


Scheme 5

substituents on **10d** and **3** are different. Hence, we planned to synthesize **10d** and **3** via two different routes: the stepwise cross-coupling of **11** with arylboronic acids **12c** and **12a** or **12b**; or the iterative bromination/cross-coupling sequence of **6**.

According to the retrosynthetic analysis, we first examined the regioselective Suzuki–Miyaura cross-coupling of dibromide **11** with arylboronic acid **12c**. Initially, we tried to accomplish the cross-coupling by modifying the reaction conditions described in Table 1. The results are summarized in Table 2. When 1.5 equiv of **12c** was used for the reaction, the 1,2-diarylated product **10c** was obtained in only 62% yield (entry 1). However, when the amount of **12c** was reduced to 1.0 equiv, no monoarylated product was observed and **10c** was obtained in 39% yield, along with the unreacted **1a** (38%, entry 2). The monoarylated product was not furnished even after changing the solvent to THF and reducing the reaction temperature to 65 °C (entry 3). These results suggested that conversion of the monoarylated product into the 1,2-diarylated product **10c** proceeds much faster than the conversion of **11** into the monoarylated product. The reason for this trend is not clear at present.

Table 2. Attempted regioselective cross-coupling of **11** with **12c**



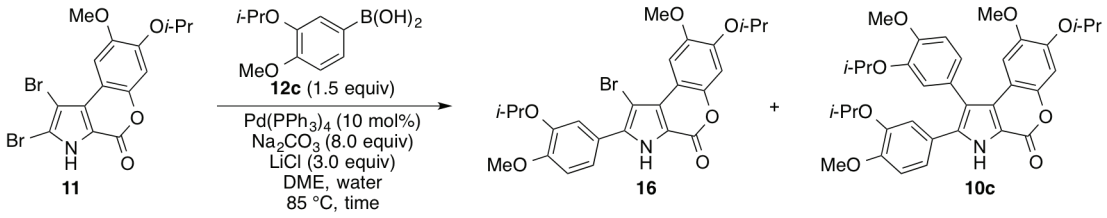
entry	**12c** (equiv)	solvent	temp. (°C)	**10c** (%)[a]	**11** (%)[a]
1	1.5	DME	85	62	0
2	1.0	DME	85	39	38
3	1.0	THF	65	14	55

[a] Isolated yield.

Dodd et al. reported that 2,5-dibromo-1-(*tert*-butoxycarbonyl)-1*H*-pyrrole (**1**) could be regioselectively monoarylated under the standard cross-coupling conditions in the presence of LiCl.[9] Accordingly, we carried out the reaction of dibromide **11** with **12c** under similar conditions, as mentioned in Table 3 [$Pd(PPh_3)_4$ (10 mol%), Na_2CO_3 (8.0 equiv), LiCl (3.0 equiv), DME, water, 85 °C, 3 h]; however, the desired product was not formed and **11** was recovered in 67% yield (entry 1). When the reaction time was extended to 15 h, the monoarylated product **16** was obtained in poor yield (12%), along with the 1,2-diarylated product **10c** (53%) and unreacted **11** (9%) (entry 2).

We then used the cross-coupling conditions established by Bach et al. for the conversion of methyl 4,5-dibromo-1*H*-pyrrole-2-carboxylate to 5-aryl-4-bromo-1*H*-pyrrole-2-carboxylate.[10] Dibromide **11**

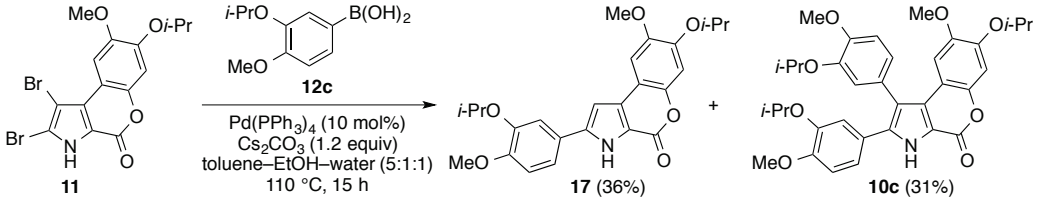
Table 3. Attempted regioselective cross-coupling of **11** with **12c** in the presence of LiCl



entry	time (h)	**16** (%)[a]	**10c** (%)[a]	**11** (%)[a]
1	3	0	0	67
2	15	12	53	9

[a] Isolated yield.

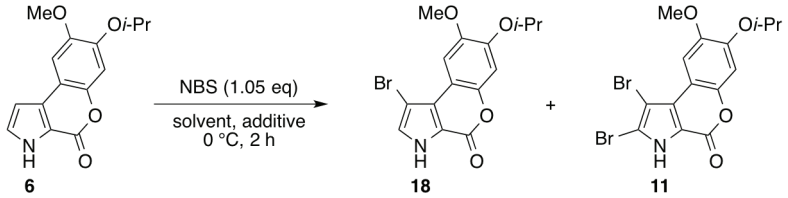
was treated under similar conditions [$Pd(PPh_3)_4$ (10 mol%), Cs_2CO_3 (1.2 equiv), toluene–EtOH–water (5:1:1), 110 °C, 15 h]. However, this reaction, too, was not very successful and afforded 1-debrominated [1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one **17** in 36% yield along with the 1,2-diaryl product **10c** in 31% yield (Scheme 6).



Scheme 6

At this stage, we discontinued the synthesis of **10d** and **3** via the stepwise cross-coupling of **11**, since the regioselective cross-coupling of **11** with **12c** was inefficient for the preparation of the monoarylated [1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one **16**. We next focused on the synthesis of **10d** and **3** via the iterative bromination/cross-coupling sequence of **6**. The results for the regioselective bromination of **6** with NBS are summarized in Table 4. Treatment of **6** with 1.05 equiv NBS in DMF at 0 °C for 2 h gave the 1-monobrominated product **18** and 1,2-dibrominated product **11** in 48% and 24% yields, respectively; the starting material **6** was recovered in 15% yield (entry 1). All attempts to separate **18**, **11**, and **6** by column chromatography failed because of the poor solubility of **18** in most of the commonly used eluents; thus, the yields of these products were estimated by ^1H NMR analysis of the mixtures. When a less polar solvent such as CH_2Cl_2 was used, the formation of **11** was suppressed (1% yield) and **18** was obtained in 68% yield (entry 2). Although the addition of 1.0 equiv pyridine promoted the reaction to afford **18** in 75% yield, compound **11** was also formed in 6% yield (entry 3). In contrast, when 1.0 equiv AcOH was used as the acidic additive, the yield of **18** improved to 79% without significant

Table 4. Regioselective bromination of [1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one **6** with NBS[a]

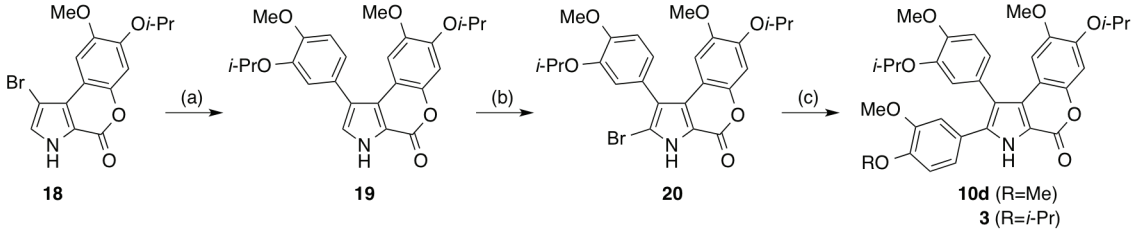


entry	solvent(s)	additive	**18** (%)	**11** (%)	**6** (%)
1	DMF	–	48	24	15
2	CH_2Cl_2	–	68	1	25
3	CH_2Cl_2	pyridine (1 equiv)	75	6	6
4	CH_2Cl_2	AcOH (1 equiv)	79	< 1	9
5	CH_2Cl_2–AcOH (4:1)	–	99[b]	0	0

[a] Unless mentioned otherwise, the yields of **18**, **11**, and **6** were estimated by ^{1}H NMR analysis of the inseparable mixture. See ref. 11. [b] Isolated yield.

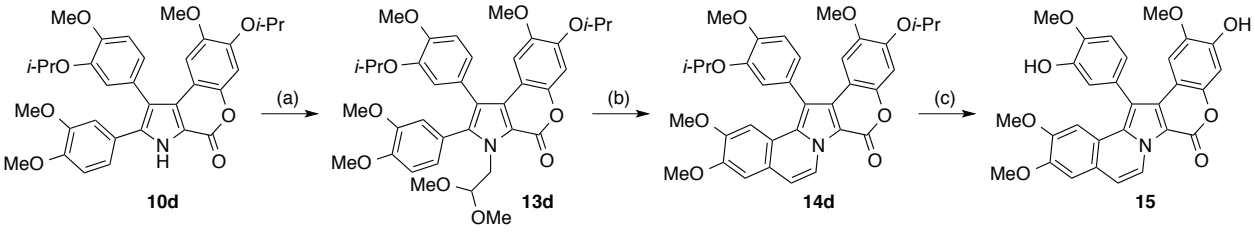
formation of **11** (entry 4). Finally, **18** was obtained as the sole product in 99% yield when a 4:1 mixture of CH_2Cl_2 and AcOH was used as the solvent system for the reaction (entry 5).

With the 1-brominated [1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one **18** in hand, we next attempted the conversion of **18** into differentially 1,2-arylated [1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-ones **10d** and **3** (Scheme 7). Suzuki–Miyaura cross-coupling of **18** with arylboronic acid **12c** under the standard conditions [$Pd(PPh_3)_4$ (10 mol%), Na_2CO_3, water, DME, reflux] afforded **19** in 76% yield. Subsequent bromination of **19** with 1.6 equiv NBS in the presence of pyridine (1.0 equiv) gave the 2-brominated product **20** in good yield (92%). When the bromination was carried out in the absence of pyridine, the reaction was slow and the addition of excess NBS was necessary to complete the reaction. Then, **20** was treated with 3.0 equiv arylboronic acids **12a** and **12b** under the standard conditions to give **10d** and **3**, respectively, in identical yields (83%). At this point, the formal synthesis of lamellarin N (**5**) was achieved since the conversion of **3** into **5** has been reported previously by us.[8u]



Scheme 7. *Reagents and conditions*: (a) **12c** (3.0 equiv), $Pd(PPh_3)_4$ (10 mol%), Na_2CO_3 (6.6 equiv), water, DME, reflux, 13 h (76%); (b) NBS (1.6 equiv), pyridine (1.0 equiv), DMF, 0 °C, 4 h (92%); (c) **12a** or **12b** (3.0 equiv), $Pd(PPh_3)_4$ (10 mol%), Na_2CO_3 (6.6 equiv), water, DME, reflux, 14 h (**10d**: 83%, **3**: 83%).

Further conversion of **10d** to lamellarin α (**15**) was achieved using the conditions indicated in Scheme 4 (Scheme 8).



Scheme 8. *Reagents and conditions*: (a) $BrCH_2CH(OMe)_2$ (6.6 equiv), Cs_2CO_3 (6.6 equiv), DMF, 110 °C, 14 h (quant); (b) cat. TfOH, CH_2Cl_2, 0 °C, 2.5 h (94%); (c) BCl_3, CH_2Cl_2, –78 °C, 0.5 h then rt, 3 h (87%).

In conclusion, we have developed a synthesis of 1,2-diarylated [1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-ones via the double cross-coupling of 1,2-dibromo-[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one **11** or iterative bromination/cross-coupling sequence of [1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one **6**. The 1,2-diarylated [1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-ones thus obtained could be converted into the corresponding lamellarins. This strategy could be useful because it can facilitate the formation of a wide range of lamellarins by simple structural modifications of the [1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one core and the arylboronic acid coupling partners.

EXPERIMENTAL

Melting points were determined with a Yanagimoto micro melting point apparatus and are reported uncorrected. IR spectra were obtained with a Thermo Nicolet Nexus 670 NT FT-IR instrument and are reported in terms of absorption frequency (cm^{-1}). NMR spectra were recorded on a JEOL JNM-AL400 instrument (400 MHz for ^1H and 100 MHz for ^{13}C) or a Varian NMR System 500PS SN instrument (500 MHz for ^1H and 126 MHz for ^{13}C). Chemical shifts for ^1H NMR are expressed in parts per million (ppm) relative to the following internal standards: $CDCl_3$ and acetone-d_6 (tetramethylsilane, δ 0.0 ppm); DMSO-d_6 (DMSO, δ 2.50 ppm). Data for ^1H NMR spectra are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, dd = double doublet, t = triplet, sep = septet, m = multiplet, br s = broad singlet), coupling constant (Hz), and integration. Chemical shifts for ^{13}C NMR are expressed in ppm relative to the following internal standards: $CDCl_3$ (tetramethylsilane, δ 0.0 ppm); DMSO-d_6 (DMSO-d_6, δ 39.52 ppm). ^{13}C NMR data are reported in terms of chemical shift. High-resolution mass spectra were recorded on a JEOL JMS-T100TD (direct analysis by real-time mass spectrometry, DARTMS). Column chromatography was conducted using silica gel 60N, 63–210 μm (Kanto Chemical Co., Inc.), Chromatorex NH-DM1020 (Fuji Silysia Chemical Ltd.), or aluminium oxide 90 (Merck

KGaA). Flash chromatography was conducted using silica gel 60N, 40–50 μm (Kanto Chemical Co., Inc.).

1,2-Dibromo-7-isopropoxy-8-methoxy[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one (11). Under an argon atmosphere, a solution of NBS (1.36 g, 7.63 mmol) in DMF (7.0 mL) was added dropwise to a solution of **6** (695 mg, 2.54 mmol) in DMF (14 mL) at 0 °C. After stirring for 15 h at 0 °C, the mixture was quenched with 10% aqueous Na_2SO_3 (14 mL) and then diluted with water (175 mL). The precipitate thus formed was collected by filtration, washed with water, and dried under reduced pressure. The crude product was recrystallized from acetone–hexane to give **11** as a colorless powder (914 mg, 83%). Mp 286.5–287.5 °C. IR (KBr): 3447, 1690, 1433, 1272, 1219, 1160, 1011 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ 1.30 (d, J = 6.0 Hz, 6H), 3.81 (s, 3H), 4.67 (sep, J = 6.0 Hz, 1H), 7.03 (s, 1H), 7.78 (s, 1H), 13.87 (br s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.7, 55.7, 70.6, 92.8, 103.2, 103.6, 107.8, 115.6, 116.5, 125.9, 145.6, 146.3, 147.5, 152.7. HRMS (*m/z*) Calcd for $C_{15}H_{14}Br_2NO_4$ [$(M+H)^+$]: 429.9290. Found: 429.9302.

1,2-Bis(3,4-dimethoxyphenyl)-7-isopropoxy-8-methoxy[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one (10a). Under an argon atmosphere, a mixture of 1,2-dibromo-7-isopropoxy-8-methoxy-[1]benzopyrano-[3,4-*b*]pyrrol-4(3*H*)-one (**11**) (500 mg, 1.16 mmol), 3,4-dimethoxyphenylboronic acid (**12a**) (633 mg, 3.48 mmol), $Pd(PPh_3)_4$ (134 mg, 0.116 mmol), Na_2CO_3 (811 mg, 7.65 mmol), DME (30 mL), and degassed water (3.0 mL) was refluxed for 12.5 h. After cooling to rt, the solvent was evaporated *in vacuo* and the residue was extracted with CH_2Cl_2. The extract was washed with water and brine, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography over silica gel 60N (hexane–EtOAc = 2:1) and subsequent column chromatography over silica gel 60N (CH_2Cl_2–EtOAc = 5:1) to give **10a** as a colorless solid (498 mg, 78%). Recrystallization from CH_2Cl_2–hexane gave a colorless powder. Mp 256–257 °C. IR (KBr): 3302, 1683, 1457, 1264, 1240, 1216, 1027 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.40 (d, J = 6.1 Hz, 6H), 3.48 (s, 3H), 3.70 (s, 3H), 3.82 (s, 3H), 3.89 (s, 3H), 3.94 (s, 3H), 4.57 (sep, J = 6.1 Hz, 1H), 6.97 (s, 1H), 6.83 (d, J = 8.3 Hz, 1H), 6.93–7.01 (m, 5H), 7.03 (dd, J = 1.5 and 8.3 Hz, 1H), 9.76 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.9, 55.7, 55.8, 55.9, 56.0, 56.1, 71.6, 103.7, 105.1, 110.6, 110.8, 111.1, 111.6, 114.1, 115.2, 117.2, 120.5, 123.5, 123.6, 127.5, 129.1, 139.4, 146.2, 146.8, 147.3, 148.7, 148.9, 149.2, 149.4, 156.2. HRMS (*m/z*) Calcd for $C_{31}H_{32}NO_8$ [$(M+H)^+$]: 546.2128. Found: 546.2151.

7-Isopropoxy-1,2-bis(4-isopropoxy-3-methoxyphenyl)-8-methoxy[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one (10b). According to the procedure described for the preparation of **10a**, bromide **11** (500 mg, 1.16 mmol) and 4-isopropoxy-3-methoxyphenylboronic acid (**12b**) (731 mg, 3.48 mmol) were reacted for 13 h. After successive purification by column chromatography over silica gel 60N (CH_2Cl_2–EtOAc =

10:1) and column chromatography over Chromatorex NH-DM1020 (CH_2Cl_2–EtOAc = 20:1), **10b** was obtained as a colorless solid (501 mg, 72%). Recrystallization from CH_2Cl_2–hexane gave a colorless powder. Mp 222.5–223.5 °C. IR (KBr): 3279, 1690, 1464, 1262, 1218, 1147, 1110 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.37 (d, J = 6.1 Hz, 6H), 1.40 (d, J = 6.1 Hz, 12H), 3.47 (s, 3H), 3.63 (s, 3H), 3.77 (s, 3H), 4.51–4.65 (m, 3H), 6.80 (s, 1H), 6.84 (d, J = 8.3 Hz, 1H), 6.91–6.94 (m, 1H), 6.94 (s, 1H), 6.95–7.01 (m, 3H), 7.03 (d, J = 8.3 Hz, 1H), 9.69 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.9, 21.9, 22.1, 22.1, 55.6, 55.8, 56.1, 71.2, 71.6, 71.7, 103.8, 105.1, 110.6, 111.3, 114.8, 114.8, 115.1, 116.6, 117.2, 120.1, 123.5, 128.1, 129.1, 139.3, 146.2, 146.8, 146.8, 147.3, 147.6, 150.0, 151.0, 156.2. HRMS (*m/z*) Calcd for $C_{35}H_{40}NO_8$ [$(M+H)^+$]: 602.2754. Found: 602.2734.

7-Isopropoxy-1,2-bis(3-isopropoxy-4-methoxyphenyl)-8-methoxy-[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one (10c). According to the procedure described for the preparation of **10a**, bromide **11** (300 mg, 0.696 mmol) and 3-isopropoxy-4-methoxyphenylboronic acid (**12c**) (439 mg, 2.09 mmol) were reacted for 15 h. After purification by flash chromatography over silica gel 60N (CH_2Cl_2–EtOAc = 10:1), **10c** was obtained as a colorless solid (303 mg, 72%). Recrystallization from Et_2O–hexane gave a colorless powder. Mp 92.5–93.5 °C. IR (KBr): 3256, 1701, 1455, 1255, 1216, 1139, 1110 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.21 (d, J = 6.0 Hz, 6H), 1.28 (br s, 3H), 1.32 (br s, 3H), 1.40 (d, J = 6.0 Hz, 6H), 3.48 (s, 3H), 3.86 (s, 3H), 3.90 (s, 3H), 4.21 (sep, J = 6.0 Hz, 1H), 4.47 (sep, J = 6.0 Hz, 1H), 4.57 (sep, J = 6.0 Hz, 1H), 6.79 (s, 1H), 6.85 (d, J = 8.4 Hz, 1H), 6.89 (d, J = 1.8 Hz, 1H), 6.95 (s, 1H), 6.95–7.03 (m, 4H), 9.48 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.9, 22.0, 22.1, 22.2, 55.7, 56.0, 56.2, 71.1, 71.2, 71.5, 103.7, 105.1, 110.6, 111.8, 112.4, 114.5, 115.0, 117.2, 118.0, 120.2, 123.4, 123.7, 127.4, 129.1, 139.3, 146.2, 146.8, 147.2, 147.3, 147.8, 149.9, 150.4, 156.2. HRMS (*m/z*) Calcd for $C_{35}H_{40}NO_8$ [$(M+H)^+$]: 602.2754. Found: 602.2744.

3-(2,2-Dimethoxyethyl)-1,2-bis(3,4-dimethoxyphenyl)-7-isopropoxy-8-methoxy[1]benzopyrano-[3,4-*b*]pyrrol-4(3*H*)-one (13a). Under an argon atmosphere, a solution of **10a** (400 mg, 0.733 mmol), 2-bromo-1,1-dimethoxyethane (572 μL, 4.84 mmol), and Cs_2CO_3 (1.58 g, 4.85 mmol) in DMF (40 mL) was stirred for 14 h at 110 °C. After cooling to rt, the mixture was diluted with water, and the products were extracted with a mixed solvent of hexane–EtOAc (1:1). The extract was washed with water and brine, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography over silica gel 60N (CH_2Cl_2–EtOAc = 5:1) to give **13a** as a colorless solid (335 mg, 72%). Recrystallization from CH_2Cl_2–hexane gave a colorless powder. Mp 196.5–197.5 °C. IR (KBr): 1709, 1464, 1438, 1262, 1139, 1027 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.40 (d, J = 6.1 Hz, 6H), 3.35 (s, 6H), 3.48 (s, 3H), 3.72 (s, 3H), 3.74 (s, 3H), 3.88 (s, 6H), 4.50 (d, J = 5.4 Hz, 2H), 4.57 (sep, J = 6.1 Hz, 1H), 4.88 (t, J = 5.4 Hz, 1H), 6.79 (d, J = 1.7 Hz, 1H), 6.81 (d, J = 8.3 Hz, 1H), 6.83 (d, J = 8.1 Hz, 1H), 6.85 (d, J = 1.7 Hz, 1H), 6.86 (dd, J = 1.7 and 8.1 Hz, 1H), 6.90 (dd, J = 1.7 and 8.3 Hz, 1H), 6.92 (s, 1H), 6.94 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8, 48.0, 55.5, 55.8, 55.8, 55.8, 55.9, 55.9, 71.5, 103.5, 104.5, 105.4, 110.2, 110.8, 111.0, 114.3, 114.6, 114.7, 118.6, 122.2, 123.6, 124.1, 126.9, 127.8, 144.1, 146.2, 146.6, 147.4, 148.2, 148.5, 148.7, 149.2, 155.7. HRMS (*m*/*z*) Calcd for $C_{35}H_{40}NO_{10}$ [(M+H)$^+$]: 634.2652. Found: 634.2671.

3-(2,2-Dimethoxyethyl)-7-isopropoxy-1,2-bis(4-isopropoxy-3-methoxyphenyl)-8-methoxy-[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one (13b). According to the procedure described for the preparation of **13a**, **10b** (350 mg, 0.582 mmol), 2-bromo-1,1-dimethoxyethane (454 μL, 3.84 mmol), and Cs_2CO_3 (1.25 g, 3.84 mmol) were reacted for 18 h. After chromatographic purification over aluminium oxide 90 (CH_2Cl_2–EtOAc = 5:1), **13b** was obtained as a colorless powder (379 mg, 94%). Recrystallization from CH_2Cl_2–hexane gave a colorless powder. Mp 165–166 °C. IR (KBr): 1702, 1467, 1440, 1231, 1135, 1074 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (d, *J* = 6.1 Hz, 6H), 1.36 (d, *J* = 6.1 Hz, 6H), 1.40 (d, *J* = 6.1 Hz, 6H), 3.34 (s, 6H), 3.47 (s, 3H), 3.66 (s, 3H), 3.68 (s, 3H), 4.47–4.69 (m, 5H), 4.88 (t, *J* = 5.4 Hz, 1H), 6.74 (d, *J* = 1.7 Hz, 1H), 6.82 (d, *J* = 8.8 Hz, 1H), 6.85–6.91 (m, 4H), 6.95 (s, 1H), 6.96 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.9, 21.9, 22.0, 22.1, 47.9, 55.4, 55.6, 55.8, 55.9, 71.2, 71.5, 71.5, 103.5, 104.5, 105.3, 110.3, 114.5, 114.7, 115.1, 115.2, 115.9, 118.6, 122.3, 123.5, 123.9, 127.5, 127.8, 144.1, 146.2, 146.3, 146.6, 147.3, 147.5, 149.6, 150.2, 155.8. HRMS (*m*/*z*) Calcd for $C_{39}H_{48}NO_{10}$ [(M+H)$^+$]: 690.3278. Found: 690.3250.

3-(2,2-Dimethoxyethyl)-7-isopropoxy-1,2-bis(3-isopropoxy-4-methoxyphenyl)-8-methoxy-[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one (13c). According to the procedure described for the preparation of **13a**, **10c** (54.4 mg, 94.8 μmol), 2-bromo-1,1-dimethoxyethane (72.1 μL, 0.626 mmol), and Cs_2CO_3 (204 mg, 0.626 mmol) were reacted for 14 h. After successive purification by column chromatography over silica gel 60N (hexane–EtOAc = 2:1) and column chromatography over silica gel 60N (toluene–EtOAc = 5:1) to give **13c** as a colorless solid (60.5 mg, 96%). Recrystallization from CH_2Cl_2–hexane gave a colorless powder. Mp 147–148 °C. IR (KBr): 1709, 1461, 1264, 1136, 1028 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.15 (br s, 3H), 1.23 (d, *J* = 6.1 Hz, 6H), 1.27 (br s, 3H), 1.40 (d, *J* = 6.1 Hz, 6H), 3.32 (s, 6H), 3.47 (s, 3H), 3.83 (s, 3H), 4.33 (sep, *J* = 6.1 Hz, 1H), 4.33 (sep, *J* = 6.1 Hz, 1H), 4.52 (d, *J* = 5.4 Hz, 2H), 4.57 (sep, *J* = 6.1 Hz, 1H), 4.85 (t, *J* = 5.4 Hz, 1H), 6.76 (d, *J* = 1.9 Hz, 1H), 6.82 (d, *J* = 8.2 Hz, 1H), 6.84 (d, *J* = 8.2 Hz, 1H), 6.87 (d, *J* = 1.9 Hz, 1H), 6.89 (dd, *J* = 1.9 and 8.2 Hz, 1H), 6.93 (dd, *J* = 1.9 and 8.2 Hz, 1H), 6.93 (s, 1H), 6.94 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 21.8, 22.2, 47.8, 55.3, 55.8, 55.9, 56.0, 71.1, 71.2, 71.4, 103.4, 104.4, 105.4, 110.3, 111.5, 111.7, 114.7, 118.6, 118.6, 118.7, 122.2, 123.9, 124.2, 126.9, 127.8, 144.1, 146.2, 146.6, 146.8, 147.0, 147.3, 149.5, 150.5, 155.8. HRMS (*m*/*z*) Calcd for $C_{39}H_{48}NO_{10}$ [(M+H)$^+$]: 690.3278. Found: 690.3491.

14-(3,4-Dimethoxyphenyl)-3-isopropoxy-2,11,12-trimethoxy-6*H*-[1]benzopyrano[4′,3′:4,5]pyrrolo-[2,1-*a*]isoquinolin-6-one (14a). Under an argon atmosphere, 1 drop of TfOH was added to a solution of

13a (15.0 mg, 23.7 μmol) in DCM (2.0 mL) at 0 °C. After stirring for 2.5 h at 0 °C, Na_2CO_3 (10 mg) and $MgSO_4$ (10 mg) was added to the mixture. The suspension was allowed to warm to rt and then passed through a pad of Celite. The filtrate was evaporated and the residue was purified by column chromatography over silica gel 60N (hexane–EtOAc = 1:1) to give **14a** as a colorless solid (13.3 mg, 99%). Recrystallization from CH_2Cl_2–hexane gave a colorless powder. Mp 238–239 °C. IR (KBr): 1708, 1430, 1269, 1226, 1043 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.41 (d, J = 6.1 Hz, 6H), 3.45 (s, 3H), 3.47 (s, 3H), 3.88 (s, 3H), 3.99 (s, 6H), 4.58 (sep, J = 6.1 Hz, 1H), 6.75 (s, 1H), 6.98 (s, 1H), 7.06 (d, J = 7.4 Hz, 1H), 7.10 (s, 1H), 7.14 (d, J = 1.8 Hz, 1H), 7.16 (d, J = 8.2 Hz, 1H), 7.17 (s, 1H), 7.23 (dd, J = 1.8 and 8.2 Hz, 1H), 9.26 (d, J = 7.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8, 21.8, 55.2, 55.6, 56.0, 56.2, 56.3, 71.5, 103.5, 105.3, 105.6, 107.4, 107.9, 109.9, 110.9, 112.0, 112.3, 114.5, 119.1, 123.3, 124.2, 124.8, 128.3, 129.5, 134.4, 146.6, 146.7, 148.0, 149.1, 149.2, 149.9, 150.1, 155.5. HRMS (*m*/*z*) Calcd for $C_{33}H_{32}NO_8$ [$(M+H)^+$]: 570.2128. Found: 570.2112.

3,11-Diisopropoxy-14-(4-isopropoxy-3-methoxyphenyl)-2,12-dimethoxy-6*H*-[1]benzopyrano-[4′,3′:4,5]pyrrolo[2,1-*a*]isoquinolin-6-one (14b). According to the procedure described for the preparation of **14a**, **13b** (100 mg, 0.145 mmol) was reacted. After purification by column chromatography over silica gel 60N (CH_2Cl_2–EtOAc = 10:1), **14b** was obtained as a colorless powder (78.5 mg, 87%). Recrystallization from CH_2Cl_2–hexane gave a colorless powder. Mp 193–194 °C (lit.[8k] Mp 191–192 °C). IR (KBr): 1705, 1431, 1418, 1267, 1223, 1036 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.40 (d, J = 6.1 Hz, 6H), 1.43 (d, J = 6.1 Hz, 12H), 3.44 (s, 3H), 3.45 (s, 3H), 3.85 (s, 3H), 4.57 (sep, J = 6.1 Hz, 1H), 4.64 (sep, J = 6.1 Hz, 1H), 4.70 (sep, J = 6.1 Hz, 1H), 6.76 (s, 1H), 6.96 (s, 1H), 7.01 (d, J = 7.4 Hz, 1H), 7.10 (s, 1H), 7.14 (s, 1H), 7.17–7.20 (m, 3H), 9.22 (d, J = 7.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8, 21.8, 21.9, 21.9, 21.9, 55.2, 55.5, 56.2, 71.2, 71.5, 71.8, 103.5, 105.5, 105.7, 107.8, 110.0, 110.5, 111.1, 112.3, 115.1, 116.9, 119.0, 123.2, 123.9, 124.7, 128.8, 129.4, 134.4, 146.5, 146.6, 147.2, 147.9, 148.5, 150.2, 151.4, 155.6. HRMS (*m*/*z*) Calcd for $C_{37}H_{40}NO_8$ [$(M+H)^+$]: 626.2754. Found: 626.2741. These physical and spectroscopic data are in good agreement with those previously reported.[8k]

3,12-Diisopropoxy-14-(3-isopropoxy-4-methoxyphenyl)-2,11-dimethoxy-6*H*-[1]benzopyrano-[4′,3′:4,5]pyrrolo[2,1-*a*]isoquinolin-6-one (14c). According to the procedure described for the preparation of **14a**, **13c** (150 mg, 0.217 mmol) was reacted. After purification by column chromatography over silica gel 60N (hexane–EtOAc = 1:1), **14c** was obtained as a colorless powder (134 mg, 99%). Recrystallization from CH_2Cl_2–hexane gave a colorless powder. Mp 207–208 °C. IR (KBr): 1692, 1446, 1269, 1221, 1042 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.18 (d, J = 6.1 Hz, 3H), 1.19 (d, J = 6.1 Hz, 3H), 1.35 (d, J = 6.1 Hz, 3H), 1.35 (d, J = 6.1 Hz, 3H), 1.41 (d, J = 6.1 Hz, 6H), 3.45 (s, 3H), 3.96 (s, 3H), 3.97 (s, 3H), 3.99 (sep, J = 6.1 Hz, 1H), 4.53 (sep, J = 6.1 Hz, 1H), 4.58 (sep, J = 6.1

Hz, 1H), 6.73 (s, 1H), 6.98 (s, 1H), 7.05 (d, J = 7.4 Hz, 1H), 7.09 (s, 1H), 7.12 (s, 1H), 7.15 (s, 2H), 7.17 (s, 1H), 9.23 (d, J = 7.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.7, 21.7, 21.8, 21.9, 22.0, 55.5, 56.0, 56.4, 70.8, 71.2, 71.4, 103.4, 105.5, 107.5, 107.7, 107.8, 110.0, 111.0, 112.3, 112.9, 117.5, 119.2, 123.1, 123.7, 124.5, 128.4, 129.5, 134.5, 146.6, 146.7, 147.6, 147.9, 148.5, 150.2, 150.9, 155.6. HRMS (m/z) Calcd for $C_{37}H_{40}NO_8$ [$(M+H)^+$]: 626.2754. Found: 626.2726.

14-(3,4-Dimethoxyphenyl)-3-hydroxy-2,11,12-trimethoxy-6*H*-[1]benzopyrano[4′,3′:4,5]pyrrolo-[2,1-*a*]isoquinolin-6-one (lamellarin η, 7). Under an argon atmosphere, a heptane solution of BCl_3 (1.0 M, 263 μL, 0.263 mmol) was added dropwise to a solution of **14a** (50.0 mg, 87.8 μmol) in DCM (13 mL) at –78 °C and the mixture was allowed to warm to rt. After stirring for 3 h at rt, the mixture was quenched with saturated aqueous $NaHCO_3$ and the precipitate thus formed was collected by filtration, washed successively with water, 1 M HCl, and water, and dried under reduced pressure. The crude product was purified by column chromatography over silica gel 60N (acetone) to give **7** as a pale gray powder (40.2 mg, 87%). Mp 258–259 °C (sealed capillary) (lit.[2m] Mp 268–272 °C). IR (KBr): 3288, 1692, 1431, 1267, 1226, 1046 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.47 (s, 3H), 3.51 (s, 3H), 3.89 (s, 3H), 3.99 (s, 3H), 4.00 (s, 3H), 5.80 (s, 1H), 6.71 (s, 1H), 7.02 (s, 1H), 7.05 (d, J = 7.3 Hz, 1H), 7.09 (s, 1H), 7.15 (d, J = 1.9 Hz, 1H), 7.15 (s, 1H), 7.16 (d, J = 8.1 Hz, 1H), 7.22 (dd, J = 1.9 and 8.1 Hz, 1H), 9.25 (d, J = 7.3 Hz, 1H). ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.32 (s, 3H), 3.36 (s, 3H), 3.76 (s, 3H), 3.86 (s, 6H), 6.65 (s, 1H), 6.85 (s, 1H), 7.06 (s, 1H), 7.12 (d, J = 8.1 Hz, 1H), 7.20–7.27 (m, 3H), 7.36 (s, 1H), 9.01 (d, J = 7.3 Hz, 1H), 9.82 (br s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 55.2, 55.6, 56.0, 56.2, 56.3, 103.6, 104.7, 105.3, 107.4, 107.9, 109.9, 110.8, 112.0, 112.3, 114.4, 119.1, 123.4, 124.2, 124.9, 128.4, 129.5, 134.4, 143.3, 146.4, 147.1, 149.1, 149.2, 149.9, 150.1, 155.5. ^{13}C NMR (100 MHz, DMSO-d_6): δ 54.5, 55.0, 55.6, 55.9, 56.0, 103.7, 104.8, 105.6, 106.6, 108.1, 108.2, 110.7, 112.6, 113.0, 114.7, 118.3, 122.2, 123.7, 124.4, 127.2, 128.9, 133.7, 144.6, 146.3, 147.9, 149.0, 149.0, 149.9, 150.0, 154.3. HRMS (m/z) Calcd for $C_{30}H_{26}NO_8$ [$(M+H)^+$]: 528.1658. Found: 528.1648. These physical and spectroscopic data are in good agreement with those previously reported.[2m,8l]

3,11-Dihydroxy-14-(4-hydroxy-3-methoxyphenyl)-2,12-dimethoxy-6*H*-[1]benzopyrano[4′,3′:4,5]-pyrrolo[2,1-*a*]isoquinolin-6-one (lamellarin D, 8). According to the procedure described for the preparation of **7**, **14b** (30.0 mg, 47.9 μmol) and BCl_3 (1.0 M, 432 μL, 0.432 mmol) were reacted. After purification by column chromatography over silica gel 60N (acetone), **8** was obtained as a pale gray powder (23.5 mg, 98%). Mp 280–300 °C (dec) (sealed capillary) [lit.[8k] Mp 280–300 °C (dec) (sealed capillary)]. IR (KBr): 3374, 1674, 1433, 1275, 1219, 1155 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.38 (s, 3H), 3.38 (s, 3H), 3.77 (s, 3H), 6.70 (s, 1H), 6.85 (s, 1H), 6.99 (dd, J = 1.7 and 8.1 Hz, 1H), 7.08 (d, J = 8.1 Hz, 1H), 7.12 (s, 1H), 7.15 (d, J = 1.7 Hz, 1H), 7.17 (d, J = 7.3 Hz, 1H), 7.17 (s, 1H), 8.97 (d,

J = 7.3 Hz, 1H), 9.33 (s, 1H), 9.81 (br s, 1H), 9.92 (br s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 54.5, 55.1, 56.0, 103.7, 105.4, 105.7, 106.4, 108.3, 110.8, 111.5, 112.3, 115.1, 116.4, 117.6, 122.0, 123.8, 124.7, 125.5, 129.0, 134.1, 144.6, 146.3, 146.8, 147.8, 148.3, 148.5, 148.7, 154.3. HRMS (*m*/*z*) Calcd for $C_{28}H_{22}NO_8$ [(M+H)$^+$]: 500.1345. Found: 500.1327. These physical and spectroscopic data are in good agreement with those previously reported.[8k]

3,12-Dihydroxy-14-(3-hydroxy-4-methoxyphenyl)-2,11-dimethoxy-6*H*-[1]benzopyrano[4′,3′:4,5]-pyrrolo[2,1-*a*]isoquinolin-6-one (5,6-dehydrolamellarin Y, 9). According to the procedure described for the preparation of **7**, **14c** (50.0 mg, 79.9 μmol) and BCl_3 (1.0 M, 719 μL, 0.719 mmol) were reacted. After purification by column chromatography over silica gel 60N (acetone), **9** was obtained as a pale gray powder (39.2 mg, 98%). Mp >300 °C (sealed capillary) (lit.[8l] Mp >250 °C). IR (KBr): 3417, 1702, 1434, 1277, 1218, 1040 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.38 (s, 3H), 3.90 (s, 3H), 3.90 (s, 3H), 6.51 (s, 1H), 6.85 (s, 1H), 6.93 (s, 1H), 6.94 (dd, *J* = 1.7 and 8.1 Hz, 1H), 7.18 (s, 1H), 7.21 (d, *J* = 8.1 Hz, 1H), 7.27 (d, *J* = 7.3 Hz, 1H), 7.39 (s, 1H), 9.02 (d, *J* = 7.3 Hz, 1H), 9.34 (br s, 1H), 9.63 (br s, 1H), 9.80 (br s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 54.9, 55.6, 55.8, 103.7, 105.5, 106.5, 108.2, 108.4, 109.0, 111.1, 112.9, 113.4, 117.9, 118.9, 121.4, 121.7, 123.6, 127.1, 129.0, 133.3, 144.5, 146.2, 147.2, 147.6, 147.7, 148.0, 149.6, 154.3. HRMS (*m*/*z*) Calcd for $C_{28}H_{22}NO_8$ [(M+H)$^+$]: 500.1345. Found: 500.1323. These physical and spectroscopic data are in good agreement with those previously reported.[8l]

Typical procedure for Suzuki–Miyaura cross-coupling of 1,2-dibromo-7-isopropoxy-8-methoxy-[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one (11) with arylboronic acid 12c (Table 2). Under an argon atmosphere, a mixture of 1,2-dibromo-7-isopropoxy-8-methoxy-[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one (**11**) (50.0 mg, 0.116 mmol), an appropriate amount of **12c**, $Pd(PPh_3)_4$ (13.4 mg, 11.6 μmol), Na_2CO_3 (81.1 mg, 0.765 mmol), DME or THF (3 mL), and degassed water (3.0 mL) was heatd at 85 °C (DME) or 65 °C (THF) for 15 h. After cooling to rt, the mixture was evaporated, and the products were extracted with CH_2Cl_2. The extract was washed with water and brine, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography over silica gel 60N (hexane–EtOAc = 2:1). The results are summarized in Table 2.

Typical procedure for Suzuki–Miyaura cross-coupling of 1,2-dibromo-7-isopropoxy-8-methoxy-[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one (11) with arylboronic acid 12c (Table 3). Under an argon atmosphere, a mixture of 1,2-dibromo-7-isopropoxy-8-methoxy-[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one (**11**) (50.0 mg, 0.116 mmol), **12c** (36.5 mg, 0.174 mmol), $Pd(PPh_3)_4$ (13.4 mg, 11.6 μmol), Na_2CO_3 (98.4 mg, 0.928 mmol), LiCl (14.8 mg, 0.348 mmol), DME (3 mL), and degassed water (3.0 mL) was heatd at 85 °C. After cooling to rt, the mixture was evaporated, and the products were extracted with CH_2Cl_2. The extract was washed with water and brine, dried over Na_2SO_4, and evaporated. The residue was

purified by column chromatography over silica gel 60N (hexane–EtOAc = 2:1). The results are summarized in Table 3.

1-Bromo-7-isopropoxy-2-(3-isopropoxy-4-methoxyphenyl)-8-methoxy-[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one (16). Mp 226–227 °C. IR (KBr): 3228, 1688, 1519, 1460, 1265, 1218 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.44 (d, J = 6.1 Hz, 6H), 1.45 (d, J = 6.1 Hz, 6H), 3.94 (s, 3H), 3.98 (s, 3H), 4.61 (sep, J = 6.1 Hz, 1H), 4.70 (sep, J = 6.1 Hz, 1H), 6.97 (s, 1H), 7.02 (d, J = 8.3 Hz, 1H), 7.38 (dd, J = 2.1 and 8.3 Hz, 1H), 7.40 (d, J = 2.1 Hz, 1H), 8.19 (s, 1H), 10.32 (br s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.9, 22.1, 56.1, 56.4, 71.6, 71.6, 89.5, 103.6, 104.7, 109.7, 111.9, 115.2, 115.4, 121.3, 122.1, 128.0, 139.8, 146.3, 147.0, 147.5, 148.0, 151.3, 155.3. HRMS (*m/z*) Calcd for $C_{25}H_{27}BrNO_6$ [$(M+H)^+$]: 516.1022. Found: 516.1021.

Procedure for Suzuki–Miyaura cross-coupling of 1,2-dibromo-7-isopropoxy-8-methoxy-[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one (11) with arylboronic acid 12c (Scheme 6). Under an argon atmosphere, a mixture of 1,2-dibromo-7-isopropoxy-8-methoxy-[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one (**11**) (50.0 mg, 0.116 mmol), **12c** (29.2 mg, 0.139 mmol), $Pd(PPh_3)_4$ (13.4 mg, 11.6 μmol), Cs_2CO_3 (37.8 mg, 0.139 mmol), toluene (1 mL), EtOH (0.2 mL), and degassed water (0.2 mL) was heated at 110 °C for 15 h. After cooling to rt, the mixture was evaporated, and the products were extracted with CH_2Cl_2. The extract was washed with water and brine, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography over silica gel 60N (hexane–EtOAc) to give **17** (18.5 mg, 36%) and **10c** (21.6 mg, 31%).

7-Isopropoxy-2-(3-isopropoxy-4-methoxyphenyl)-8-methoxy-[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one (17). Mp 221–222 °C. IR (KBr): 3259, 1697, 1519, 1473, 1278, 1259, 1149 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.44 (d, J = 6.1 Hz, 6H), 1.48 (d, J = 6.1 Hz, 6H), 3.93 (s, 3H), 3.98 (s, 3H), 4.59 (sep, J = 6.1 Hz, 1H), 4.96 (sep, J = 6.1 Hz, 1H), 6.85 (d, J = 2.2 Hz, 1H), 6.96 (s, 1H), 6.99 (d, J = 8.4 Hz, 1H), 7.23 (s, 1H), 7.42 (dd, J = 2.1 and 8.4 Hz, 1H), 7.60 (d, J = 2.1 Hz, 1H), 11.20 (br s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.9, 22.2, 56.1, 56.5, 71.4, 71.7, 98.8, 103.8, 105.0, 110.3, 112.2, 112.8, 116.2, 119.0, 123.7, 132.0, 143.5, 146.1, 147.5, 147.8, 147.8, 151.0, 156.1. HRMS (*m/z*) Calcd for $C_{25}H_{28}NO_6$ [$(M+H)^+$]: 438.1917. Found: 438.1935.

Typical procedure for regioselective bromination of 7-isopropoxy-8-methoxy-[1]benzopyrano-[3,4-*b*]pyrrol-4(3*H*)-one (6) with 1.05 equiv of NBS (Table 4). Under an argon atmosphere, NBS (13.7 mg, 76.8 μmol) was added portionwise to a mixture of **6** (20 mg, 73.2 μmol), an appropriate additive, and solvent (2 mL) at 0 °C. After stirring for 2 h at 0 °C, the mixture was quenched with 10% aqueous Na_2SO_3 and evaporated if necessary. The precipitate was collected by filtration, washed with water, and dried under reduced pressure. Since all attempts to separate of **18**, **11**, and **6** by column chromatography failed, the yields of **18**, **11**, and **6** were estimated by integration of ^1H NMR absorption of

H9 of each compound (δ H9 of **18**: 8.07; δ H9 of **11**: 8.03; δ H9 of **6**: 7.46).[11] The results are shown in Table 4.

1-Bromo-7-isopropoxy-8-methoxy-[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one (18). Under an argon atmosphere, NBS (82.1 mg, 0.461 mmol) was added portionwise to a solution of **6** (120 mg, 0.439 mmol) in CH_2Cl_2 (9.6 mL) and AcOH (2.4 mL) at 0 °C. After stirring for 2 h at 0 °C, the mixture was quenched with 10% aqueous Na_2SO_3 (2 mL) and evaporated. The precipitate was collected by filtration, washed with water, and dried under reduced pressure. The crude product was recrystallized from acetone–EtOAc to give **18** as a colorless powder (153 mg, 99%). Mp 263.5–265.5 °C. IR (KBr): 3175, 1689, 1499, 1423, 1278, 1221, 1109 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ 1.29 (d, J = 6.0 Hz, 6H), 3.83 (s, 3H), 4.69 (sep, J = 6.0 Hz, 1H), 7.12 (s, 1H), 7.70 (s, 1H), 7.93 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.7, 55.8, 70.6, 89.8, 103.5, 104.0, 109.0, 115.9, 124.8, 130.3, 145.5, 146.4, 147.2, 153.8. HRMS (m/z) Calcd for $C_{15}H_{15}BrNO_4$ [$(M+H)^+$]: 352.0184. Found: 352.0158.

7-Isopropoxy-1-(3-isopropoxy-4-methoxyphenyl)-8-methoxy-[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one (19). Under an argon atmosphere, a mixture of bromide **18** (1.00 g, 2.84 mmol), 3-isopropoxy-4-methoxyphenylboronic acid (**12c**) (1.79 g, 8.52 mmol), $Pd(PPh_3)_4$ (328 mg, 0.284 mmol), Na_2CO_3 (1.99 g, 18.7 mmol), DME (60 mL), and degassed water (6 mL) was refluxed for 13 h. After cooling to rt, the solvent was evaporated *in vacuo* and the residue was extracted with CH_2Cl_2. The extract was washed with water and brine, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography over silica gel 60N (hexane–EtOAc = 2:1) and subsequently by recrystallization from CH_2Cl_2–hexane to give **19** as a colorless powder (941 mg, 76%). Mp 168–169.5 °C. IR (KBr): 3209, 1693, 1492, 1269, 1220, 1107 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.38 (d, J = 6.0 Hz, 6H), 1.41 (d, J = 6.0 Hz, 6H), 3.59 (s, 3H), 3.92 (s, 3H), 4.56 (sep, J = 6.0 Hz, 1H), 4.58 (sep, J = 6.0 Hz, 1H), 6.99 (d, J = 8.3 Hz, 1H), 6.99 (s, 1H), 7.08 (s, 1H), 7.09 (dd, J = 1.7 and 8.3 Hz, 1H), 7.19 (s, 1H), 7.37 (d, J = 2.7 Hz, 1H), 11.16 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8, 22.2, 56.0, 56.1, 71.5, 71.5, 103.8, 105.4, 110.7, 111.9, 116.4, 117.2, 121.4, 122.5, 126.8, 126.9, 128.2, 145.9, 146.9, 147.3, 147.4, 149.9, 156.8. HRMS (m/z) Calcd for $C_{25}H_{28}NO_6$ [$(M+H)^+$]: 438.1917. Found: 438.1889.

2-Bromo-7-isopropoxy-1-(3-isopropoxy-4-methoxyphenyl)-8-methoxy-[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one (20). Under an argon atmosphere, a solution of NBS (530 mg, 2.98 mmol) in DMF (5 mL) was added dropwise to a mixture of **19** (814 mg, 1.86 mmol), pyridine (150 μL, 1.85 mmol), and DMF (20 mL) at 0 °C. After stirring for 4 h at 0 °C, the mixture was quenched with 10% aqueous Na_2SO_3 (2 mL), diluted with water, and the products were extracted with EtOAc. The extract was washed with water and brine, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography over silica gel 60N (CH_2Cl_2–EtOAc = 20:1) to give **20** as a colorless solid (887 mg, 92%). Recrystallization from CH_2Cl_2–hexane gave a colorless powder. Mp 228.5–229.5 °C. IR

(KBr): 3143, 1697, 1488, 1422, 1261, 1219, 1155, 1133, 1112 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.39 (d, J = 6.1 Hz, 6H), 1.40 (d, J = 6.1 Hz, 6H), 3.51 (s, 3H), 3.93 (s, 3H), 4.56 (sep, J = 6.1 Hz, 1H), 4.57 (sep, J = 6.1 Hz, 1H), 6.93 (s, 1H), 6.99 (s, 1H), 7.01 (d, J = 1.7 Hz, 1H), 7.02 (d, J = 8.3 Hz, 1H), 7.05 (dd, J = 1.7 and 8.3 Hz, 1H), 11.56 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8, 22.0, 22.2, 55.8, 56.1, 71.4, 71.5, 103.6, 104.9, 109.6, 111.8, 114.3, 116.5, 117.8, 120.5, 123.4, 124.9, 128.3, 146.1, 146.9, 147.3, 147.8, 150.2, 155.6. HRMS (*m*/*z*) Calcd for $C_{25}H_{27}BrNO_6$ [$(M+H)^+$]: 516.1022. Found: 516.1023.

2-(3,4-Dimethoxyphenyl)-7-isopropoxy-1-(3-isopropoxy-4-methoxyphenyl)-8-methoxy-[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one (10d). Under an argon atmosphere, a mixture of bromide **20** (100 mg, 0.194 mmol), 3,4-dimethoxyphenylboronic acid (**12a**) (52.8 mg, 0.290 mmol), $Pd(PPh_3)_4$ (22.4 mg, 19.4 μmol), Na_2CO_3 (135 mg, 1.28 mmol), DME (6.0 mL), and degassed water (0.6 mL) was heated in a sealed tube at 85 °C for 14 h. After cooling to rt, the solvent was evaporated *in vacuo* and the residue was extracted with CH_2Cl_2. The extract was washed with water and brine, dried over Na_2SO_4, and evaporated. The residue was purified by flash chromatography over silica gel 60N (hexane–EtOAc = 1:1) to give **10d** as a colorless solid (92.4 mg, 83%). Recrystallization from CH_2Cl_2–hexane gave a colorless powder. Mp 215–216 °C. IR (KBr): 3297, 1684, 1458, 1437, 1265, 1135, 1107 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.28 (br d, J = 6.1 Hz, 3H), 1.33 (br d, J = 6.1 Hz, 3H), 1.41 (d, J = 6.1 Hz, 6H), 3.49 (s, 3H), 3.85 (s, 3H), 3.88 (s, 3H), 3.92 (s, 3H), 4.48 (sep, J = 6.1 Hz, 1H), 4.57 (sep, J = 6.1 Hz, 1H), 6.80 (d, J = 8.2 Hz, 1H), 6.81 (s, 1H), 6.92 (s, 1H), 6.98 (d, J = 2.0 Hz, 1H), 7.01 (d, J = 8.2 Hz, 1H), 7.04 (dd, J = 2.0 and 8.2 Hz, 1H), 7.04 (dd, J = 2.0 and 8.2 Hz, 1H), 7.22 (d, J = 2.0 Hz, 1H), 11.01 (br s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.8, 21.9, 22.1, 55.7, 55.8, 55.9, 56.2, 71.2, 71.5, 103.6, 105.1, 110.6, 110.9, 111.1, 112.3, 115.1, 117.2, 118.2, 120.5, 123.5, 123.8, 127.4, 129.1, 139.4, 146.1, 146.8, 147.3, 147.7, 148.9, 149.1, 149.9, 156.2. HRMS (*m*/*z*) Calcd for $C_{33}H_{36}NO_8$ [$(M+H)^+$]: 574.2441. Found: 574.2425.

7-Isopropoxy-1-(3-isopropoxy-4-methoxyphenyl)-2-(4-isopropoxy-3-methoxyphenyl)-8-methoxy-[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one (3). According to the procedure described for the preparation of **10d**, bromide **20** (100 mg, 0.194 mmol) and 4-isopropoxy-3-methoxyphenylboronic acid (**12b**) (61.0 mg, 0.290 mmol) were reacted. After purification by flash chromatography over silica gel 60N (hexane–EtOAc = 3:1 to 1:1), **3** was obtained as a colorless solid (97.0 mg, 83%). Recrystallization from CH_2Cl_2–hexane gave a colorless powder. Mp 212–213 °C (lit.[8u] Mp 216–217 °C). IR (KBr): 3282, 1692, 1464, 1440, 1264, 1147, 1110 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.26 (br d, J = 6.1 Hz, 3H), 1.32 (br d, J = 6.1 Hz, 3H), 1.37 (d, J = 6.1 Hz, 6H), 1.41 (d, J = 6.1 Hz, 6H), 3.49 (s, 3H), 3.80 (s, 3H), 3.92 (s, 3H), 4.47 (sep, J = 6.1 Hz, 1H), 4.54 (sep, J = 6.1 Hz, 1H), 4.57 (sep, J = 6.1 Hz, 1H), 6.81 (d, J = 8.4 Hz, 1H), 6.81 (s, 1H), 6.92 (s, 1H), 6.97 (d, J = 1.8 Hz, 1H), 7.00 (dd, J = 2.1 and 8.4 Hz, 1H),

7.01 (d, *J* = 8.2 Hz, 1H), 7.04 (dd, *J* = 1.8 and 8.2 Hz, 1H), 7.19 (d, *J* = 2.1 Hz, 1H), 10.88 (br s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.9, 22.0, 55.7, 55.8, 56.2, 71.2, 71.2, 71.5, 103.7, 105.1, 110.7, 111.3, 112.3, 114.8, 115.1, 117.2, 118.2, 120.3, 123.5, 123.8, 127.5, 129.1, 139.4, 146.1, 146.8, 147.2, 147.5, 147.6, 149.9, 150.0, 156.2. HRMS (*m*/*z*) Calcd for $C_{35}H_{40}NO_8$ [(M+H)$^+$]: 602.2754. Found: 602.2738. These physical and spectroscopic data are in good agreement with those previously reported.[8u]

3-(2,2-Dimethoxyethyl)-2-(3,4-dimethoxyphenyl)-7-isopropoxy-1-(3-isopropoxy-4-methoxyphenyl)-8-methoxy-[1]benzopyrano[3,4-*b*]pyrrol-4(3*H*)-one (13d). According to the procedure described for the preparation of **13a**, **10d** (57.4 mg, 0.100 mmol), 2-bromo-1,1-dimethoxyethane (78.0 μL, 0.660 mmol), and Cs_2CO_3 (215 mg, 0.660 mmol) were reacted for 14 h. After chromatographic purification over silica gel 60N (hexane–EtOAc = 1:1), **13d** was obtained as a colorless powder (66.2 mg, quant). Recrystallization from CH_2Cl_2–Et_2O gave a colorless powder. Mp 165–166.5 °C. IR (KBr): 1702, 1465, 1438, 1267, 1245, 1137, 1032 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.16 (br d, *J* = 6.1 Hz, 3H), 1.27 (br d, *J* = 6.1 Hz, 3H), 1.40 (d, *J* = 6.1 Hz, 6H), 3.35 (br s, 6H), 3.48 (s, 3H), 3.73 (s, 3H), 3.85 (s, 3H), 3.86 (s, 3H), 4.34 (sep, *J* = 6.1 Hz, 1H), 4.50 (d, *J* = 5.5 Hz, 2H), 4.57 (sep, *J* = 6.1 Hz, 1H), 4.88 (t, *J* = 5.5 Hz, 1H), 6.77 (d, *J* = 1.8 Hz, 1H), 6.80 (d, *J* = 8.3 Hz, 1H), 6.85 (d, *J* = 8.3 Hz, 1H), 6.89 (dd, *J* = 1.8 and 8.3 Hz, 1H), 6.90 (dd, *J* = 1.8 and 8.3 Hz, 1H), 6.93 (d, *J* = 1.8 Hz, 1H), 6.93 (s, 1H), 6.93 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.5, 21.8, 22.2, 48.0, 55.5, 55.8, 55.8, 56.0, 71.2, 71.4, 103.4, 104.5, 105.4, 110.3, 110.8, 111.6, 114.5, 114.7, 118.6, 118.8, 122.2, 123.9, 124.1, 126.8, 127.9, 144.0, 146.2, 146.6, 146.9, 147.3, 148.5, 149.2, 149.6, 155.8. HRMS (*m*/*z*) Calcd for $C_{37}H_{44}NO_{10}$ [(M+H)$^+$]: 662.2965. Found: 662.2936.

3-Isopropoxy-14-(3-isopropoxy-4-methoxyphenyl)-2,11,12-trimethoxy-6*H*-[1]benzopyrano-[4′,3′:4,5]pyrrolo[2,1-*a*]isoquinolin-6-one (14d). According to the procedure described for the preparation of **14a**, **13d** (20.0 mg, 0.0302 mmol) was reacted. After purification by column chromatography over silica gel 60N (hexane–EtOAc = 1:1), **14d** was obtained as a colorless powder (17.0 mg, 94%). Recrystallization from CH_2Cl_2–hexane gave a colorless powder. Mp 214.5–215.5 °C (lit.[3c] Mp 211–212 °C). IR (KBr): 1702, 1429, 1267, 1225, 1167, 1044 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.35 (d, *J* = 6.1 Hz, 3H), 1.36 (d, *J* = 6.1 Hz, 3H), 1.41 (d, *J* = 6.1 Hz, 6H), 3.46 (s, 3H), 3.48 (s, 3H), 3.96 (s, 3H), 3.99 (s, 3H), 4.55 (sep, *J* = 6.1 Hz, 1H), 4.58 (sep, *J* = 6.1 Hz, 1H), 6.75 (s, 1H), 6.97 (s, 1H), 7.05 (d, *J* = 7.4 Hz, 1H), 7.09 (s, 1H), 7.14 (d, *J* = 1.8 Hz, 1H), 7.16 (d, *J* = 8.1 Hz, 1H), 7.17 (s, 1H), 7.20 (dd, *J* = 1.8 and 8.1 Hz, 1H), 9.24 (d, *J* = 7.4 Hz, 1H). ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.21 (d, *J* = 6.0 Hz, 3H), 1.22 (d, *J* = 6.0 Hz, 3H), 1.27 (d, *J* = 6.0 Hz, 6H), 3.35 (s, 3H), 3.35 (s, 3H), 3.86 (s, 3H), 3.88 (s, 3H), 4.57 (sep, *J* = 6.0 Hz, 1H), 4.69 (sep, *J* = 6.0 Hz, 1H), 6.70 (s, 1H), 7.10 (s, 1H), 7.14 (s, 1H), 7.17 (dd, *J* = 1.9 and 8.0 Hz, 1H), 7.18 (d, *J* = 1.9 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.33 (d, *J* = 7.4 Hz, 1H), 7.44 (s, 1H), 9.08 (d, *J* = 7.4 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.8, 22.0, 22.0, 55.2, 55.5,

56.0, 56.4, 71.3, 71.4, 103.4, 105.3, 105.5, 107.4, 107.8, 110.0, 111.1, 112.3, 112.8, 118.2, 119.2, 123.4, 124.1, 124.8, 128.2, 129.5, 134.4, 146.6, 146.7, 147.9, 148.2, 149.2, 150.1, 150.3, 155.6. ^{13}C NMR (126 MHz, DMSO-d_6): δ 21.6, 21.7, 21.7, 21.8, 54.4, 54.9, 55.7, 56.0, 70.4, 70.6, 103.3, 104.7, 105.4, 106.8, 108.3, 109.2, 111.0, 112.9, 113.6, 118.0, 118.3, 122.3, 123.7, 124.5, 127.0, 128.6, 133.8, 146.1, 146.2, 147.6, 147.8, 149.0, 150.1, 150.2, 154.3. HRMS (*m*/*z*) Calcd for $C_{35}H_{36}NO_8$ [(M+H)$^+$]: 598.2441. Found: 598.2441. These physical and spectroscopic data are in good agreement with those previously reported.[3c]

3-Hydroxy-14-(3-hydroxy-4-methoxyphenyl)-2,11,12-trimethoxy-6*H*-[1]benzopyrano[4′,3′:4,5]-pyrrolo[2,1-*a*]isoquinolin-6-one (lamellarin α, 15). According to the procedure described for the preparation of **7**, **14d** (30.0 mg, 50.2 μmol) and BCl_3 (1.0 M, 301 μL, 0.301 mmol) were reacted. After purification by column chromatography over silica gel 60N (acetone), **15** was obtained as a pale gray powder (22.4 mg, 87%). Mp >300 °C (sealed capillary) (lit.[4] Mp >300 °C). IR (KBr) 1690, 1429, 1270, 1227, 1160, 1045 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6): δ 3.35 (s, 3H), 3.39 (s, 3H), 3.84 (s, 3H), 3.85 (s, 3H), 6.72 (s, 1H), 6.85 (s, 1H), 6.95 (dd, *J* = 2.0 and 8.2 Hz, 1H), 7.00 (d, *J* = 2.0 Hz, 1H), 7.12 (s, 1H), 7.17 (d, *J* = 8.2 Hz, 1H), 7.20 (d, *J* = 7.4 Hz, 1H), 7.31 (s, 1H), 8.96 (d, *J* = 7.4 Hz, 1H), 9.37 (br s, 1H), 9.82 (br s, 1H). ^{13}C NMR (126 MHz, DMSO-d_6): δ 54.5, 55.1, 55.6, 56.1, 103.7, 104.8, 105.7, 106.6, 108.1, 108.2, 110.7, 112.5, 113.5, 118.2, 118.3, 122.1, 124.3, 127.3, 128.7, 133.5, 144.6, 146.3, 147.7, 147.8, 148.0, 148.9, 149.9, 154.3. HRMS (*m*/*z*) Calcd for $C_{29}H_{24}NO_8$ [(M+H)$^+$]: 514.1502. Found: 514.1494. These physical and spectroscopic data are in good agreement with those previously reported.[4]

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11. In case x mol of **6** was reacted to give y g of a mixture of monobromide **18**, dibromide **11**, and **6** and the molar fractions of **18**, **11**, and **6** in the mixture were determined to be N_{18}, N_{11}, and N_6 (see Supporting Information), the yields of **18**, **11** and **6** were estimated by using the following equations:

$$\text{The yield of } \mathbf{18}\ (Y_{18}) = \frac{yN_{18}}{x\,(MW_{18}N_{18} + MW_{11}N_{11} + MW_6N_6)} \times 100\ (\%)$$

$$\text{The yield of } \mathbf{11}\ (Y_{11}) = \frac{yN_{11}}{x\,(MW_{18}N_{18} + MW_{11}N_{11} + MW_6N_6)} \times 100\ (\%)$$

$$\text{The yield of } \mathbf{6}\ (Y_6) = \frac{yN_6}{x\,(MW_{18}N_{18} + MW_{11}N_{11} + MW_6N_6)} \times 100\ (\%)$$

where MW_{18}, MW_{11}, and MW_6 are molecular weights of **18**, **11** and **6**.