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SYNTHESIS OF PYRROLO[2,3-*c*]QUINOLINE ALKALOID MARINOQUINOLINES

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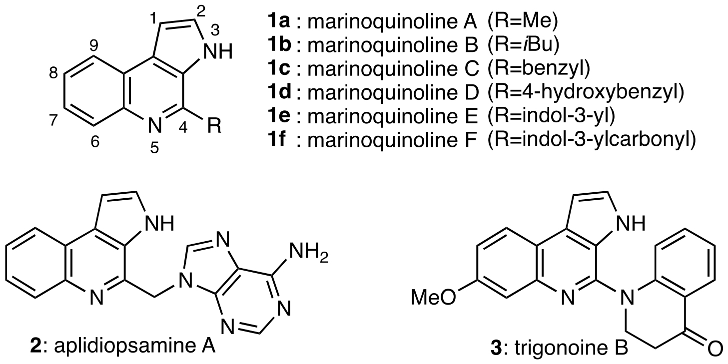
We dedicate this paper to Professor Dr. Yasuyuki Kita on the celebration of his 77th birthday.

Abstract – In this study, the synthesis of pyrrolo[2,3-*c*]quinoline as a common skeleton, is described. The process is based on the thermal electrocyclization of 3-phenylpyrrole containing isocyanate as 2-azahexatriene. Using this approach, the total synthesis of three natural marinoquinolines A, B, and E can be successfully achieved.

INTRODUCTION

Quinoline is an important nitrogen-containing heterocycle; it is a common component in pharmaceutical agents and biologically active natural products.[1] Among them, marinoquinolines A-F,[2] aplidiopsamine A,[3] and trigonoine B[4] have been reported as marine natural products possessing the pyrrolo[2,3-*c*]quinoline skeleton (Figure 1).



1a : marinoquinoline A (R=Me)
1b : marinoquinoline B (R=*i*Bu)
1c : marinoquinoline C (R=benzyl)
1d : marinoquinoline D (R=4-hydroxybenzyl)
1e : marinoquinoline E (R=indol-3-yl)
1f : marinoquinoline F (R=indol-3-ylcarbonyl)

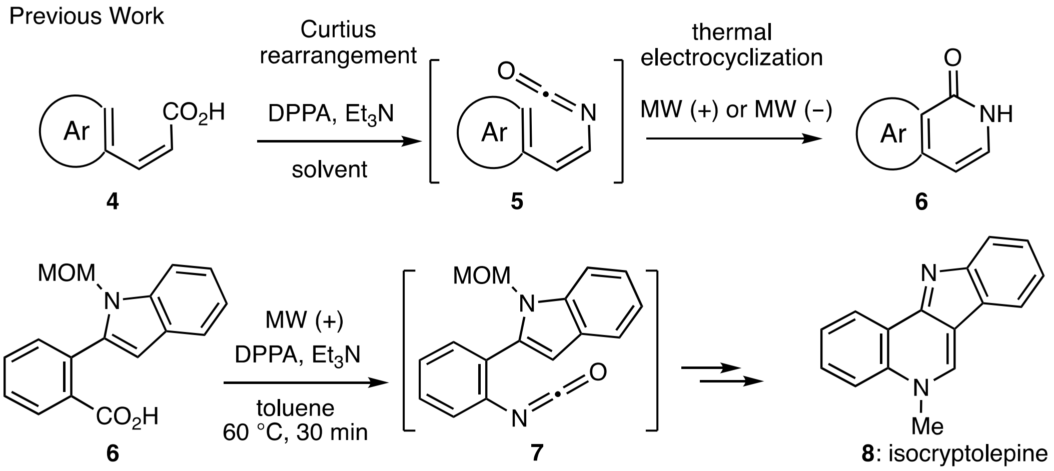
2: aplidiopsamine A

3: trigonoine B

Figure 1

Marinoquinoline A has been isolated from *Rapidithrix thailandica* by Srisukchayakul et al. in 2007. In addition, marinoquinolines B–F have been isolated from *Ohtaekwangia kribbensis* by Okanya et al. in Marinoquinolines A–F exhibit antibacterial, antifungal, and acetylcholinesterase inhibiting activities.[2] Aplidiopsamine A is a potent antimalarial agent.[3] Trigonoine B has been reported to exhibit anti-HIV activity.[4] Furthermore, some 4-substituted pyrroloquinoline derivatives have been reported to exhibit antitubercular activity.[5] The development of a convenient and efficient synthetic method to construct the pyrrolo[2,3-*c*]quinoline skeleton has attracted considerable attention from organic and medicinal chemists owing to their unique structures, characteristics, and biological activities. Therefore, the total synthesis of marinoquinolines and aplidiopsamine A has been achieved via various synthetic strategies using the pyridine ring formation from 3-arylpyrroles via the Morgen–Walls reaction,[6] Pictet–Spengler reaction,[7] tandem reductive cyclization,[8] Pd-catalyzed imine cyclization,[9] Bishler–Napieralski reaction,[10] and arene–ynamide cyclization.[11] Furthermore, the total synthesis of marinoquinolines C and E has been reported via synthetic strategy using the pyrrole ring formation from 2-chloro-3-nitroquinoline by Bartoli indolization.[12]

We are interested in the synthesis of heterocyclic compounds by constructing fused pyridine ring systems using the thermal electrocyclization of an azahexatriene system.[13] Furthermore, we have been searching for stronger biologically active compounds using these natural compounds and their derivatives.[14] We have recently reported a one-pot reaction wherein carboxylic acid **4** was converted to isocyanate **5** as 2-azahexatriene using Curtius rearrangement followed by a microwave-assisted electrocyclization to construct a fused pyridone ring (Scheme 1).[15] In fact, a convenient total synthesis of isocryptolepine (**8**) has been achieved using this method.[16]

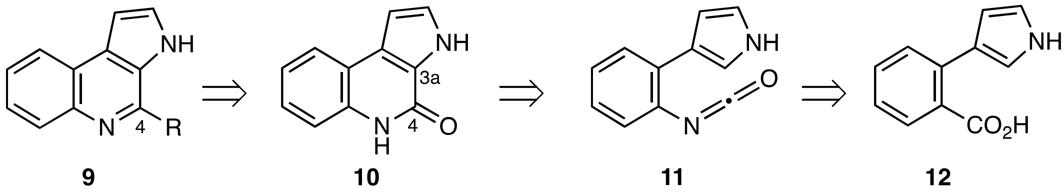


Scheme 1

RESULTS AND DISCUSSION

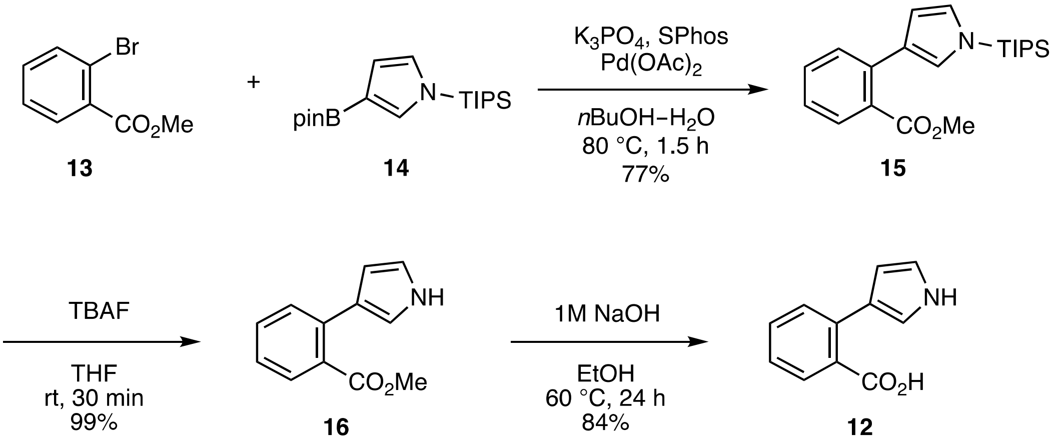
In this paper, we disclose the total synthesis of marinoquinolines by constructing a pyrrolo[2,3-*c*]quinoline framework via the electrocyclization of 2-(pyrrol-3-yl)phenyl isocyanate as the 2-azahexatiriene system.

Our retrosynthetic analysis of marinoquinolines is depicted in Scheme 2. We planned to introduce a side chain via a coupling reaction to the C4-position of marinoquinolines **9** in the final step. We anticipated the formation of a common pyrrolo[3,2-*c*]quinoline nucleus **10** using the thermal electrocyclization of 2-(pyrrol-3-yl)phenyl isocyanate **11** as the 2-azahexatiriene system, which is derived from the cleavage at the C3a–C4 bond position of **10**. Isocyanate **11** will be prepared by the Curtius rearrangement of 2-(pyrrol-3-yl)benzoic acid (**12**), which is easily obtained from methyl 2-(pyrrol-3-yl)benzoate.



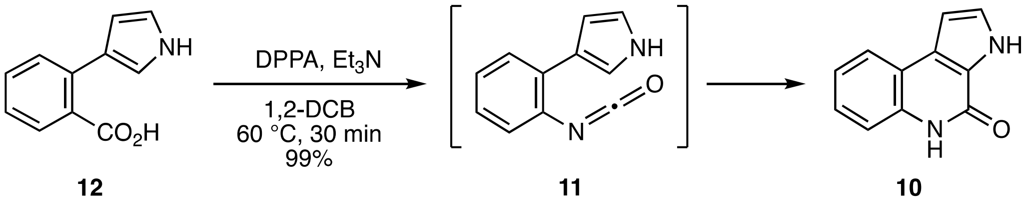
Scheme 2

As shown in Scheme 3, methyl 2-(pyrrol-3-yl)benzoate **15** was synthesized using the Suzuki–Miyaura coupling reaction of methyl 2-bromobenzoate (**13**) and 1-(triisopropylsilyl)-1*H*-pyrrole-3-boronic acid pinacol ester (**14**) using Guido's conditions.[7a] Subsequently, the TIPS group of **15** was removed with TBAF to obtain methyl 2-(pyrrol-3-yl)benzoate (**16**) with 99% yield. The hydrolysis of the obtained ester **16** with 1 M NaOH produced benzoic acid **12** in 84% yield.

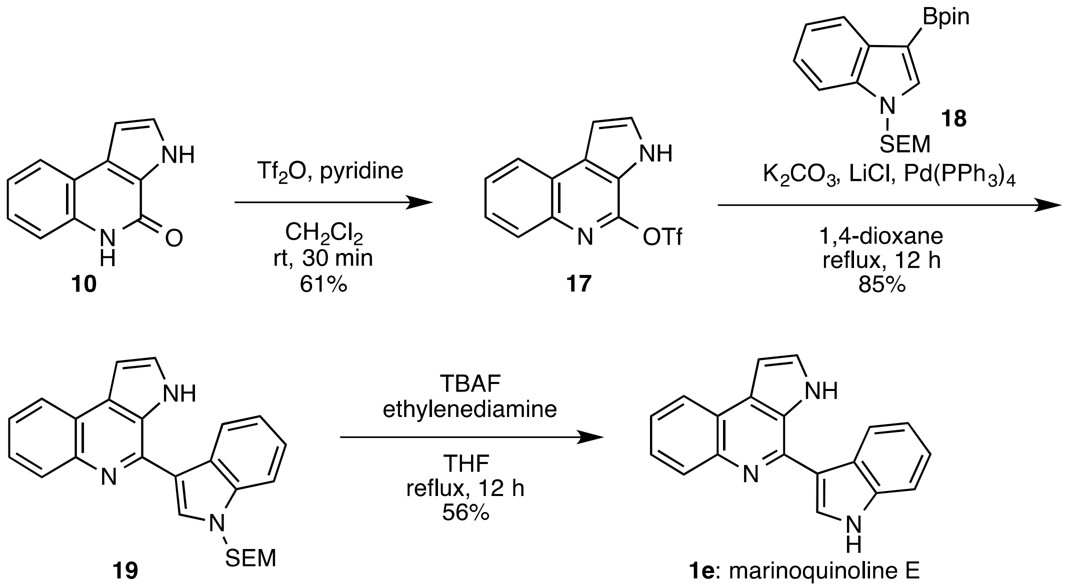


Scheme 3

Next, the synthesis of a pyrrolo[2,3-*c*]quinoline skeleton via electrocyclization was examined (Scheme 4). Carboxylic acid **12** was reacted with DPPA and Et$_3$N in 1,2-dichlorobenzene (1,2-DCB) at 60 °C for 30 min to obtain isocyanate **11** via the Curtius rearrangement. The reactant was purified to obtain pyrrolo[3,2-*c*]quinolin-4-one **10** instead of isocyanate **11** in 99% yield. Surprisingly, this result showed that electrocyclization proceeded immediately at the same temperature after the rearrangement reaction to form isocyanate. In addition, electrocyclization under microwave irradiation was performed; however, this approach was not more effective than the conventional one for substrate **12**. As described above, pyrroloquinolinone **10** was efficiently synthesized in a four-step sequence.



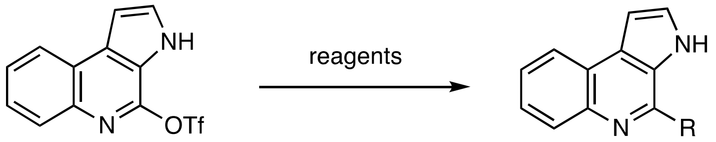
Scheme 4



Scheme 5

Next, to investigate substituent introduction at the C4 position of the obtained pyrroloquinolinone **10** (Scheme 5), treatment of **10** with trifluoromethanesulfonic anhydride (Tf$_2$O) and pyridine afforded triflate **17** in 61% yield. Sperry et al. have reported the synthesis of marinoquinolines C and E using the Suzuki–Miyaura reaction between 4-chloropyrrolo[2,3-*c*]quinoline and boronic acid MIDA esters (benzyl and indol-3-yl).[12] Therefore, we attempted to synthesize marinoquinoline E via the Suzuki–Miyaura reaction between triflate **17** and *N*-SEM-indol-3-ylboric acid pinacol ester **18**. The treatment of triflate **17** with **18** in the presence of $Pd(PPh_3)_4$ produced 4-(indol-3-yl)pyrrolo[2,3-*c*]quinoline **19** in 85% yield. Finally, the SEM group of **19** was removed with TBAF to obtain marinoquinoline E (**1e**) in 56% yield.

Table 1. Synthesis of Marinoquinolines A, B, and C



17 **1a-1c**: marinoquinolines A-C, **20**

run	reagents (eq)	conditions (eq)	No.	R	yield (%)
1	$MeB(OH)_2$ (1.5)	K_2CO_3 (3), $Pd(PPh_3)_4$ (0.01) 1,4-dioxane, reflux, 12 h	**1a**	Me	–
2	trimethylboroxine (2)	K_2CO_3 (2), $Pd(PPh_3)_4$ (0.01) 1,4-dioxane, reflux, 12 h	**1a**	Me	–
3	Me_3Al (7)	$Pd(PPh_3)_4$ (0.01) THF, reflux, 12 h	**1a**	Me	96
4	*i*BuB(OH)$_2$ (1.5)	K_2CO_3 (2), $Pd(PPh_3)_4$ (0.01) 1,4-dioxane/H_2O, 80 °C, 1.5 h	**1b**	*i*Bu	–
5	*i*Bu$_3$Al (7)	$Pd(PPh_3)_4$ (0.01) THF, reflux, 15 h	**1b**	*i*Bu	59
6	Bn-Bpin (1.5)	K_2CO_3 (2), $Pd(PPh_3)_4$ (0.01) 1,4-dioxane, reflux, 12 h	**1c**	Bn	–
7	Bn_3Al (7)	$Pd(PPh_3)_4$ (0.01) THF, reflux, 15 h	**1c**	Bn	–
8	–	MeOH (20), CO (1 atm), Et_3N (2) $Pd(OAc)_2$ (0.05), dppf (0.1), DMF, 80 °C, 12 h	**20**	CO_2Me	67

Next, we attempted to synthesize marinoquinolines A, B, and C by introducing an alkyl group at the C4 position of **17**. As shown in Table 1, the synthesis of marinoquinolines was examined using the Suzuki–Miyaura reaction between triflate **17** with commercial boric acid derivatives; however, desired marinoquinolines could not be obtained (runs 1, 2, 4, and 6). The abovementioned results showed that the borane reagent has low reactivity with substrate **17**. Therefore, we decided to examine the coupling reaction using trialkylaluminums reported by Hirota et al.[17] The coupling reaction of **17** with trimethylaluminum in the presence of $Pd(PPh_3)_4$ produced marinoquinoline A (**1a**) in 96% yield (run 3). Subsequently, the treatment of **17** with triisobutylaluminum under the same condition produced marinoquinoline B (**1b**) in 59% yield (run 5). Next, the introduction of a benzyl group was examined using tribenzylaluminum; however, marinoquinoline C (**1c**) was not obtained because the triflate moiety of **17** was hydrolyzed (run 7). The introduction of an alkyl group into **17** was determined to be optimal with an aluminum reagent. Furthermore, we performed the three-component cross-coupling reaction of triflate **17** with CO and MeOH in the presence of Pd catalyst and obtained methyl ester **20** in 67% yield (run 8). If compound **20** is used, the synthesis of other marinoquinolines and aplidiopsamine A is thought to be possible. The physical and spectroscopic data of our synthesized marinoquinolines A, B, and E are identical to those of natural and synthetic compounds.

CONCLUSION

This paper describes the synthesis of a common pyrrolo[2,3-*c*]quinoline skeleton using the thermal electrocyclization of 3-phenylpyrrole containing isocyanate as 2-azahexatriene. Using this approach, the total synthesis of three natural marinoquinolines was successfully achieved. Marinoquinoline E was synthesized by performing a coupling reaction with triflate and a borane reagent via a seven-step sequence with 18% overall yield. In addition, marinoquinolines A and B were synthesized using trialkylaluminum as a coupling reagent via a six-step sequence with 37% and 23% overall yields, respectively. Further applications and biological evaluation of their analogues are ongoing in our laboratory.

EXPERIMENTAL

General Methods: All non-aqueous reactions were carried out under an atmosphere of nitrogen in dried glassware unless otherwise noted. Solvents were dried and distilled according to standard protocols. Analytical thin-layer chromatography was performed with Silica gel 60PF$_{254}$ (Merck). Silica gel column chromatography was performed with Silica gel 60 (70–230 mesh, Kanto Co. Lit.). All melting points were determined on Yanagimoto micro melting point apparatus and are uncorrected. Proton nuclear magnetic resonance (^{1}H-NMR) spectra were recorded on a JEOL AL-300 at 300 MHz. Chemical shifts are reported relative to Me4Si (δ 0.00). NMR spectra were measured with $CDCl_3$ unless otherwise noted. Multiplicity is indicated by one or more of the following: s (singlet); d (doublet); t (triplet); q (quartet); m (multiplet); br (broad). Carbon nuclear magnetic resonance (^{13}C-NMR) spectra were recorded on a JEOL AL-300 at 75 MHz. Chemical shifts are reported relative to $CDCl_3$ (δ 77.0) and DMSO-*d*$_6$ (δ 39.7). Infrared spectra were recorded with ATR method using a Shimadzu FTIR-8000 spectrophotometer and Technologies DuraScop. Low and high-resolution mass spectra were recorded on JEOL JMS-700 spectrometers by direct inlet system.

Methyl 2-(*N*-triisopropylsilylpyrrol-3-yl)benzoate (15)

A mixture of methyl 2-bromobenzoate (**13**) (483 μL, 3.44 mmol), 1-(triisopropylsilyl)-1*H*-pyrrole-3-boronic acid pinacol ester (**14**) (1 g, 2.87 mmol), K_3PO_4 (973 mg, 4.59 mmol), $Pd(OAc)_2$ (19 mg, 0.09 mmol), and SPhos (71 mg, 0.17 mmol) in *n*-BuOH/H_2O (20 mL/ 10 mL) was stirred at 80 °C for 1.5 h under N_2 atmosphere. The reaction mixture was quenched with water, and then the mixture was extracted with EtOAc. The EtOAc layer was washed with water and brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was purified by column chromatography using EtOAc–hexane (1:99 v/v) to give methyl 2-(pyrrol-3-yl)benzoate **15** (800 mg, 77%) as colorless oil. IR (ATR) ν = 1720 cm^{-1}. ^1H-NMR (300 MHz, $CDCl_3$) δ: 1.12 (18H, d, *J* = 7.7 Hz), 1.46 (3H, sept, *J* = 7.7 Hz), 3.73 (3H, s), 6.39 (1H, dd, *J* = 1.5, 2.8 Hz), 6.77 (1H, dd, *J* = 1.8, 2.8 Hz), 6.86 (1H, dd, *J* = 1.5, 2.8 Hz), 7.23 (1H, t, *J* = 7.8 Hz), 7.42 (1H, t, *J* = 7.8 Hz), 7.47 (1H, d, *J* = 7.8 Hz), 7.56 (1H, d, *J* = 7.8 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 11.7, 17.8, 52.0, 110.9, 122.4, 124.4, 125.3, 125.4, 128.6, 129.7, 130.5, 131.1, 135.5, 170.9. MS *m/z*: 357 (M^+). HRMS (EI): calcd for $C_{21}H_{31}NO_2Si$ 357.2124; found 357.2134.

Methyl 2-(pyrrol-3-yl)benzoate (16)

A solution of TBAF (1.0 M in THF, 3.4 mL, 3.43 mmol) was added dropwise to a solution of methyl 2-(pyrrol-3-yl)benzoate **15** (818 mg, 2.29 mmol) in THF (30 mL) at 0 °C under N_2 atmosphere. After stirring at rt for 0.5 h, the reaction mixture was quenched with water, and then was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was purified by column chromatography using EtOAc-hexane (1:4, v/v) as an eluent to give methyl 2-(pyrrol-3-yl)benzoate (**16**) (455 mg, 99%) as yellow solid. Mp 68–70 °C (EtOAc–hexane). IR (ATR) ν = 1712 cm^{-1}. ^1H-NMR (300 MHz, $CDCl_3$) δ: 3.79 (3H, s), 6.32 (1H, dd, *J* = 2.7, 4.3 Hz), 6.82 (1H, dd, *J* = 2.4, 4.3 Hz), 6.94 (1H, dd, *J* = 2.4, 2.7 Hz), 7.24–7.29 (1H, m), 7.43–7.45 (2H, m), 7.60 (1H, d, *J* = 7.7 Hz), 8.28 (1H, br s). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 52.0, 108.7, 116.3, 118.2, 123.1, 125.6, 128.7, 129.9, 130.7, 130.8, 135.5, 170.6. MS *m/z*: 201 (M^+). HRMS (EI): calcd for $C_{12}H_{11}NO_2$ 201.0790; found 201.0783.

2-(Pyrrol-3-yl)benzoic acid (12)

To an ester **16** (250 mg, 1.24 mmol) in EtOH (12 mL) was added 1 M NaOH aqueous solution (12 mL), and then was stirred at 60 °C for 24 h. The reaction mixture was diluted with water, and then was acidified with 10% HCl aqueous solution to precipitate the carboxylic acid. The precipitation was filtrated off to give the crude benzoic acid **12** (194 mg, 84%) as white solid. Mp 125–127 °C (EtOAc–hexane). IR (ATR) ν = 1666 cm^{-1}. ^1H-NMR (300 MHz, $CDCl_3$) δ: 6.39 (1H, dd, *J* = 1.9, 4.8 Hz), 6.87 (1H, dd, *J* = 2.4, 4.8 Hz), 6.98 (1H, dd, *J* = 1.9, 2.4 Hz), 7.32 (1H, t, *J* = 7.7 Hz), 7.44 (1H, t, *J* = 7.7 Hz), 7.50 (1H, d, *J* = 7.7 Hz), 7.89 (1H, d, *J* = 7.7 Hz), 8.39 (1H, br s). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 109.4, 116.9, 118.4, 122.7, 126.0, 129.2, 130.3, 130.8, 131.8, 136.5, 173.1. MS *m/z*: 187 (M^+). HRMS (EI): calcd for $C_{11}H_9NO_2$ 187.0633; found 187.0645.

Pyrrolo[2, 3-*c*]quinolin-4-one (10)

A solution of benzoic acid **12** (338 mg, 1.81 mmol), DPPA (1.2 mL, 5.42 mmol), and Et_3N (0.75 mL, 5.42 mmol) in 1,2-dichlorobenzene (3 mL) were stirred at 60 °C for 30 min. After cooling to an ambient temperature, the solvent was removed, and the residue was purified by column chromatography using

EtOAc–hexane (1:3 v/v) as an eluent to give the pyrroloquinolinone **10** (398 mg, 99%) as white solid. Mp 146–148 °C (EtOAc–hexane). IR (ATR) ν = 1635 cm^{-1}. ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 6.87–6.89 (1H, m), 7.18 (1H, t, *J* = 7.8 Hz), 7.32 (1H, t, *J* = 7.8 Hz), 7.36–7.38 (2H, m), 7.93 (1H, d, *J* = 7.8 Hz), 11.34 (1H, br s), 12.21 (1H, br s). ^{13}C-NMR (75 MHz, DMSO-d_6) δ: 102.3, 115.8, 117.4, 121.6, 122.5, 122.9, 126.2, 126.5, 127.2, 135.4, 155.1. MS *m/z*: 184 (M$^+$). HRMS (EI): calcd for $C_{11}H_8N_2O$ 184.0637; found 184.0652.

4-(Trifluoromethylsulfonyloxy)pyrrolo[2,3-*c*]quinoline (17)

Tf_2O (71 μL, 0.43 mmol) was added to a stirred solution of the pyrroloquinolinone **10** (61 mg, 0.29 mmol) and pyridine (69 μL, 0.86 mmol) in CH_2Cl_2 under cooling with ice. After stirring at rt for 30 min, the solution was treated with water. The mixture was extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with water and brine and then dried over Na_2SO_4. The solvent was removed, and the residue was purified by column chromatography (silica gel, 10 g) using EtOAc–hexane (1:4, v/v) as an eluent to give the triflate **17** (55 mg, 61%) as white solid. Mp 135–137 °C (EtOAc–hexane). IR (ATR) ν = 1041, 1481 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.13–7.15 (1H, m), 7.52 (1H, t, *J* = 2.8 Hz), 7.61–7.67 (2H, m), 8.06–8.09 (1H, m), 8.19–8.22 (1H, m), 9.10 (1H, br s). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 103.4, 116.6, 118.4, 120.8, 123.0, 123.7, 127.1, 127.4, 128.2, 128.9, 130.1, 134.5, 139.9, 141.2 MS *m/z*: 316 (M$^+$). HRMS (EI): calcd for $C_{12}H_7F_3N_2O_3S$ 316.0129; found 316.0129

4-[*N*-(Trimethylsilylethoxymethyl)indol-3-yl]pyrrolo[2,3-*c*]quinoline (19)

A mixture of triflate **17** (71 mg, 0.23 mmol), *N*-SEM-indol-3-ylboronic acid **18** (168 mg, 0.45 mmol), 2 M K_2CO_3 aqueous solution (0.23 mL, 0.45 mmol), LiCl (19 mg, 0.45 mmol), and $Pd(PPh_3)_4$ (12 mg, 1 μmol) in dioxane (3 mL) was refluxed for 12 h under N_2 atmosphere. The reaction mixture was quenched with water and extracted with EtOAc. The organic layer was washed with water and brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was purified by column chromatography using EtOAc–hexane (3:7 v/v) as an eluent to give the 4-(indol-3-yl)pyrroloquinoline **19** (79 mg, 85%) as white solid. Mp 130–132 °C (EtOAc–hexane). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: –0.06 (9H, s), 0.89 (2H, t, *J* = 8.3 Hz), 3.53 (2H, t, *J* = 8.3 Hz), 5.51 (2H, s), 7.14 (1H, d, *J* = 3.0 Hz), 7.27 (1H, t, *J* = 7.5 Hz), 7.35 (1H, t, *J* = 7.5 Hz), 7.42 (1H, d, *J* = 3.0 Hz), 7.54–7.65 (3H, m), 7.79 (1H, s), 8.05 (1H, d, *J* = 7.5 Hz), 8.22–8.27 (2H, m), 9.10 (1H, br s). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: –1.41, 17.7, 66.3, 76.0, 102.1, 110.6, 114.8, 120.9, 121.5, 122.8, 122.9, 123.1, 125.3, 125.7, 126.1, 127.2, 127.9, 128.3, 128.7, 129.4, 137.1, 142.3, 143.1. MS *m/z*: 413 (M$^+$). HRMS (EI): calcd for $C_{25}H_{27}N_3OSi$; 413.1923; found 413.1938.

Marinoquinoline E (1e)

TBAF (1.0 M in THF, 0.3 mL, 0.32 mmol) was added dropwise to a solution of 4-(indol-3-yl)pyrroloquinoline **19** (44 mg, 0.11 mmol) and ethylenediamine (21 μL, 0.32 mmol) in THF (2 mL) under N_2 atmosphere. After refluxing for 12 h, the reaction mixture was quenched with water, and then was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was purified by column chromatography using EtOAc–hexane (1:1, v/v) as an eluent to give marinoquinoline E (**1e**) (17 mg, 56%) as yellow solid. Mp 263–264 °C (EtOAc–hexane). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.15 (1H, d, *J* = 2.7 Hz), 7.23–7.34 (2H, m), 7.44 (1H, d, *J* = 2.9 Hz), 7.51 (1H, d, *J* = 7.4 Hz), 7.57–7.65 (2H, m), 7.84 (1H, s), 8.03 (1H, d, *J* = 7.4 Hz), 8.23–8.27 (2H, m), 8.74 (1H, br s), 8.94 (1H, br s). ^{1}H-NMR (300 MHz, acetone–*d*$_6$) δ: 7.18–7.26 (3H, m), 7.47–7.57 (3H, m), 7.61 (1H, d, *J* = 7.1 Hz), 8.18 (1H, d, *J* = 7.8 Hz), 8.22–8.28 (2H, m), 8.72 (1H, d, *J* = 7.8 Hz), 10.88 (1H, br s), 11.06 (1H, br s). ^{13}C-NMR (75 MHz, acetone–*d*$_6$) δ: 102.2, 112.3, 114.7, 121.1, 123.3, 123.46, 123.52, 123.6, 125.6, 126.5, 127.1, 127.7, 127.8, 128.0, 129.6, 129.7, 137.9, 143.5, 144.3. MS *m/z*: 283 (M^+). HRMS (EI): calcd for $C_{19}H_{13}N_3$ 283.1109; found 283.1113.

Marinoquinoline A (1a)

A mixture of triflate **17** (20 mg, 0.063 mmol), trimethylaluminum (28 μL, 0.43 mmol) and $Pd(PPh_3)_4$ (7 mg, 6.3 μmol) in THF (2 mL) was refluxed for 12 h under N_2 atmosphere. The reaction mixture was quenched with water and extracted with EtOAc. The organic layer was washed with water and brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was purified by column chromatography using EtOAc–hexane (1:3 v/v) as an eluent to give marinoquinoline A (**1a**) (11 mg, 96%) as white solid. Mp 231–233 °C (EtOAc–hexane). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.88 (3H, s), 7.09 (1H, d, *J* = 3.0 Hz), 7.43 (1H, d, *J* = 3.0 Hz), 7.51–7.61 (2H, m), 8.10–8.13 (1H, m), 8.16–8.19 (1H, m), 9.01 (1H, br s). ^{1}H-NMR (300 MHz, acetone–*d*$_6$) δ: 2.82 (3H, s) 7.12 (1H, d, *J* = 2.9 Hz), 7.46–7.53 (2H, m), 7.58 (1H, d, *J* = 2.9 Hz), 7.98–8.01 (1H, m), 8.20–8.23 (1H, m), 11.15 (1H, br s). ^{13}C-NMR (75 MHz, acetone–*d*$_6$) δ: 21.1, 102.0, 123.7, 124.1, 125.7, 126.1, 127.2, 128.3, 128.4, 129.7, 143.6, 146.8. MS *m/z*: 182 (M^+). HRMS (EI): calcd for $C_{12}H_{10}N_2$ 182.0844; found 182.0845.

Marinoquinoline B (1b)

Marinoquinoline B (**1b**) (yield 59%) was prepared according to a synthetic method for **1a** as white solid. Mp 182–183 °C (EtOAc–hexane). ^{1}H-NMR (300 MHz, $CDCl_3$) δ:1.03 (6H, d, *J* = 7.1 Hz), 2.41 (1H, sept, *J* = 7.1 Hz), 3.04 (2H, d, *J* = 7.3 Hz), 7.09 (1H, d, *J* = 3.0 Hz), 7.44 (1H, d, *J* = 3.0 Hz), 7.52–7.62 (2H, m), 8.14–8.20 (2H, m), 8.82 (1H, br s). ^{1}H-NMR (300 MHz, acetone–*d*$_6$) δ: 0.99 (6H, d, *J* = 6.6 Hz), 2.43 (1H, sept, *J* = 6.6 Hz), 3.06 (2H, d, *J* = 7.3 Hz), 7.12 (1H, d, *J* = 2.7 Hz), 7.47–7.52 (2H, m), 7.55 (1H, d, *J* = 2.7 Hz), 7.79–8.02 (1H, m), 8.21–8.24 (1H, m), 11.13 (1H, br s). ^{13}C-NMR (75 MHz, acetone–*d*$_6$) δ: 23.0, 29.0, 44.0, 101.9, 123.7, 124.0, 125.6, 126.0, 127.0, 128.6, 129.8, 130.0, 143.7, 150.0. MS *m/z*: 224 (M^+). HRMS (EI): calcd for $C_{15}H_{16}N_2$ 224.1313; found 224.1322.

Methyl pyrrolo[2,3-*c*]quinoline-4-carboxylate (20)

Carbon monoxide was bubbled for 5 min to a mixture of the triflate **17** (102 mg, 0.33 mmol), MeOH (0.27 mL, 6.58 mmol), Et_3N (0.09 mL, 0.66 mmol), dppf (18 mg, 0.033 mmol), and $Pd(OAc)_2$ (13 mg, 0.017 mmol) in DMF (7 mL) at rt. The resulting mixture was stirred at 80 °C for 12 h under a CO atmosphere. After cooling to an ambient temperature, the mixture was quenched with water and then the mixture was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was purified by column chromatography using EtOAc–hexane (3:7, v/v) as an eluent to give the methyl ester **20** (50 mg, 67%) as yellow solid. Mp 151–153 °C (EtOAc–hexane). IR (ATR) $\nu = 1701$ cm^{-1}. ^1H-NMR (300 MHz, $CDCl_3$) δ: 4.16 (3H, s), 7.12–7.14 (1H, m), 7.58 (1H, t, J = 2.7 Hz), 7.66–7.70 (2H, m), 8.24–8.27 (1H, m), 8.34–8.38 (1H, m), 10.33 (1H, br s). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 53.3, 101.5, 123.1, 125.1, 126.8, 127.8, 128.2, 128.8, 130.8, 130.9, 133.4, 141.7, 166.9. MS *m/z*: 226 (M^+). HRMS (EI): $C_{13}H_{10}N_2O_2$ calcd for 226.0742; found 226.0752.

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