Total Synthesis of Nortopsentins A—D, Marine Alkaloids

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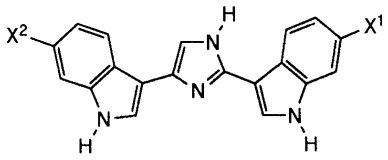
Nortopsentins A—D, antifungal 1,4-bisindolylimidazole marine alkaloids isolated from a sponge, were synthesized through palladium-catalyzed cross-coupling of 3-indolylboronic and 6-bromo-3-indolylboronic acids with halogenoimidazoles as the key reaction.

Key words imidazole; marine alkaloid; Suzuki reaction; palladium catalyst; arylboronic acid; nortopsentin

Many imidazole marine alkaloids exhibit biological activities, such as antibacterial and antitumorigenic activities.[1-3] Nortopsentins A—C (**1**—**3**), having a characteristic 2,4-bisindolylimidazole skeleton, are cytotoxic and antifungal constituents of a marine sponge, *Spongosorites ruetzleri*,[2] and nortopsentin D (**4**), obtained by hydrogenation of **1**—**3**, retains these biological activities.[3] We are interested in the synthesis and biological activities of imidazole compounds,[4] and in this paper we would like to report a total synthesis of **1**—**4** starting from 1-protected 1*H*-imidazoles.

First, we planned a total synthesis of nortopsentin D (**4**), which has the simplest structure among these bisindolylimidazoles (**1**—**4**), *via* arylation of the imidazole ring. Regioselective introduction of carbogenic substituents at the 4- and/or 5-position of the imidazole nucleus has been examined,[5] but selective arylation of the imidazole ring is undeveloped.[6] 2,4,5-Tribromo-1-methoxymethyl- and 1-[[2-(trimethylsilyl)ethoxy]methyl]-1*H*-imidazoles (**5a**, **b**) were prepared,[7,8] and arylation of these compounds with various arylmetals in the presence of tetrakis(triphenylphosphine)palladium was examined. The results are summarized in Table 1. In the cases of organozinc (run 1) and Grignard reagents (run 2), the 2-phenylimidazole (**6a**) was produced in low yields accompanied with a considerable amount of the 2,2′-bi(4,5-dibromoimidazole) (**7**). Under the conditions of the Suzuki reaction[9] (runs 3—7), an equimolar amount of arylboronic acids[10] reacted with **5a** and **5b** to give the corresponding aryldibromides (**6a—d**), but when two



Nortopsentin A (**1**): $X^1=X^2=Br$
B (**2**): $X^1=Br$, $X^2=H$
C (**3**): $X^1=H$, $X^2=Br$
D (**4**): $X^1=X^2=H$

Fig. 1

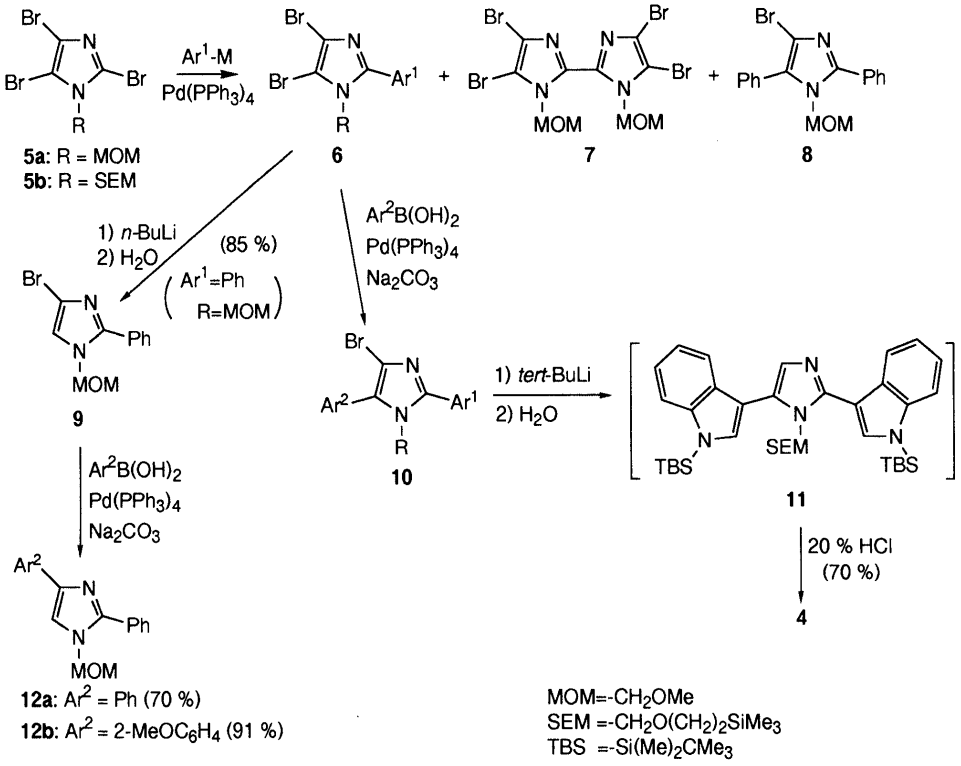


Chart 1

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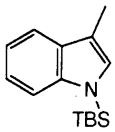
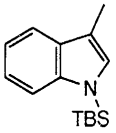
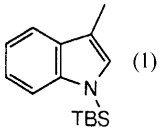
Table 1. Introduction of Aryl Group into **5** and **6** with ArM

Entry	Ar^1-M (eq)		$Ar^2B(OH)_2$ (eq)	R (Substrate)	Reaction time (h)	Yield (%) (product)
	Ar^1-	M				
1	Ph-	ZnCl (1)	—	MOM (**5a**)	5	45[a] (**6a**), 9[b] (**7**)
2	Ph-	MgBr (1)	—	MOM (**5a**)	10	15[a] (**6a**), 27[b] (**7**)
3	Ph-	$B(OH)_2$ (1)	—	MOM (**5a**)	8	94[b] (**6a**)
4	Ph-	$B(OH)_2$ (2)	—	MOM (**5a**)	15	65[a] (**6a**), 30[b] (**8**)
5	2-$MeOC_6H_4$–	$B(OH)_2$ (1)	—	MOM (**5a**)	8	92[b] (**6b**)
6		$B(OH)_2$ (1)	—	MOM (**5a**)	8	80[b] (**6c**)
7		$B(OH)_2$ (1)	—	SEM (**5b**)	8	89[b] (**6d**)
8	Ph-	—	Ph (1)	MOM (**6a**)	10	70[b] (**8**)
9	Ph-	—	2-$MeOC_6H_4$ (1)	MOM (**6a**)	10	71[b] (**10a**)
10		—	 (1)	SEM (**6d**)	10	68[b] (**10b**)

a) Determined by GLC with an internal standard. *b*) Isolated yield.

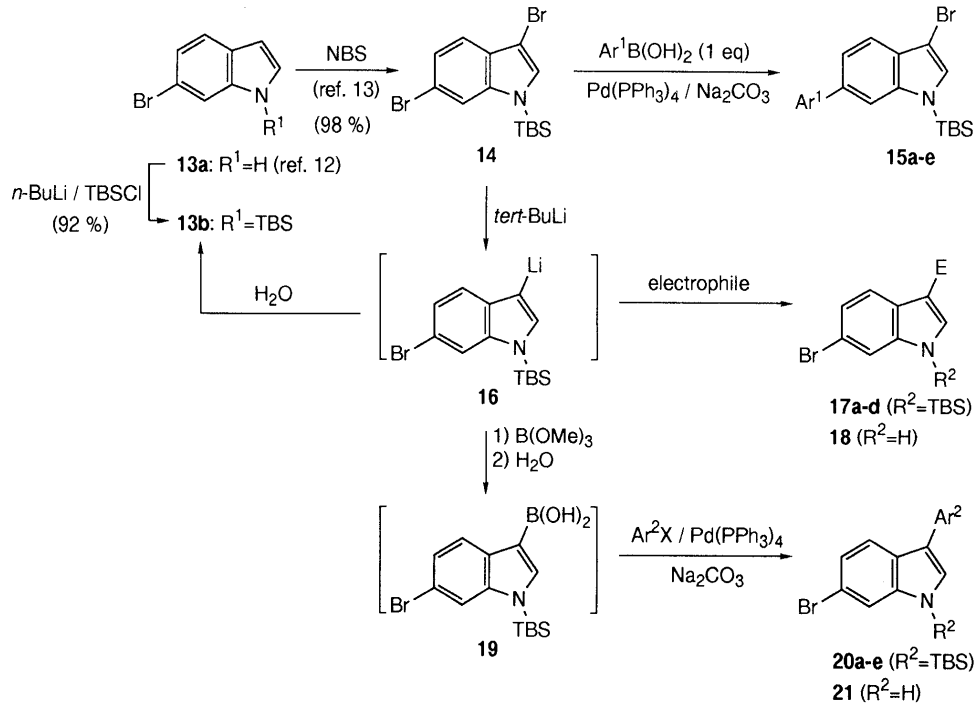


Chart 2

equivalents of phenylboronic acid and a prolonged reaction time were used, the 2,5-diphenylimidazole (**8**) was produced to a considerable extent (run 4). The results listed in Table 1 agreed with reported data on lithio imidazole[11] and nucleophilic substitution.[7] Reaction of the 2- aryldibromoimidazoles (**6a**, **d**) with an equimolar amount of arylboronic acids gave the corresponding 2,5-diarylimidazoles (**8**, **10a**, **b**) in satisfactory yields (runs 8—10), and it was also found that **10a** could be produced conveniently in a one-pot procedure starting from the tribromide (**5a**) by successive addition of equimolar amounts of these two kinds of arylboronic acids, phenylboronic and 2-methoxyphenylboronic acids, with an appropriate interval. The product (**10b**) was treated with *tert*-butyllithium, followed by quenching with water and removal of the silyl protecting groups by treatment with diluted hydrochloric acid to give nortopsentin D (**4**) in 70% yield.

We examined the reaction of various arylboronic acids with an equimolar amount of 1-*tert*-butyldimethylsilyl-3,6-dibromoindole (**14**) in the presence of palladium(0) catalyst and aqueous sodium carbonates as an approach to total synthesis of the bromine-containing alkaloids, nortopsentins A—C (**1**—**3**). The reaction proceeded

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almost exclusively at the 6-position of the indole (**14**) to give the 6-aryl-3-bromoindoles (**15a—e**) (Table 2), which is inappropriate for the synthesis of **1—3**.

Next, the 3,6-dibromoindole (**14**) was treated with *tert*-butyllithium (1.2 eq) in tetrahydrofuran (THF) at −78 °C followed by treatment with appropriate electrophiles to give the corresponding 3-substituted 6-bromoindoles (**17**, **18**) in moderate to good yields (Table 3). Generation of the 3-lithioindole (**16**) was confirmed by production of the 6-bromoindole (**13b**) after treatment with water as an electrophile. This procedure could be conveniently applied to the preparation of the 6-bromo-3-indolylboronic acid (**19**) *via* treatment of **16** with trimethoxyborane followed by aqueous work-up.[14] The crude boronic acid (**19**) was heated at 70 °C in the presence of arylbromide and the palladium(0) catalyst in benzene and methanol, but only a complex mixture was obtained (Table 4, runs 1—3).

On the other hand, it was found that iodoarenes such as iodobenzene, 4-iodotoluene and 4-fluoroiodobenzene smoothly reacted with 6-bromo-3-indolylboronic acid (**19**) as shown in Table 4 (runs 4—6). Thus, the 1-protected monoiodoimidazoles (**22a—c**) were prepared *via* the corresponding lithioimidazoles[4e,16] and treated with **19** to afford the 6-bromo-3-imidazolylindoles (**20d, e**, **21**) (runs 7—9).

Next, the 2,5-diiodoimidazole (**23**) was prepared from **22a** by lithiation with lithium 2,2,6,6-tetramethylpiperidide (LTMP)[17] followed by addition of iodine. Reaction of **23** with 2.2 eq of **19** followed by treatment of the product with tetrabutylammonium fluoride (TBAF) gave the 1-protected nortopsentin A (**25**) in only 9% yield, and removal of the SEM group of **25** was achieved by treatment

Table 2. Reaction Products of **14** with Various Arylboronic Acids

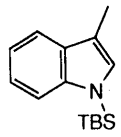
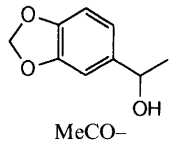
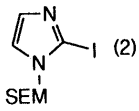
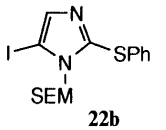
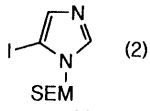
Run	Ar^1	Yield (%) (product)	mp (°C)
1	Phenyl	61 (**15a**)	121—123
2	2-Thienyl	78 (**15b**)	102—104
3	4-F–C_6H_4–	74 (**15c**)	133—134
4	2-MeO–C_6H_4–	70 (**15d**)	96—97
5		52 (**15e**)	172—174

Table 3. Reaction of the 3-Lithioindole (**16**) with Various Electrophiles

Run	Electrophile	E	Yield (%) (product)
1	H_2O	H–	60 (**13b**)
2	MeI	Me–	81 (**17a**)
3	EtI	Et–	71 (**17b**)
4	Piperonal		84 (**17c**)
5	$MeCONMe_2$	MeCO–	53 (**17d**)
6	$HCONMe_2$	HCO–	64[a] (**18**)

a) **18**, a natural product (un-named; see ref. 15), was obtained by treatment of the initial reaction product with tetrabutylammonium fluoride (TBAF).

Table 4. Reaction of the 6-Bromo-3-indolylboronic Acid (**19**) with Bromo- or Iodoarenes

Run	Ar^2-X (eq)	Yield (%) (product)
1	Ph-Br (3)	—[a]
2	2-MeO–C_6H_4Br (5)	—[a]
3	4-MeO–C_6H_4Br (3)	—[a]
4	Ph-I (3)	85 (**20a**)
5	4-Me–C_6H_4I (3)	81 (**20b**)
6	4-F–C_6H_4I (3)	73 (**20c**)
7	 **22a**	54[b] (**21**)
8	 **22b**	67 (**20d**)
9	 **22c**	58 (**20e**)

a) A complex mixture was obtained. *b*) Desilylation occurred during work-up.

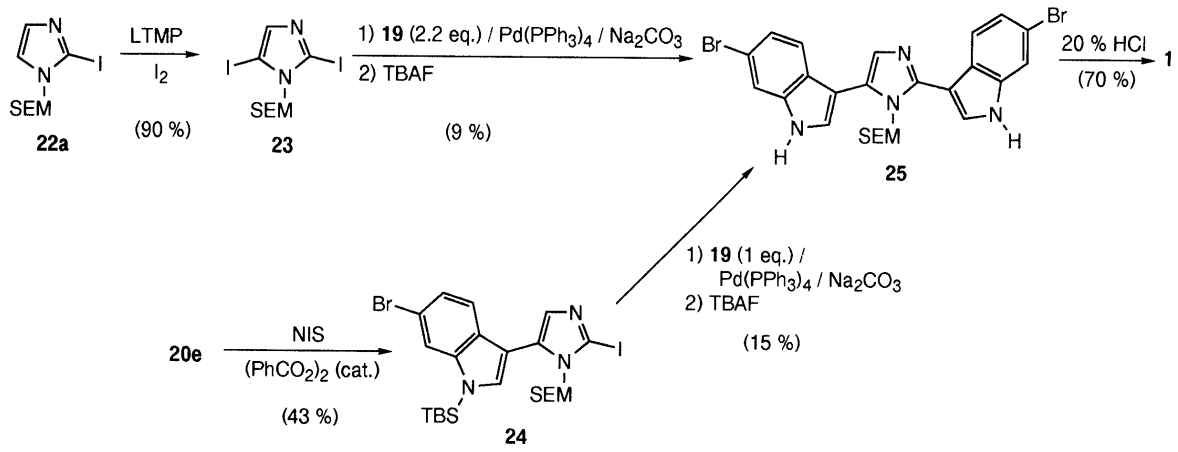


Chart 3

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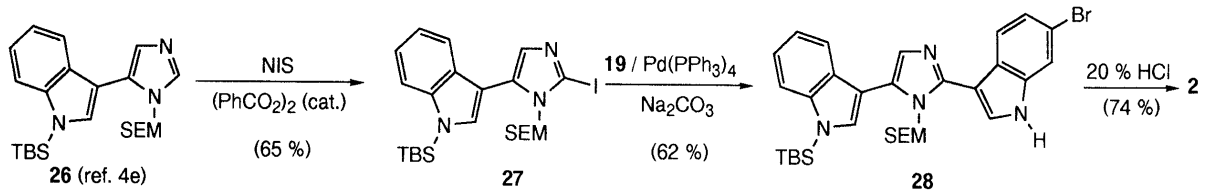

Chart 4

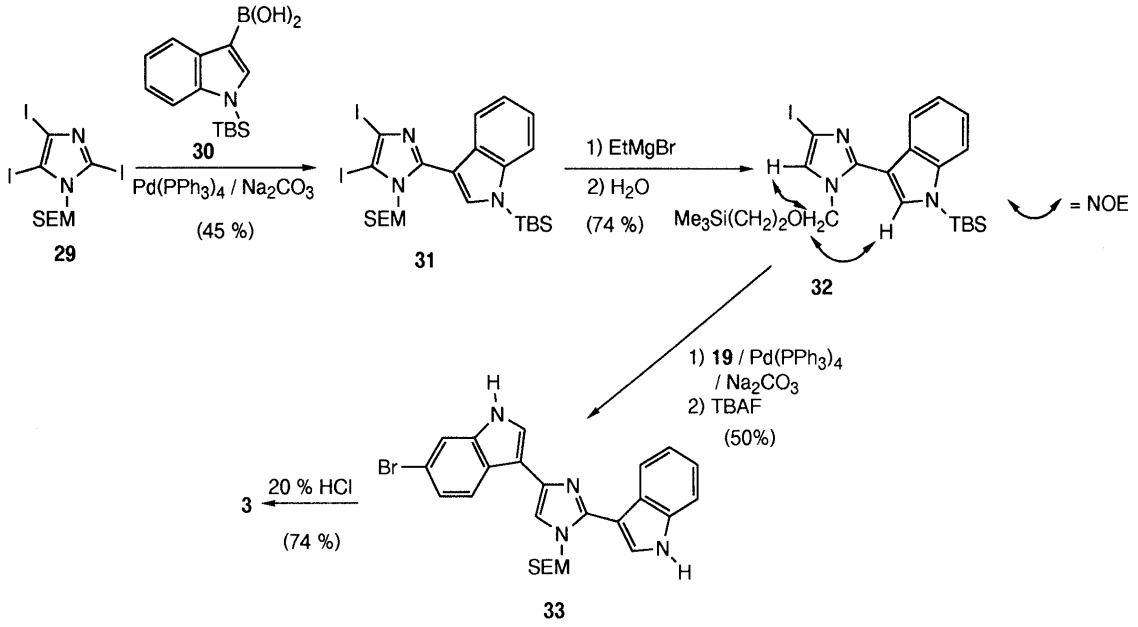

Chart 5

with diluted hydrochloric acid to give nortopsentin A (**1**) in 70% yield (Chart 3).[18] Compound **25** was also obtained in the following way. The imidazolylindole (**20e**) was treated with *N*-iodosuccinimide (NIS) in the presence of dibenzoyl peroxide to give the 2-iodoimidazol-5-ylindole (**24**) in 43% yield, and **24** was subsequently subjected to the coupling reaction with **19** in the above-mentioned manner followed by treatment with TBAF to give **25** in 15% yield.

Nortopsentin B (**2**) was synthesized in the following way. The 3-imidazolylindole (**26**)[4e] was treated with NIS to give the indolyliodoimidazole (**27**) in 65% yield, and the product was coupled with **19** followed by deprotection with 20% hydrochloric acid to give nortopsentin B (**2**) in 46% overall yield from **27** (Chart 4).[18]

Nortopsentin C (**3**) was synthesized in the following way. The 1-protected 2,4,5-triiodoimidazole (**29**) was prepared,[19] and the iodide (**29**) was coupled with the 3-indolylboronic acid (**30**)[4d,e] in the above-mentioned manner to give the indolyldiiodoimidazole (**31**) in 45% yield. Treatment of **31** with ethylmagnesium bromide gave the indolylmonoiodoimidazole (**32**) in 74% yield. The structure of **32** was confirmed on the basis of nuclear Overhauser effects (NOE), as shown in Chart 5.[20] The indolyliodoimidazole (**32**) was coupled with **19** in the above-mentioned manner, followed by deprotection of the product with TBAF and then with 20% hydrochloric acid to give nortopsentin C (**3**) in 37% overall yield from **32** (Chart 5).[18]

Experimental

All melting points were measured with a Yanaco MP micro-melting point apparatus, without correction. Infrared (IR) spectra were taken with a Shimadzu IR-410 spectrometer. ^{1}H-NMR spectra and ^{13}C-NMR spectra were obtained on a Varian XL-300 (300 MHz for ^{1}H and 75.4 MHz for ^{13}C). The chemical shifts are given in δ (ppm) values with tetramethylsilane as an internal standard. Abbreviations of ^{1}H-NMR signal patterns are as follows: s (singlet); d (doublet); t (triplet); m (multiplet). High-resolution mass spectra (HR-MS) and low-resolution mass spectra (LR-MS) were obtained on a JEOL JMS-SX 102A QQ spectrometer. Silica gel (Merck Art. 7734 and Nacalai Tesque Silica gel 60 PF254) was used for column chromatography and preparative thin-layer chromatography (PTLC), respectively.

Representative Procedure for Arylation of Imidazole Ring: a) Synthesis of 4,5-Dibromo-1-methoxymethyl-2-phenyl-1*H*-imidazole (6a) from 5a and Phenylboronic Acid A mixture of phenylboronic acid (61 mg, 0.5 mmol), **5a**[7] (174 mg, 0.5 mmol), benzene (10 ml), methanol (2 ml), 2 M sodium carbonate (0.5 ml) and tetrakis(triphenylphosphine)palladium (58 mg, 0.05 mmol) was refluxed for 8 h under an N_2 atmosphere. The reaction mixture was cooled to room temperature and anhydrous sodium sulfate was added. The mixture was filtered and the filtrate was evaporated under reduced pressure to give an oily residue, which was subjected to PTLC with *n*-hexane to give **6a** (163 mg, 94%), which was recrystallized from cyclohexane. mp 92—93 °C (colorless crystals). IR ($CHCl_3$): 1497, 1460, 1376, 1180, 1105 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 3.45 (3H, s), 5.27 (2H, s), 7.45—7.47 (3H, m), 7.74—7.77 (2H, m). ^{13}C-NMR ($CDCl_3$): 56.6, 76.2, 105.3, 117.9, 128.7, 128.9, 129.1, 129.9, 149.9. LR-MS *m/z*: (relative intensity): 45 (100), 344 (5), 346 (12), 348 (6). *Anal.* Calcd for $C_{11}H_{10}Br_2N_2O$: C, 38.18; H, 2.91; N, 8.10. Found: C, 38.29; H, 2.90; N, 8.19.

b) 4,4′,5,5′-Tetrabromo-1,1′-bis(methoxymethyl)-2,2′-biimidazolyl (7) and 6a from 5a and PhMgBr A mixture of phenylmagnesium bromide (0.3 ml, 0.3 mmol, 1 M solution in THF), **5a** (105 mg, 0.3 mmol), tetrakis(triphenylphosphine)palladium (35 mg, 0.03 mmol) and THF (4 ml) was stirred for 2 h at room temperature under an N_2 atmosphere, then refluxed for 2 h. The reaction mixture was cooled to room

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temperature. The yield of **6a** was measured by GLC analysis, and water (5 ml) was added to the mixture. The crude **7** was extracted with AcOEt, and the organic layer was dried and evaporated to give a solid residue, which was subjected to PTLC (AcOEt/*n*-hexane = 1/5) to give **7** (44 mg, 27%). This product was recrystallized from AcOEt–*n*-hexane. mp 222—240 °C (dec.) (colorless crystals). IR ($CHCl_3$): 2920, 1481, 1376, 1109, 967 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 3.32 (6H, s), 5.91 (4H, s). ^{13}C-NMR ($CDCl_3$): 56.6, 76.9, 107.9, 117.7, 137.6. LR-MS *m/z*: (relative intensity): 45 (100), 463 (8), 465 (8), 493 (9), 495 (14), 534 (1), 536 (5), 538 (8), 540 (5), 542 (1). HR-MS *m/z*: Calcd for $C_{10}H_{10}Br_4N_4O_2$, 533.7540. Found, 533.7567 (M^+).

4,5-Dibromo-1-methoxymethyl-2-(2-methoxyphenyl)-1*H*-imidazole (**6b**): This compound was obtained from **5a** and 2-methoxyphenylboronic acid[21] in a similar manner to that used for the above synthesis of **6a**. The crude product was purified by PTLC (AcOEt/*n*-hexane = 1/2). Yield, 92%. Colorless viscous oil. IR ($CHCl_3$): 1496, 1463, 1220, 1119, 1107 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 3.08 (3H, s), 3.81 (3H, s), 5.18 (2H, s), 6.98 (1H, d, J = 8.1 Hz), 7.06 (1H, dd, J = 1.0, 7.5 Hz), 7.43—7.49 (2H, m). ^{13}C-NMR ($CDCl_3$): 55.6, 56.3, 76.9, 104.1, 111.1, 117.8, 118.6, 121.1, 131.9, 132.3, 146.8, 157.0. LR-MS *m/z*: (relative intensity): 45 (100), 170 (36), 215 (11), 374 (10), 376 (19), 378 (10). HR-MS *m/z*: Calcd for $C_{12}H_{12}Br_2N_2O_2$, 373.9270. Found, 373.9263 (M^+).

4,5-Dibromo-1-methoxymethyl-2-(2-thienyl)-1*H*-imidazole (**6c**): This compound was obtained from **5a** and 2-thienylboronic acid[22] in a similar manner to that used for the above synthesis of **6a**. The crude product was purified by PTLC (AcOEt/*n*-hexane = 1/3). Yield, 80%. Colorless viscous oil. IR ($CHCl_3$): 2940, 1495, 1260, 1100, 781 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 3.48 (3H, s), 5.39 (2H, s), 7.11 (1H, dd, J = 3.7, 5.1 Hz), 7.44 (1H, dd, J = 1.1, 5.1 Hz), 7.58 (1H, dd, J = 1.1, 3.7 Hz). ^{13}C-NMR ($CDCl_3$): 56.6, 76.2, 105.4, 117.9, 127.8, 128.0, 128.3, 131.0, 144.3. LR-MS *m/z*: (relative intensity): 45 (100), 350 (9), 352 (17), 354 (9). HR-MS *m/z*: Calcd for $C_9H_8Br_2N_2OS$, 349.8720. Found, 349.8711 (M^+).

Preparation of 3-[1-(*tert*-Butyldimethylsilyl)indolyl]boronic Acid (30)[4d,e] A solution of *tert*-BuLi in *n*-pentane (1.9 M; 0.53 ml, 1 mmol) was added dropwise to a solution of 3-bromo-1-(*tert*-butyldimethylsilyl)indole[13,23] (**34**) (155 mg, 0.5 mmol) in THF (10 ml) under an N_2 atmosphere at −78 °C. The mixture was stirred for 15 min at −78 °C, then a solution of trimethoxyborane (208 mg, 2 mmol) in THF (10 ml) was added dropwise at −78 °C. Stirring was continued for 1 h at −78 °C, methanol (0.25 ml) and water (0.25 ml) were added, and the whole was stirred at room temperature for 3 h. Water (10 ml) was added, and the mixture was extracted with ether. The organic layer was dried over anhydrous sodium sulfate and evaporated to give a solid residue, which was used for the next reaction without further purification.

4,5-Dibromo-2-[3-[1-(*tert*-butyldimethylsilyl)indolyl]]-1-[[2-(trimethylsilyl)ethoxy]methyl]-1*H*-imidazole (**6d**): This compound was obtained from **5b**[8] (131 mg, 0.3 mmol) and **30** (from 0.5 mmol of **34**) in a similar manner to that used for the above synthesis of **6a**. After purification by PTLC (AcOEt/*n*-hexane = 1/10), the product was recrystallized from EtOH–H_2O. Yield, 156 mg (89%). Colorless crystals, mp 101—103 °C. IR ($CHCl_3$): 2920, 1140, 1100, 824 cm^{-1}. ^{1}H-NMR ($CDCl_3$): −0.16 (9H, s), 0.48 (6H, s), 0.78 (9H, s), 0.79 (2H, t, J = 7.1 Hz), 3.49 (2H, t, J = 7.1 Hz), 5.16 (2H, s), 7.04—7.09 (2H, m), 7.36 (1H, t, J = 5.6 Hz), 7.66 (1H, s), 7.96 (1H, dd, J = 3.6, 5.9 Hz). ^{13}C-NMR ($CDCl_3$): −4.0, −1.5, 18.0, 19.3, 26.2, 68.4, 74.5, 103.2, 108.0, 113.8, 117.5, 120.6, 121.0, 122.6, 129.2, 132.5, 141.1, 145.8. LR-MS *m/z*: (relative intensity): 73 (100), 103 (12), 446 (12), 448 (14), 525 (7), 527 (13), 529 (8), 583 (6), 585 (10), 587 (7). HR-MS *m/z*: Calcd for $C_{23}H_{35}Br_2N_3OSi_2$, 583.0690. Found, 583.0662 (M^+).

4-Bromo-2,5-diphenyl-1-methoxymethyl-1*H*-imidazole (**8**): This compound was obtained from **6a** and phenylboronic acid in a similar manner to that used for the above synthesis of **6a**. The reaction mixture was refluxed for 15 h. The crude product was purified by PTLC (AcOEt/*n*-hexane = 1/2). Yield, 70%. Colorless viscous oil. IR ($CHCl_3$): 1480, 1380, 1127, 1082, 692 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 3.24 (3H, s), 4.99 (2H, s), 7.45—7.62 (8H, m), 7.82—7.85 (2H, m). ^{13}C-NMR ($CDCl_3$): 55.5, 75.4, 115.4, 128.3, 128.6, 128.7, 128.9, 128.9, 129.1, 129.5, 130.3, 131.1, 149.0. LR-MS *m/z*: (relative intensity): 45 (100), 218 (9), 342 (9), 344 (9). HR-MS *m/z*: Calcd for $C_{17}H_{15}BrN_2O$, 342.0370. Found, 342.0373 (M^+).

4-Bromo-1-methoxymethyl-5-(2-methoxyphenyl)-2-phenyl-1*H*-imidazole (**10a**): This compound was obtained from **6a** and 2-methoxyphenylboronic acid in a similar manner to that used for the above synthesis of **6a**. The reaction mixture was refluxed for 15 h. The crude product was purified by PTLC (AcOEt/*n*-hexane = 1/2). Yield, 71%. Colorless viscous oil. IR ($CHCl_3$): 2920, 1480, 1462, 1240, 1097 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 2.95 (3H, s), 3.82 (3H, s), 5.07 (2H, s), 6.98—7.10 (2H, m), 7.43—7.60 (7H, m). ^{13}C-NMR ($CDCl_3$): 55.6, 55.9, 75.9, 111.1, 119.0, 121.0, 121.1, 128.3, 128.7, 130.3, 130.8 (×2), 131.5, 132.6, 150.0, 157.1. LR-MS *m/z*: (relative intensity): 45 (100), 248 (46), 293 (19), 372 (48), 373 (10), 374 (49), 375 (9). HR-MS *m/z*: Calcd for $C_{18}H_{17}BrN_2O_2$, 372.0470. Found, 372.0490 (M^+).

4-Bromo-2,5-bis[3-[1-(*tert*-butyldimethylsilyl)indolyl]]-1-[[2-(trimethylsilyl)ethoxy]methyl]-1*H*-imidazole (**10b**): This compound was obtained from **6d** (176 mg, 0.3 mmol) and **30** (from 0.5 mmol of **34**) in a similar manner to that used for the above synthesis of **6a**. After purification by PTLC (AcOEt/*n*-hexane = 1/10), the product was recrystallized from EtOH–H_2O. Yield, 150 mg (68%). Colorless crystals, mp 154—156 °C. IR ($CHCl_3$): 2910, 1940, 1447, 1142, 837 cm^{-1}. ^{1}H-NMR ($CDCl_3$): −0.14 (9H, s), 0.65 (6H, s), 0.67 (6H, s), 0.84 (2H, t, J = 7.4 Hz), 0.96 (9H, s), 0.98 (9H, s), 3.23 (2H, t, J = 7.4 Hz), 5.18 (2H, s), 7.18—7.28 (4H, m), 7.42 (1H, s), 7.51—7.62 (3H, m), 7.82 (1H, s), 8.27 (1H, dd, J = 2.1, 5.8 Hz). LR-MS *m/z*: (relative intensity): 178 (100), 290 (19), 603 (19), 605 (22), 734 (13), 735 (9), 736 (18), 737 (7). HR-MS *m/z*: Calcd for $C_{37}H_{55}BrN_4OSi_3$, 734.2870. Found, 734.2852 (M^+).

4-Bromo-1-methoxymethyl-2-phenyl-1*H*-imidazole (9) A solution of *n*-BuLi in *n*-hexane (1.6 M; 0.44 ml, 0.7 mmol) was added dropwise under N_2 at −78 °C to a solution of **6a** (242 mg, 0.7 mmol) in THF (2 ml) and ether (14 ml). The mixture was stirred for 1 min at −78 °C, then water (10 ml) was added, and the whole was extracted with ether. The organic layer was dried over anhydrous sodium sulfate and evaporated to give an oily residue. The crude product was purified by PTLC (AcOEt/*n*-hexane = 1/2). Yield, 159 mg (85%). Colorless viscous oil. IR ($CHCl_3$): 2910, 1495, 1462, 1177, 1100 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 3.39 (3H, s), 5.20 (2H, s), 7.12 (1H, s), 7.44—7.46 (3H, m), 7.71—7.75 (2H, m). ^{13}C-NMR ($CDCl_3$): 56.5, 77.3, 115.6, 120.3, 125.1, 128.7, 128.9, 129.5, 148.7. LR-MS *m/z*: (relative intensity): 45 (100), 266 (30), 268 (30). HR-MS *m/z*: Calcd for $C_{11}H_{11}BrN_2O$, 266.0060. Found, 266.0028 (M^+).

1-Methoxymethyl-2,4-diphenyl-1*H*-imidazole (**12a**): This compound was obtained from **9** and phenylboronic acid in a similar manner to that used for the above synthesis of **6a**. The reaction mixture was refluxed for 15 h. The crude product was purified by PTLC (AcOEt/*n*-hexane = 1/2). Yield, 70%. Colorless viscous oil. IR ($CHCl_3$): 1723, 1460, 1241, 1173, 1101 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 3.34 (3H, s), 5.21 (2H, s), 7.23 (1H, tt, J = 1.3, 7.5 Hz), 7.35—7.48 (6H, m), 7.77—7.87 (4H, m). ^{13}C-NMR ($CDCl_3$): 56.3, 77.3, 116.9, 125.0, 126.9, 128.5, 128.6, 129.0, 129.1, 129.9, 133.7, 141.2, 148.9. HR-MS *m/z*: Calcd for $C_{17}H_{16}N_2O$, 264.1260. Found, 264.1256 (M^+).

1-Methoxymethyl-4-(2-methoxyphenyl)-2-phenyl-1*H*-imidazole (**12b**): This compound was obtained from **9** and 2-methoxyphenylboronic acid in a similar manner to that used for the above synthesis of **6a**. The reaction mixture was refluxed for 15 h. The crude product was purified by PTLC (AcOEt/*n*-hexane = 1/2). Yield, 91%. Colorless viscous oil. IR ($CHCl_3$): 2920, 1721, 1460, 1239, 1098 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 3.41 (3H, s), 3.97 (3H, s), 5.27 (2H, s), 6.95—7.27 (3H, m), 7.43—7.51 (3H, m), 7.74 (1H, s), 7.83 (2H, dd, J = 1.8, 8.2 Hz), 8.34 (1H, dd, J = 1.8, 7.7 Hz). ^{13}C-NMR ($CDCl_3$): 55.3, 56.2, 77.3, 110.6, 120.9, 121.4, 127.5, 127.7, 128.6, 128.9, 129.0, 129.1, 130.3, 136.6, 147.8, 156.1. HR-MS *m/z*: Calcd for $C_{18}H_{18}N_2O_2$, 294.1370. Found, 294.1359 (M^+).

Nortopsentin D (4)[3] A solution of *tert*-BuLi in *n*-pentane (1.57 M; 0.127 ml, 0.2 mmol) was added dropwise to a solution of **10b** (74 mg, 0.1 mmol) in THF (150 ml) under N_2 at −78 °C. The mixture was stirred for 30 min at −78 °C, then water (10 ml) was added and the whole was extracted with ether. The organic layer was dried over anhydrous sodium sulfate and evaporated to give an oily residue. The residue was dissolved in ethanol (6 ml) and hydrochloric acid (20%; 3 ml), and the mixture was refluxed for 1 h, then cooled to room temperature and neutralized by the addition of saturated sodium bicarbonate. The mixture was extracted with AcOEt, and the organic layer was dried and evaporated to give an oily residue. This was subjected to PTLC (AcOEt/MeOH = 10/1) to give **4** (21 mg, 70%), which was recrystallized from acetone–AcOEt. mp 195—227 °C (dec.) (colorless plates). IR (KBr): 3361, 3194, 1652, 1451, 1332, 1253, 1097, 739 cm^{-1}. ^{1}H-NMR (acetone-d_6): 7.08—7.19 (4H, m), 7.44—7.51 (2H, m), 7.56 (1H, s), 7.94 (1H, d, J = 7.6 Hz), 8.15 (1H, br), 8.34—8.39 (2H, m), 10.55 (1H, br), 10.92 (1H, br). ^{13}C-NMR (acetone-d_6): 105.4, 110.1, 113.1, 113.3, 114.8, 121.1, 121.8, 121.9, 123.2, 123.3, 123.8, 124.7, 124.8 (×2), 126.4, 132.3, 138.0, 138.1, 143.6. HR-MS *m/z*: Calcd for $C_{19}H_{14}N_4$, 298.1220. Found, 298.1211

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(M^+).

6-Bromo-1-(*tert*-butyldimethylsilyl)indole (13b) A solution of *n*-BuLi in *n*-hexane (1.6 M; 6.25 ml, 10 mmol) was added dropwise to a solution of **13a**[12] (1.96 g, 10 mmol) in THF (150 ml) under an N_2 atmosphere at −78 °C. The mixture was stirred for 15 min at −78 °C, then *tert*-butyldimethylsilyl chloride (1.51 g, 10 mmol) was added at −78 °C. Stirring was continued for 4 h at ambient temperature. Water (10 ml) was added, and the mixture was extracted with ether. The organic layer was dried over anhydrous sodium sulfate and evaporated to give a solid residue, which was subjected to column chromatography with *n*-hexane to give **13b** (2.852 g, 92%). Recrystallized from *n*-hexane. mp 90—91 °C (colorless crystals). IR ($CHCl_3$): 3031, 1450, 1273, 1143, 805 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.60 (6H, s), 0.92 (9H, s), 6.58 (1H, dd, J=0.9, 3.2 Hz), 7.14 (1H, d, J=3.2 Hz), 7.21 (1H, dd, J=1.7, 8.4 Hz), 7.47 (1H, d, J=8.4 Hz), 7.63 (1H, dd, J=0.9, 1.7 Hz). ^{13}C-NMR ($CDCl_3$): −4.0, 19.4, 26.2, 104.8, 115.0, 116.6, 121.7, 123.0, 130.2, 131.6, 141.9. LR-MS *m/z*: (relative intensity): 172 (40), 173 (27), 252 (89), 253 (70), 254 (100), 255 (70), 256 (12), 309 (78), 310 (15), 311 (80), 312 (14). *Anal.* Calcd for $C_{14}H_{20}BrNSi$: C, 54.19; H, 6.50; N, 4.51. Found: C, 53.98; H, 6.54; N, 4.43.

3,6-Dibromo-1-(*tert*-butyldimethylsilyl)indole (14) *N*-Bromosuccinimide (890 mg, 5 mmol) was added to a solution of **13b** (1.55 g, 5 mmol) in THF (200 ml) under an N_2 atmosphere at −78 °C, and the mixture was stirred for 4 h at −78 °C. The organic solvent was removed by evaporation to give a solid residue, which was subjected to column chromatography with *n*-hexane to give **14** (1.910 g, 98%). Recrystallized from *n*-hexane. mp 92—93 °C (colorless crystals). IR ($CHCl_3$): 2918, 1133, 1101, 1027, 806 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.59 (6H, s), 0.93 (9H, s), 7.13 (1H, s), 7.29 (1H, dd, J=1.6, 8.5 Hz), 7.42 (1H, d, J=8.5 Hz), 7.60 (1H, d, J=1.6 Hz). ^{13}C-NMR ($CDCl_3$): −4.0, 19.3, 26.1, 93.7, 116.2, 116.8, 120.4, 123.9, 128.9, 130.3, 141.0. LR-MS *m/z*: (relative intensity): 73 (70), 144 (38), 331 (38), 332 (50), 333 (75), 334 (34), 335 (38), 387 (50), 388 (10), 389 (100), 390 (11), 391 (52). *Anal.* Calcd for $C_{14}H_{19}Br_2NSi$: C, 43.20; H, 4.92; N, 3.60. Found: C, 43.12; H, 4.94; N, 3.48.

Representative Procedure for Arylation at the 6-Position of 14: Synthesis of 3-Bromo-1-(*tert*-butyldimethylsilyl)-6-phenylindole (15a) from 14 and Phenylboronic Acid A mixture of phenylboronic acid (61 mg, 0.5 mmol), **14** (195 mg, 0.5 mmol), benzene (10 ml), methanol (2 ml), 2 M sodium carbonate (0.5 ml) and tetrakis(triphenylphosphine)palladium (58 mg, 0.05 mmol) was refluxed for 8 h under an N_2 atmosphere. The reaction mixture was cooled to room temperature and anhydrous sodium sulfate was added. The mixture was filtered and the filtrate was evaporated under reduced pressure to give an oily residue, which was subjected to PTLC with *n*-hexane to give **15a** (118 mg, 61%). Recrystallized from EtOH–H_2O. mp 121—123 °C (colorless crystals). IR ($CHCl_3$): 2943, 2920, 1128, 939, 921 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.62 (6H, s), 0.96 (9H, s), 7.19 (1H, s), 7.35 (1H, td, J=1.6, 7.5 Hz), 7.42—7.48 (3H, m), 7.58—7.63 (3H, m), 7.68 (1H, d, J=0.9 Hz). ^{13}C-NMR ($CDCl_3$): −3.9, 19.4, 26.3, 93.6, 112.7, 119.3, 120.5, 126.8, 127.4, 128.8, 129.3, 130.3, 136.1, 140.8, 142.2. LR-MS *m/z*: (relative intensity): 73 (65), 248 (100), 249 (28), 329 (46), 331 (47), 385 (73), 386 (21), 387 (75), 388 (20). *Anal.* Calcd for $C_{20}H_{24}BrNSi$: C, 62.17; H, 6.26; N, 3.63. Found: C, 62.28; H, 6.35; N, 3.56.

3-Bromo-1-(*tert*-butyldimethylsilyl)-6-(2-thienyl)indole (**15b**): This compound was obtained from **14** and 2-thienylboronic acid in a similar manner to that used for the above synthesis of **15a**. Yield, 78%. Colorless crystals, mp 102—104 °C. IR ($CHCl_3$): 2917, 1431, 1135, 1019, 808 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.63 (6H, s), 0.96 (9H, s), 7.09 (1H, dd, J=3.7, 5.1 Hz), 7.17 (1H, s), 7.25 (1H, dd, J=1.2, 5.1 Hz), 7.28 (1H, dd, J=1.2, 3.6 Hz), 7.47 (1H, dd, J=1.4, 8.3 Hz), 7.54 (1H, dd, J=0.6, 8.3 Hz), 7.72 (1H, dd, J=0.6, 1.4 Hz). ^{13}C-NMR ($CDCl_3$): −3.9, 19.4, 26.2, 93.7, 111.6, 119.4, 119.5, 122.5, 124.1, 128.0, 129.2, 129.5, 130.5, 140.7, 145.7. *Anal.* Calcd for $C_{18}H_{22}BrNSSi$: C, 55.09; H, 5.65; N, 3.57. Found: C, 54.85; H, 5.62; N, 3.69.

3-Bromo-1-(*tert*-butyldimethylsilyl)-6-(4-fluorophenyl)indole (**15c**): This compound was obtained from **14** and 4-fluorophenylboronic acid[24] in a similar manner to that used for the above synthesis of **15a**. Yield, 74%. Colorless crystals, mp 133—134 °C. IR ($CHCl_3$): 2907, 1508, 1463, 1138, 840 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.62 (6H, s), 0.96 (9H, s), 7.11—7.16 (2H, m), 7.20 (1H, s), 7.38 (1H, dd, J=1.4, 8.4 Hz), 7.51—7.61 (4H, m). ^{13}C-NMR ($CDCl_3$): −3.9, 19.4, 26.3, 93.6, 112.6, 115.5, 115.8, 119.4, 120.4, 128.8, 128.9, 129.3, 130.4, 135.1, 140.9. LR-MS *m/z*: (relative intensity): 73 (19), 266 (43), 346 (22), 347 (36), 348 (30), 349 (37), 403 (96), 404 (26), 405 (100), 406 (27). HR-MS *m/z*: Calcd for $C_{20}H_{23}BrFNSi$, 403.0770. Found, 403.0787 (M^+).

3-Bromo-1-(*tert*-butyldimethylsilyl)-6-(2-methoxyphenyl)indole (**15d**): This compound was obtained from **14** and 2-methoxyphenylboronic acid in a similar manner to that used for the above synthesis of **15a**. After purification by PTLC (AcOEt/*n*-hexane = 1/10), the product was recrystallized from EtOH–H_2O. Yield, 70%. Colorless crystals, mp 96—97 °C. IR ($CHCl_3$): 2907, 1480, 1241, 1139, 1021 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.58 (6H, s), 0.96 (9H, s), 3.78 (3H, s), 6.83—7.07 (2H, m), 7.18 (1H, s), 7.28—7.40 (3H, m), 7.59 (1H, dd, J=0.7, 8.3 Hz), 7.72 (1H, dd, J=0.7, 1.3 Hz). ^{13}C-NMR ($CDCl_3$): −4.0, 19.3, 26.3, 55.4, 93.6, 111.3, 115.4, 118.5, 120.9, 122.6, 128.2, 128.9, 130.0, 131.2, 131.4, 132.7, 140.1, 156.5. LR-MS *m/z*: (relative intensity): 73 (15), 359 (22), 360 (15), 361 (23), 415 (95), 416 (26), 417 (100), 418 (27). *Anal.* Calcd for $C_{21}H_{26}BrNOSi$: C, 60.57; H, 6.29; N, 3.36. Found: C, 60.54; H, 6.36; N, 3.33.

3-Bromo-1-(*tert*-butyldimethylsilyl)-6-[3-[1-(*tert*-butyldimethylsilyl)-indolyl]]indole (**15e**): This compound was obtained from **14** and **30** (from 0.5 mmol of **34**) in a similar manner to that used for the above synthesis of **15a**. After purification by PTLC (*n*-hexane), the product was recrystallized from EtOH. Yield, 140 mg (52%). Colorless crystals, mp 172—174 °C. IR ($CHCl_3$): 2930, 2909, 1247, 1104, 819 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.63 (6H, s), 0.65 (6H, s), 0.98 (9H, s), 0.99 (9H, s), 7.17 (1H, s), 7.19—7.24 (2H, m), 7.31 (1H, s), 7.46 (1H, dd, J=1.3, 8.2 Hz), 7.56—7.62 (2H, m), 7.78 (1H, d, J=1.3 Hz), 7.90 (1H, dd, J=2.4, 7.6 Hz). ^{13}C-NMR ($CDCl_3$): −3.9, −3.8, 19.4, 19.5, 26.3, 26.3, 93.7, 113.0, 114.3, 119.2, 119.4, 120.2, 121.0, 121.3, 121.7, 128.4, 128.7, 129.4, 129.6, 130.1, 140.9, 141.9. LR-MS *m/z*: (relative intensity): 73 (100), 85 (83), 101 (50), 147 (35), 538 (7), 540 (9). *Anal.* Calcd for $C_{28}H_{39}BrN_2Si_2$: C, 62.31; H, 7.28; N, 5.19. Found: C, 62.13; H, 7.32; N, 4.97.

Representative Procedure for Synthesis of 3-Substituted Indoles (17, 18): Synthesis of 6-Bromo-1-(*tert*-butyldimethylsilyl)-3-methylindole (17a) from 14 and Methyl Iodide A solution of 1.57 M *tert*-BuLi in *n*-pentane (0.38 ml, 0.6 mmol) was added dropwise under an N_2 atmosphere at −78 °C to a solution of **14** (195 mg, 0.5 mmol) in THF (3 ml). The mixture was stirred for 15 min at −78 °C, then methyl iodide (142 mg, 1 mmol) was added at −78 °C, and the mixture was stirred for 2 h at ambient temperature. Water (5 ml) was added, and the product was extracted with ether. The organic layer was dried and evaporated to give a solid residue, which was subjected to PTLC with *n*-hexane to give **17a** (131 mg, 81%). Recrystallized from EtOH–H_2O. mp 63—64 °C (colorless crystals). IR ($CHCl_3$): 2911, 1459, 1252, 1140, 821 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.57 (6H, s), 0.92 (9H, s), 2.28 (3H, d, J=1.1 Hz), 6.89 (1H, d, J=1.1 Hz), 7.21 (1H, dd, J=1.7, 8.5 Hz), 7.39 (1H, d, J=8.5 Hz), 7.57 (1H, d, J=1.7 Hz). ^{13}C-NMR ($CDCl_3$): −4.0, 9.6, 19.4, 26.2, 113.6, 115.0, 116.5, 119.9, 122.4, 128.9, 130.6, 142.2. LR-MS *m/z*: (relative intensity): 266 (80), 267 (64), 268 (100), 269 (65), 323 (40), 325 (42). *Anal.* Calcd for $C_{15}H_{22}BrNSi$: C, 55.55; H, 6.84; N, 4.32. Found: C, 55.45; H, 6.51; N, 4.25.

6-Bromo-1-(*tert*-butyldimethylsilyl)-3-ethylindole (**17b**): This compound was obtained from **14** and ethyl iodide in a similar manner to that used for the above synthesis of **17a**. The crude product was purified by PTLC (*n*-hexane). Yield, 71%. Colorless viscous oil. IR ($CHCl_3$): 2923, 2906, 1453, 1140, 810 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.58 (6H, s), 0.92 (9H, s), 1.30 (3H, t, J=7.5 Hz), 2.73 (2H, qd, J=7.5, 1.0 Hz), 6.89 (1H, d, J=1.0 Hz), 7.20 (1H, dd, J=1.7, 8.4 Hz), 7.42 (1H, dd, J=0.3, 8.4 Hz), 7.58 (1H, dd, J=0.3, 1.7 Hz). ^{13}C-NMR ($CDCl_3$): −3.9, 14.3, 18.2, 19.4, 26.2, 115.0, 116.6, 119.9, 120.6, 122.3, 127.7, 129.8, 142.4. LR-MS *m/z*: (relative intensity): 186 (34), 280 (96), 281 (47), 282 (100), 283 (48), 337 (93), 338 (22), 339 (95), 340 (21). HR-MS *m/z*: Calcd for $C_{16}H_{24}BrNSi$, 337.0860. Found, 337.0840 (M^+).

6-Bromo-1-(*tert*-butyldimethylsilyl)-3-[1-hydroxy-1-(3,4-methylenedioxyphenyl)methyl]indole (**17c**): This compound was obtained from **14** and piperonal in a similar manner to that used for the above synthesis of **17a**. After purification by PTLC (AcOEt/*n*-hexane = 1/10), the product was recrystallized from *n*-hexane. Yield, 84%. Colorless crystals, mp 92—97 °C. IR ($CHCl_3$): 3582, 2908, 1428, 1142, 1039 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.58 (6H, s), 0.92 (9H, s), 2.21 (1H, br), 5.92 (2H, s), 5.99 (1H, d, J=0.8 Hz), 6.77 (1H, d, J=7.9 Hz), 6.89 (1H, d, J=1.7 Hz), 6.92 (1H, dd, J=1.7, 7.9 Hz), 7.06 (1H, d, J=0.8 Hz), 7.13 (1H, dd, J=1.7, 8.5 Hz), 7.29 (1H, d, J=8.5 Hz), 7.59 (1H, d, J=1.7 Hz). ^{13}C-NMR ($CDCl_3$): −4.0, 19.4, 26.2, 70.4, 101.0, 107.2, 108.0, 115.4, 116.8, 120.0, 120.8, 121.3, 123.0, 127.8, 129.4, 137.4, 142.7, 147.0, 147.7. *Anal.* Calcd for $C_{22}H_{26}BrNO_3Si$: C, 57.39; H, 5.69; N, 3.04. Found: C, 57.33; H, 5.71; N, 3.10.

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3-Acetyl-6-bromo-1-(*tert*-butyldimethylsilyl)indole (**17d**): This compound was obtained from **14** and *N*,*N*-dimethylacetamide in a similar manner to that used for the above synthesis of **17a**. The crude product was purified by PTLC (AcOEt/*n*-hexane = 1/10). Yield, 53%. Colorless viscous oil. IR ($CHCl_3$): 2910, 1662, 1429, 1282, 1143 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.65 (6H, s), 0.94 (9H, s), 2.65 (3H, s), 7.34 (1H, s), 7.65 (1H, d, J = 8.2 Hz), 7.74 (1H, dd, J = 1.4, 8.2 Hz), 8.22 (1H, d, J = 1.4 Hz). ^{13}C-NMR ($CDCl_3$): −3.9, 19.7, 26.2, 26.7, 105.1, 114.7, 118.9, 120.3, 120.9, 131.9, 135.0, 140.4, 198.2. LR-MS *m/z*: (relative intensity): 202 (45), 216 (85), 217 (98), 218 (32), 273 (100), 274 (36), 351 (9), 353 (10). HR-MS *m/z*: Calcd for $C_{16}H_{22}BrNOSi$, 351.0660. Found, 351.0615 (M^+).

3-(6-Bromo)indolylcarbaldehyde (**18**)[15,18]: This compound was obtained from **14** and *N*,*N*-dimethylformamide in a similar manner to that used for the above synthesis of **17a**. The crude product was dissolved in THF (10 ml), and 1 M TBAF in THF (3 ml, 3 mmol) was added to the solution. The mixture was stirred for 1 h at room temperature. Water (10 ml) was added, the organic solvent was evaporated, and the remaining solution was extracted with AcOEt. The organic layer was dried and evaporated to give a solid residue, which was subjected to PTLC (AcOEt/*n*-hexane = 1/1) to give **18** (72 mg, 64%). Recrystallized from AcOEt–*n*-hexane. mp 198—200 °C (colorless prisms). IR (KBr): 3148, 2896, 1632, 1423, 803 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 7.43 (1H, dd, J = 1.7, 8.6 Hz), 7.62 (1H, d, J = 1.7 Hz), 7.84 (1H, d, J = 3.1 Hz), 8.20 (1H, d, J = 8.6 Hz), 8.78 (1H, br), 10.05 (1H, s). ^{13}C-NMR ($CDCl_3$): 114.5, 117.9, 120.0, 123.3, 126.1, 126.4, 135.4, 136.8, 184.9. LR-MS *m/z*: (relative intensity): 223 (100), 224 (10), 225 (98), 226 (11). HR-MS *m/z*: Calcd for C_9H_6BrNO, 222.9630. Found, 222.9613 (M^+). *Anal.* Calcd for C_9H_6BrNO: C, 48.25; H, 2.70; N, 6.25. Found: C, 48.43; H, 2.70; N, 6.10.

Preparation of 3-[6-Bromo-1-(*tert*-butyldimethylsilyl)indolyl]boronic Acid (19) A solution of 1.57 M *tert*-BuLi in *n*-pentane (0.38 ml, 0.6 mmol) was added dropwise to a solution of **14** (195 mg, 0.5 mmol) in THF (5 ml) under an N_2 atmosphere at −78 °C. The mixture was stirred for 15 min at −78 °C, then a solution of trimethoxyborane (208 mg, 2 mmol) in THF (5 ml) was added dropwise at −78 °C. Stirring was continued for 30 min at −78 °C, methanol (0.25 ml) and water (0.25 ml) were added, and the whole was stirred at room temperature for 3 h. Water (10 ml) was added, and the mixture was extracted with ether. The organic layer was dried over anhydrous sodium sulfate and evaporated to give a solid residue, which was used for the next reaction without further purification.

Representative Procedure for Arylation at the 3-Position of 14: Synthesis of 6-Bromo-1-(*tert*-butyldimethylsilyl)-3-phenylindole (20a) from 19 and Iodobenzene A mixture of **19** (from 0.5 mmol of **14**), iodobenzene (306 mg, 1.5 mmol), benzene (20 ml), methanol (4 ml), 2 M sodium carbonate (0.5 ml) and tetrakis(triphenylphosphine)palladium (58 mg, 0.05 mmol) was refluxed for 8 h under an N_2 atmosphere. The reaction mixture was cooled to room temperature and anhydrous sodium sulfate was added. The mixture was filtered and the filtrate was evaporated under reduced pressure to give an oily residue, which was subjected to PTLC with *n*-hexane to give **20a** (164 mg, 85%). Recrystallized from EtOH–H_2O. mp 92—94 °C (colorless crystals). IR ($CHCl_3$): 2915, 1463, 1144, 905, 820 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.64 (6H, s), 0.97 (9H, s), 7.25—7.33 (3H, m), 7.42—7.45 (2H, m), 7.59—7.63 (2H, m), 7.66 (1H, d, J = 1.7 Hz), 7.95 (1H, d, J = 8.6 Hz). ^{13}C-NMR ($CDCl_3$): −3.9, 19.4, 26.2, 115.4, 117.0, 120.3, 120.8, 123.5, 126.3, 127.6, 128.1, 128.8, 129.1, 135.0, 142.7. LR-MS *m/z*: (relative intensity): 73 (53), 249 (52), 328 (57), 329 (59), 330 (69), 331 (60), 385 (94), 386 (27), 387 (100), 388 (26). *Anal.* Calcd for $C_{20}H_{24}BrNSi$: C, 62.17; H, 6.26; N, 3.63. Found: C, 62.03; H, 6.28; N, 3.57.

6-Bromo-1-(*tert*-butyldimethylsilyl)-3-(4-methylphenyl)indole (**20b**): This compound was obtained from **19** and 4-iodotoluene in a similar manner to that used for the above synthesis of **20a**. The crude product was purified by PTLC (*n*-hexane). Yield, 81%. Colorless viscous oil. IR ($CHCl_3$): 2909, 1557, 1144, 1003, 820 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.63 (6H, s), 0.96 (9H, s), 2.40 (3H, s), 7.23—7.28 (4H, m), 7.48—7.52 (2H, m), 7.65 (1H, d, J = 1.7 Hz), 7.73 (1H, d, J = 8.6 Hz). ^{13}C-NMR ($CDCl_3$): −3.9, 19.4, 21.2, 26.2, 115.3, 116.9, 120.2, 120.8, 123.3, 127.5, 128.2, 128.8, 129.5, 132.0, 136.0, 142.7. LR-MS *m/z*: (relative intensity): 73 (18), 264 (17), 332 (28), 333 (29), 334 (34), 335 (29), 399 (96), 400 (27), 401 (100), 402 (27). HR-MS *m/z*: Calcd for $C_{21}H_{26}BrNSi$, 399.1020. Found, 399.0983 (M^+).

6-Bromo-1-(*tert*-butyldimethylsilyl)-3-(4-fluorophenyl)indole (**20c**): This compound was obtained from **19** and 4-fluoroiodobenzene in a similar manner to that used for the above synthesis of **20a**. Yield, 73%. Colorless crystals, mp 87—89 °C. IR ($CHCl_3$): 2906, 1499, 1252, 1143, 839 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.63 (6H, s), 0.96 (9H, s), 7.10—7.15 (2H, m), 7.22 (1H, s), 7.27 (1H, dd, J = 1.6, 8.6 Hz), 7.52—7.57 (2H, m), 7.66 (1H, d, J = 1.6 Hz), 7.67 (1H, d, J = 8.6 Hz). ^{13}C-NMR ($CDCl_3$): −3.9, 19.4, 26.2, 115.5, 115.8, 117.0, 119.3, 120.5, 123.5, 128.0, 128.9, 129.0, 129.1, 131.0, 142.6. LR-MS *m/z*: (relative intensity): 73 (20), 267 (23), 268 (20), 346 (38), 347 (37), 348 (47), 349 (37), 403 (96), 404 (26), 405 (100), 406 (26). HR-MS *m/z*: Calcd for $C_{20}H_{23}BrFNSi$, 403.0770. Found, 403.0732 (M^+).

2-[3-(6-Bromo)indolyl]-1-[[2-(trimethylsilyl)ethoxy]methyl]-1*H*-imidazole (**21**): This compound was synthesized from **19** (obtained from 0.5 mmol of **14**) and **22a**[16] (324 mg, 1 mmol) in a similar manner to that used for the above synthesis of **20a**. The crude product was purified by PTLC (AcOEt/*n*-hexane = 1/3). Yield, 105 mg (54%). Colorless viscous oil. IR ($CHCl_3$): 3449, 2959, 1435, 1171, 1118 cm^{-1}. ^{1}H-NMR ($CDCl_3$): −0.1 (9H, s), 0.94 (2H, t, J = 8.3 Hz), 3.60 (2H, t, J = 8.3 Hz), 5.30 (2H, s), 7.10 (1H, d, J = 1.3 Hz), 7.22 (1H, d, J = 1.3 Hz), 7.31 (1H, dd, J = 1.7, 8.5 Hz), 7.54 (1H, d, J = 1.7 Hz), 7.72 (1H, d, J = 2.7 Hz), 8.11 (1H, d, J = 8.5 Hz), 8.64 (1H, br). ^{13}C-NMR ($CDCl_3$): −1.4, 17.8, 66.2, 75.2, 110.7, 113.9, 116.6, 120.5, 122.8, 124.2, 124.9, 125.4, 128.4, 136.7, 143.8. LR-MS *m/z*: (relative intensity): 73 (100), 332 (37), 333 (20), 334 (40), 345 (21), 391 (30), 393 (31). HR-MS *m/z*: Calcd for $C_{17}H_{22}BrN_3OSi$, 391.0720. Found, 391.0730 (M^+).

5-[3-[6-Bromo-1-(*tert*-butyldimethylsilyl)indolyl]]-1-[[2-(trimethylsilyl)ethoxy]methyl]-2-phenylthio-1*H*-imidazole (**20d**): This compound was obtained from **19** (obtained from 0.5 mmol of **14**) and **22b**[4e] (432 mg, 1 mmol) in a similar manner to that used for the above synthesis of **20a**. The crude product was purified by PTLC (AcOEt/*n*-hexane = 1/10). Yield, 205 mg (67%). Colorless viscous oil. IR ($CHCl_3$): 2947, 1466, 1243, 1042, 837 cm^{-1}. ^{1}H-NMR ($CDCl_3$): −0.01 (9H, s), 0.63 (6H, s), 0.84 (2H, t, J = 8.5 Hz), 0.95 (9H, s), 3.50 (2H, t, J = 8.5 Hz), 5.34 (2H, s), 7.15—7.32 (6H, m), 7.44 (1H, s), 7.60 (1H, d, J = 8.4 Hz), 7.66 (1H, d, J = 1.9 Hz), 7.67 (1H, s). ^{13}C-NMR ($CDCl_3$): −4.0, −1.5, 18.1, 21.1, 26.2, 66.0, 73.2, 105.5, 114.2, 116.9, 120.6, 123.9, 126.7, 126.8, 128.1, 128.3, 128.5, 129.1, 129.2, 131.8, 138.4, 142.0. LR-MS *m/z*: (relative intensity): 73 (100), 477 (21), 535 (38), 613 (19), 615 (21). HR-MS *m/z*: Calcd for $C_{29}H_{40}BrN_3OSSi_2$, 613.1620. Found, 613.1620 (M^+).

5-Iodo-1-[[2-(trimethylsilyl)ethoxy]methyl]-1*H*-imidazole (22c) A solution of *n*-BuLi in *n*-hexane (1.6 M; 3.75 ml, 6 mmol) was added dropwise to a solution of 1-[[2-(trimethylsilyl)ethoxy]methyl]-1*H*-imidazole[25] (990 mg, 5 mmol) in THF (50 ml) under an N_2 atmosphere at −78 °C. The mixture was stirred for 30 min at −78 °C, then triethylsilyl chloride (904 mg, 6 mmol) was added at −78 °C, and the whole was stirred for 1 h at room temperature. The mixture was cooled again to −78 °C, and a solution of *sec*-BuLi in cyclohexane (1.1 M; 5.91 ml, 6.5 mmol) was added dropwise to it. The whole was stirred for 30 min at −78 °C, then iodine (1.650 g, 6.5 mmol) was added, and the reaction was continued under stirring for 2 h at ambient temperature. A solution of 1 M TBAF in THF (20 mmol, 20 ml) was added dropwise. Stirring was continued for 1 h at room temperature, and then sodium thiosulfate (5%; 30 ml) was added to the mixture. The organic solvent was evaporated, the residue was extracted with AcOEt, and the organic layer was dried over anhydrous sodium sulfate then evaporated to give an oily residue. The crude product was purified by column chromatography (AcOEt/*n*-hexane = 1/3). Yield, 1.183 g (73%). Colorless viscous oil. IR ($CHCl_3$): 2944, 1247, 1105, 857, 835 cm^{-1}. ^{1}H-NMR ($CDCl_3$): −0.01 (9H, s), 0.92 (2H, t, J = 8.4 Hz), 3.52 (2H, t, J = 8.4 Hz), 5.27 (2H, s), 7.15 (1H, d, J = 0.9 Hz), 7.75 (1H, s). ^{13}C-NMR ($CDCl_3$): −1.4, 17.7, 66.4, 69.5, 76.2, 137.5, 140.3. HR-MS *m/z*: Calcd for $C_9H_{17}IN_2OSi$, 324.0160. Found, 324.0146 (M^+).

5-[3-[6-Bromo-1-(*tert*-butyldimethylsilyl)indolyl]]-1-[[2-(trimethylsilyl)ethoxy]methyl]-1*H*-imidazole (**20e**): This compound was obtained from **19** (from 0.5 mmol of **14**) and **22c** (324 mg, 1 mmol) in a similar manner to that used for the above synthesis of **20a**. The crude product was purified by PTLC (AcOEt/*n*-hexane = 1/1). Yield, 147 mg (58%). Colorless viscous oil. IR ($CHCl_3$): 2949, 1256, 1159, 1083 cm^{-1}. ^{1}H-NMR ($CDCl_3$): −0.02 (9H, s), 0.64 (6H, s), 0.92 (2H, t, J = 8.3 Hz), 0.96 (9H, s), 3.53 (2H, t, J = 8.3 Hz), 5.23 (2H, s), 7.27 (1H, s), 7.29 (1H, dd, J = 1.7, 8.6 Hz), 7.55 (1H, s), 7.56 (1H, d, J = 8.6 Hz), 7.67 (1H, d, J = 1.7 Hz), 7.71 (1H, s). ^{13}C-NMR ($CDCl_3$): −4.0, −1.5, 17.8, 19.4, 26.2, 65.9, 73.9, 107.2, 114.1, 115.8, 116.8, 120.7, 123.8, 128.1, 128.7, 131.2, 138.1, 142.1. LR-MS *m/z*: (relative intensity): 73 (100), 333 (11), 335 (12), 391 (14) 393 (15), 505 (23), 507 (26). HR-MS *m/z*: Calcd for

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$C_{23}H_{36}BrN_3OSi_2$, 505.1580. Found, 505.1592 (M^+).

2,5-Diiodo-1-[[2-(trimethylsilyl)ethoxy]methyl]-1*H*-imidazole (23) A solution of 1.6 M *n*-BuLi in *n*-hexane (0.69 ml, 1.1 mmol) was added dropwise to a solution of 2,2,6,6-tetramethylpiperidine (170 mg, 1.2 mmol) in THF (15 ml) under an N_2 atmosphere at −78 °C. The mixture was stirred for 30 min at −78 °C, then a solution of **22a** (324 mg, 1 mmol) in THF (5 ml) was added dropwise at −78 °C. Stirring was continued for 30 min at −78 °C, iodine (508 mg, 2 mmol) was added, and the whole was stirred at room temperature for 3 h. Sodium thiosulfate (5%; 15 ml) was added, and the mixture was extracted with AcOEt. The organic layer was dried over anhydrous sodium sulfate and evaporated to give an oily residue. The crude product was purified by column chromatography (AcOEt/*n*-hexane = 1/1). Yield, 405 mg (90%). Colorless viscous oil. IR ($CHCl_3$): 2945, 1727, 1247, 1219, 855 cm^{-1}. ^{1}H-NMR ($CDCl_3$): −0.01 (9H, s), 0.93 (2H, t, J = 8.2 Hz), 3.59 (2H, t, J = 8.2 Hz), 5.32 (2H, s), 7.18 (1H, s). ^{13}C-NMR ($CDCl_3$): −1.4, 17.8, 66.8, 71.5, 77.5, 90.4, 140.7. HR-MS *m/z*: Calcd for $C_9H_{16}I_2N_2OSi$, 449.9120. Found, 449.9117 (M^+).

5-[3-[6-Bromo-1-(*tert*-butyldimethylsilyl)indolyl]]-2-iodo-1-[[2-(trimethylsilyl)ethoxy]methyl]-1*H*-imidazole (24) NIS (135 mg, 0.6 mmol) was added to a solution of **20e** (152 mg, 0.3 mmol) and dibenzoyl peroxide (7 mg, 0.03 mmol) in THF (30 ml) under an N_2 atmosphere. The mixture was refluxed for 9 h, then cooled to room temperature. Sodium thiosulfate (5%; 10 ml) was added to it, and the whole was extracted with AcOEt. The organic layer was dried over anhydrous sodium sulfate and evaporated to give an oily residue. The crude product was purified by column chromatography (AcOEt/*n*-hexane = 1/3). Yield, 82 mg (43%). Colorless viscous oil. IR ($CHCl_3$): 2941, 1249, 1151, 1081, 836 cm^{-1}. ^{1}H-NMR ($CDCl_3$): −0.01 (9H, s), 0.64 (6H, s), 0.93 (2H, t, J = 8.3 Hz), 0.96 (9H, s), 3.59 (2H, t, J = 8.3 Hz), 5.20 (2H, s), 7.28 (1H, s), 7.28 (1H, dd, J = 1.7, 8.5 Hz), 7.50 (1H, d, J = 8.5 Hz), 7.54 (1H, s), 7.66 (1H, d, J = 1.7 Hz). ^{13}C-NMR ($CDCl_3$): −4.0, −1.4, 18.1, 19.3, 26.2, 66.4, 75.3, 90.7, 107.3, 115.9, 116.9, 120.5, 124.0, 128.6, 130.4, 131.2, 131.9, 141.9. LR-MS *m/z*: (relative intensity): 73 (100), 573 (23), 575 (25), 631 (54), 632 (19), 633 (61), 634 (20). HR-MS *m/z*: Calcd for $C_{23}H_{35}BrIN_3OSi_2$, 631.0550. Found, 631.0563 (M^+).

2,5-Bis[3-(6-bromo)indolyl]-1-[[2-(trimethylsilyl)ethoxy]methyl]-1*H*-imidazole (**25**): This compound was obtained from **19** (from 0.3 mmol of **14**) and **24** (190 mg, 0.3 mmol) in a similar manner to that used for the above synthesis of **20a**. The crude product was dissolved in THF (5 ml), and 1 M TBAF in THF (1 ml, 1 mmol) was added to the solution. The reaction mixture was stirred for 1 h at room temperature. Water (15 ml) was added to it, and the organic solvent was evaporated, then the residue was extracted with AcOEt. The organic layer was dried over anhydrous sodium sulfate and evaporated to give an oily residue. The crude product was purified by PTLC ($CHCl_3$/MeOH = 20/1, then AcOEt). Yield, 26 mg (15%). Colorless viscous oil. IR ($CHCl_3$): 3447, 2945, 1449, 1247, 1090, 835 cm^{-1}. ^{1}H-NMR ($CDCl_3$): −0.18 (9H, s), 0.76 (2H, t, J = 8.5 Hz), 3.22 (2H, t, J = 8.5 Hz), 5.21 (2H, s), 7.22—7.27 (2H, m), 7.34—7.37 (2H, m), 7.40 (1H, d, J = 1.7 Hz), 7.47 (1H, d, J = 1.6 Hz), 7.52 (1H, d, J = 2.6 Hz), 7.57 (1H, d, J = 8.6 Hz), 7.97 (1H, d, J = 8.6 Hz), 9.66 (1H, br), 10.00 (1H, br). ^{13}C-NMR ($CDCl_3$): −1.6, 17.9, 65.7, 72.5, 105.5, 106.5, 114.4 (×2), 116.1, 116.2, 120.8, 121.8, 123.7, 123.9, 125.0, 125.5, 125.8, 126.0, 126.8, 127.2, 136.8, 136.9, 144.5. LR-MS *m/z*: (relative intensity): 73 (100), 455 (22), 526 (25), 527 (27), 528 (52), 529 (25), 530 (27), 584 (24), 586 (50), 588 (27). HR-MS *m/z*: Calcd for $C_{25}H_{26}Br_2N_4OSi$, 584.0240. Found, 584.0214 (M^+).

Nortopsentin A (1)[2] A solution of hydrochloric acid (20%; 5 ml) was added to a solution of **25** (52 mg, 0.09 mmol) in ethanol (9 ml), and the mixture was refluxed for 2 h. It was then cooled to room temperature, neutralized by the addition of saturated sodium bicarbonate, and extracted with AcOEt. The organic layer was dried over anhydrous sodium sulfate and evaporated to give an oily residue. The crude product was purified by PTLC ($CHCl_3$/MeOH = 5/1). Yield, 32 mg (70%). Colorless viscous oil. IR (KBr): 3394, 1652, 1609, 1449, 1326, 892, 797 cm^{-1}. ^{1}H-NMR (acetone-d_6): 7.25 (1H, dd, J = 1.8, 8.5 Hz), 7.30 (1H, dd, J = 1.8, 8.6 Hz), 7.42 (1H, s), 7.63 (1H, d, J = 1.8 Hz), 7.65 (1H, d, J = 1.8 Hz), 7.77 (1H, d, J = 2.5 Hz), 7.93 (1H, d, J = 2.6 Hz), 8.04 (1H, d, J = 8.5 Hz), 8.53 (1H, d, J = 8.5 Hz), 10.55 (1H, br), 10.72 (1H, br). LR-MS *m/z*: (relative intensity): 128 (32), 155 (19), 454 (50), 455 (18), 456 (100), 457 (25), 458 (52). HR-MS *m/z*: Calcd for $C_{19}H_{12}Br_2N_4$, 453.9430. Found, 453.9439 (M^+).

5-[3-[1-(*tert*-Butyldimethylsilyl)indolyl]]-2-iodo-1-[[2-(trimethylsilyl)ethoxy]methyl]-1*H*-imidazole (**27**): This compound was obtained from **26**[4e] (299 mg, 0.7 mmol), NIS (315 mg, 1.4 mmol), dibenzoyl peroxide (17 mg, 0.07 mmol) and THF (70 ml) in a similar manner to that used for the above synthesis of **24**. The crude product was purified by PTLC (AcOEt/*n*-hexane = 1/3). Yield, 252 mg (65%). Colorless viscous oil. IR ($CHCl_3$): 2940, 2901, 1242, 1364, 1248, 1040 cm^{-1}. ^{1}H-NMR ($CDCl_3$): −0.02 (9H, s), 0.64 (6H, s), 0.92 (2H, t, J = 8.4 Hz), 0.96 (9H, s), 3.58 (2H, t, J = 8.4 Hz), 5.22 (2H, s), 7.17—7.23 (2H, m), 7.31 (1H, s), 7.53—7.57 (2H, m), 7.64 (1H, dd, J = 1.6, 7.0 Hz). ^{13}C-NMR ($CDCl_3$): −4.0, −1.4, 18.1, 19.4, 26.3, 66.3, 75.3, 90.2, 107.2, 114.1, 119.4, 120.7, 122.4, 129.8, 131.1, 131.1, 131.4, 141.1. HR-MS *m/z*: Calcd for $C_{23}H_{36}IN_3OSi_2$, 553.1440. Found, 553.1471 (M^+).

2-[3-(6-Bromo)indolyl]-5-[3-[1-(*tert*-butyldimethylsilyl)indolyl]]-1-[[2-(trimethylsilyl)-ethoxy]methyl]-1*H*-imidazole (**28**): This compound was obtained from **19** (from 0.2 mmol of **14**) and **27** (221 mg, 0.4 mmol) in a similar manner to that used for the above synthesis of **20a**. The crude product was purified by PTLC ($CHCl_3$/MeOH = 50/1). Yield, 77 mg (62%). Colorless viscous oil. IR ($CHCl_3$): 3441, 2943, 1449, 1254, 1074, 836 cm^{-1}. ^{1}H-NMR ($CDCl_3$): −0.01 (9H, s), 0.66 (6H, s), 0.90 (2H, t, J = 8.7 Hz), 0.98 (9H, s), 3.33 (2H, t, J = 8.7 Hz), 5.27 (2H, s), 7.17—7.25 (2H, m), 7.31 (1H, dd, J = 1.7, 8.5 Hz), 7.38 (1H, s), 7.45 (1H, s), 7.53 (1H, d, J = 1.5 Hz), 7.57 (1H, dd, J = 1.6, 7.2 Hz), 7.67 (1H, d, J = 2.6 Hz), 7.72 (1H, dd, J = 1.6, 6.1 Hz), 8.12 (1H, d, J = 8.5 Hz), 9.06 (br, 1H). ^{13}C-NMR ($CDCl_3$): −3.9, −1.5, 18.2, 19.5, 26.3, 65.4, 72.9, 107.4, 107.9, 114.0, 114.1, 116.4, 119.6, 120.6, 122.3, 122.6, 124.0, 125.0, 125.6, 127.1, 127.5, 130.4, 130.6, 136.8, 141.2, 144.3. LR-MS *m/z*: (relative intensity): 73 (100), 489 (24), 491 (26), 562 (19), 564 (20), 620 (44), 621 (20), 622 (48), 623 (21). HR-MS *m/z*: Calcd for $C_{31}H_{41}BrN_4OSi_2$, 620.2010. Found, 620.1998 (M^+).

Nortopsentin B (2)[2] This compound was obtained from **28** (62 mg, 0.1 mmol) in a similar manner to that used for the above synthesis of **1**. After purification by PTLC (AcOEt/MeOH = 10/1), the product was recrystallized from $CHCl_3$–AcOEt. Yield, 28 mg (74%). Colorless plates, mp 249—258 °C (dec.) (lit. mp[2]: 250—270 (dec.)). IR (KBr): 3372, 1451, 1326, 1250, 1098, 892, 738 cm^{-1}. ^{1}H-NMR (acetone-d_6): 7.10—7.20 (2H, m), 7.31 (1H, dd, J = 1.8, 8.6 Hz), 7.47 (1H, br d, J = 6.9 Hz), 7.49 (1H, s), 7.64 (1H, d, J = 1.8 Hz), 7.84 (1H, d, J = 1.5 Hz), 8.01 (1H, br d, J = 7.0 Hz), 8.04 (1H, d, J = 1.4 Hz), 8.48 (1H, d, J = 8.6 Hz), 10.43 (1H, br), 10.80 (1H, br). LR-MS *m/z*: (relative intensity): 44 (35), 128 (25), 155 (21), 297 (17), 376 (100), 377 (25), 378 (97), 379 (22). HR-MS *m/z*: Calcd for $C_{19}H_{13}BrN_4$, 376.0330. Found, 376.0323 (M^+).

2,4,5-Triiodo-1-[[2-(trimethylsilyl)ethoxy]methyl]-1*H*-imidazole (29) 2,4,5-Triiodo-1*H*-imidazole was prepared from 1*H*-imidazole according to Brunings' procedure.[19] [2-(Trimethylsilyl)ethoxy]methyl chloride (367 mg, 2.2 mmol) was added dropwise to a mixture of 2,4,5-triiodo-1H-imidazole (892 mg, 2 mmol), triethylamine (304 mg, 3 mmol) and 4-*N*,*N*-dimethylaminopyridine (244 mg, 2 mmol) in *N*,*N*-dimethylformamide (5 ml) under an N_2 atmosphere. The mixture was stirred at 100 °C for 2 h and then cooled to room temperature. Water (10 ml) was added, and the whole was extracted with AcOEt. The organic layer was dried over anhydrous sodium sulfate and evaporated to give an oily residue, which was subjected to column chromatography (AcOEt/*n*-hexane = 1/3) to give **29** (139 mg, 12%). Recrystallized from *n*-hexane. mp 110—111 °C (colorless crystals). IR ($CHCl_3$): 2941, 1247, 1179, 1102, 834 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.02 (9H, s), 0.93 (2H, t, J = 8.4 Hz), 3.58 (2H, t, J = 8.3 Hz), 5.35 (2H, s). ^{13}C-NMR ($CDCl_3$): −1.3, 17.8, 67.0, 79.2, 84.7, 90.7, 98.7. *Anal.* Calcd for $C_9H_{15}I_3N_2OSi$: C, 18.77; H, 2.62; N, 4.86. Found: C, 18.92; H, 2.63; N, 5.22.

2-[3-[1-(*tert*-Butyldimethylsilyl)indolyl]]-4,5-diiodo-1-[2-(trimethylsilyl)ethoxy]methyl-1*H*-imidazole (**31**): This compound was obtained from **29** (173 mg, 0.3 mmol) and **30** (from 0.5 mmol of **34**) in a similar manner to that used for the above synthesis of **6a**. After purification by PTLC (AcOEt/*n*-hexane = 1/10), the product was recrystallized from EtOH–H_2O. Yield, 91 mg (45%). Colorless crystals, mp 136—139 °C. IR ($CHCl_3$): 2947, 2918, 1471, 1246, 1021 cm^{-1}. ^{1}H-NMR ($CDCl_3$): −0.01 (9H, s), 0.63 (6H, s), 0.93 (2H, t, J = 8.4 Hz), 0.94 (9H, s), 3.63 (2H, t, J = 8.4 Hz), 5.35 (2H, s), 7.20—7.23 (2H, m), 7.52 (1H, t, J = 4.7 Hz), 7.77 (1H, s), 8.05 (1H, t, J = 4.7 Hz). ^{13}C-NMR ($CDCl_3$): −4.0, −1.4, 18.1, 19.4, 26.2, 66.4, 76.7, 82.1, 97.1, 108.1, 113.8, 120.9, 121.2, 122.6, 129.3, 132.6, 141.1, 149.2. *Anal.* Calcd for $C_{23}H_{35}I_2N_3OSi_2$: C, 40.65; H, 5.19; N, 6.18. Found: C, 40.55; H, 5.09; N, 5.81.

2-[3-[1-(*tert*-Butyldimethylsilyl)indolyl]]-4-iodo-1-[2-(trimethylsilyl)-ethoxy]methyl-1*H*-imidazole (32) A solution of ethylmagnesium bromide in THF (0.9 M; 0.56 ml, 0.5 mmol) was added dropwise to a solution of **31** (340 mg, 0.5 mmol) in THF (25 ml) and ether (14 ml) under an N_2 atmosphere at −78 °C. The mixture was stirred for 30 min at

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−78 °C, then water (15 ml) was added to it. The whole was extracted with AcOEt. The organic layer was dried over anhydrous sodium sulfate and evaporated to give an oily residue, which was purified by PTLC (AcOEt/*n*-hexane = 1/5). Yield, 205 mg (74%). Colorless viscous oil. IR ($CHCl_3$): 2951, 2945, 1370, 1240, 1021 cm^{-1}. ^{1}H-NMR ($CDCl_3$): −0.01 (9H, s), 0.63 (6H, s), 0.93 (2H, t, J = 8.3 Hz), 0.94 (9H, s), 3.54 (2H, t, J = 8.3 Hz), 5.35 (2H, s), 7.19—7.23 (3H, m), 7.52 (1H, t, J = 4.7 Hz), 7.69 (1H, s), 8.07 (1H, t, J = 4.7 Hz). ^{13}C-NMR ($CDCl_3$): −4.0, −1.4, 17.8, 19.4, 26.2, 66.3, 75.2, 82.1, 107.6, 113.8, 121.0 (×2), 122.5, 125.5, 129.5, 132.1, 141.2, 146.3. HR-MS *m/z*: Calcd for $C_{23}H_{36}IN_3OSi_2$, 553.1440. Found, 553.1443 (M^+).

4-[3-(6-Bromo)indolyl]-2-(3-indolyl)-1-[[2-(trimethylsilyl)ethoxy]-methyl]-1*H*-imidazole (**33**): This compound was synthesized from **19** (obtained from 0.2 mmol of **14**) and **32** (221 mg, 0.4 mmol) in a similar manner to that used for the above synthesis of **20a.** The crude product was dissolved in THF (5 ml), and 1 M TBAF in THF (1 ml, 1 mmol) was added to the solution. The reaction mixture was stirred for 1 h at room temperature. Water (15 ml) was added, the organic solvent was evaporated, and the residue was extracted with AcOEt. The organic layer was dried over anhydrous sodium sulfate and evaporated to give an oily residue, which was subjected to PTLC with AcOEt to give **33** (51 mg, 50%). Recrystallized from AcOEt–*n*-hexane. mp 204—207 °C (colorless crystals). IR (KBr): 3412, 2938, 1448, 1242, 1082 cm^{-1}. ^{1}H-NMR (acetone-d_6): −0.05 (9H, s), 0.95 (2H, t, J = 8.1 Hz), 3.75 (2H, t, J = 8.1 Hz), 5.47 (2H, s), 7.12—7.21 (3H, m), 7.44 (1H, dd, J = 2.0, 7.1 Hz), 7.61 (1H, dd, J = 1.5, 8.3 Hz), 7.63 (1H, s), 7.77 (1H, d, J = 1.4 Hz), 7.88 (1H, d, J = 1.6 Hz), 8.09 (1H, d, J = 8.7 Hz), 8.48 (1H, dd, J = 1.7, 6.4 Hz), 10.45 (1H, br), 10.61 (1H, br). ^{13}C-NMR (acetone-d_6): −0.8, 18.9, 67.0, 76.4, 107.9, 112.5, 112.6, 115.5, 115.6, 115.7, 116.5, 121.2, 123.2, 123.4, 123.5, 123.6, 123.9, 124.1, 125.9, 126.1, 137.1, 138.0, 145.3. LR-MS *m/z*: (relative intensity): 73 (100), 375 (30), 377 (31), 447 (21), 448 (35), 449 (31), 450 (35), 506 (42), 507 (15), 508 (46), 509 (16). HR-MS *m/z*: Calcd for $C_{25}H_{27}BrN_4OSi$, 506.1140. Found, 506.1115 (M^+).

Nortopsentin C (3)[2] This compound was obtained from **33** (51 mg, 0.1 mmol) in a similar manner to that used for the above synthesis of **1**. The crude product was purified by PTLC ($CHCl_3$/MeOH = 10/1). Yield, 28 mg (74%). Colorless viscous oil. IR (KBr): 3371, 1610, 1448, 1329, 1254, 736 cm^{-1}. ^{1}H-NMR (acetone-d_6): 7.11—7.18 (2H, m), 7.21 (1H, dd, J = 1.7, 8.5 Hz), 7.42 (1H, s), 7.44 (1H, br, d, J = 7.2 Hz), 7.61 (1H, d, J = 1.7 Hz), 7.78 (1H, d, J = 1.9 Hz), 7.94 (1H, d, J = 2.5 Hz), 8.01 (1H, d, J = 8.5 Hz), 8.49 (1H, br, d, J = 8.4 Hz), 10.51 (1H, br), 10.56 (1H, br). LR-MS *m/z*: (relative intensity): 128 (24), 155 (18), 297 (14), 376 (100), 377 (30), 378 (98), 379 (21). HR-MS *m/z*: Calcd for $C_{19}H_{13}BrN_4$, 376.0330. Found, 376.0314 (M^+).

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