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Total Synthesis of the Neuronal Cell-Protecting Carbazole Alkaloids Carbazomadurin A and (*S*)-(+)-Carbazomadurin B

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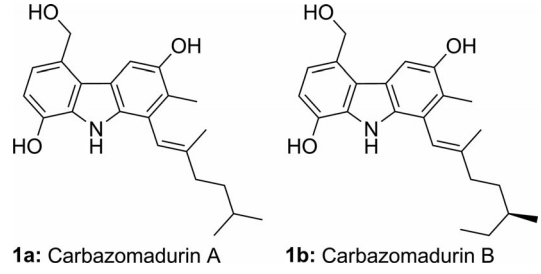
The total syntheses of the neuronal cell-protecting carbazole alkaloids carbazomadurin A and (*S*)-(+)-carbazomadurin B were achieved. The key step of the synthesis of the polysubstituted carbazole rings included an allene-mediated electrocyclic reaction of the 6π-electron system that involved the indole 2,3-bond. The cleavage of the alkoxy groups of the resulting 3-ethoxy-8-isopropoxycarbazole successfully gave the 3,8-dihydroxycarbazole, which was converted into the 3,8-bis(OSEM)-carbazole (SEM = 2-trimethylsilylethoxymethyl). A Suzuki–Miyaura cross-coupling reaction of the 3,8-bis(OSEM)-carbazole with the corresponding alkenyl pinacol borates afforded the 1-alkenylcarbazoles, which were treated with tetra-*n*-butylammonium fluoride (TBAF) followed by reduction with $NaBH_4$ to provide carbazomadurin A and (*S*)-(+)-carbazomadurin B, respectively.

Introduction

Carbazole alkaloids have attracted much interest among synthetic organic chemists because of their broad range of biological activities.[1,2] Since 1979, several groups have found new types of highly substituted carbazole alkaloids from different natural resources.[1,2] In 1997, the structurally unique carbazole alkaloids carbazomadurin A (**1a**) and B (**1b**, see Figure 1) were isolated by Seto and co-workers from the microorganism *Actinomadura madurae* 2808-SV1.[3] These alkaloids exhibit strong neuronal cell-protecting activities against cell death, which is induced by L-glutamate.[3] On the basis of their spectroscopic data, the structures of both alkaloids were determined to have the new 3,8-dioxygenated and highly functionalized carbazole framework. The absolute configuration of (+)-carbazomadurin B (**1b**), however, remained unknown.[3] In 2003, the first total synthesis of carbazomadurin A (**1a**) was reported by the Knölker group, which used a palladium-catalyzed sequence of the Buchwald–Hartwig amination, an oxidative cyclization, and a Stille coupling reaction.[4] A few years later, the same group reported the first enantioselective total synthesis of (+)-carbazomadurin B (**1b**), and the stereogenic center at the C-11 position was assigned as having the *S* configuration.[5]



1a: Carbazomadurin A **1b:** Carbazomadurin B

Figure 1. Carbazomadurins A (**1a**) and B (**1b**).

We are interested in the syntheses of bioactive nitrogen-containing fused heteroaromatic compounds, which includes natural products, through the employment of a thermal electrocyclic reaction that uses either a 6π- or an aza 6π-electron system and in principle involves an aromatic or heteroaromatic double bond.[6] Among these, we have reported the total syntheses of the hyellazoles, carazostatin, the carbazoquinocins,[7] murrayaquinone, furocarbazole, carbazomycin G,[8] the calothrixins,[9] mukonine,[10] and the carquinostatins[11] by using an allene-mediated thermal electrocyclic reaction that involves the indole 2,3-bond. Recently, we reported a new total synthesis of carbazomadurin A (**1a**) by using our methodology through the construction of a highly substituted carbazole framework.[12] Herein, we describe the detailed total synthesis of carbazomadurin A (**1a**) and a new asymmetric total synthesis of (*S*)-(+)-carbazomadurin B (**1b**). Our synthetic strategy for **1a** and **1b** is illustrated by the retrosynthetic analysis in Scheme 1, in which the 1,3,8-trioxygenated carbazole framework **2** is obtained from 2-allenylindole intermediate **4** that is generated from 2-propargylindole **5**. Furthermore, we plan to introduce an alkenyl side chain with the *E* con-

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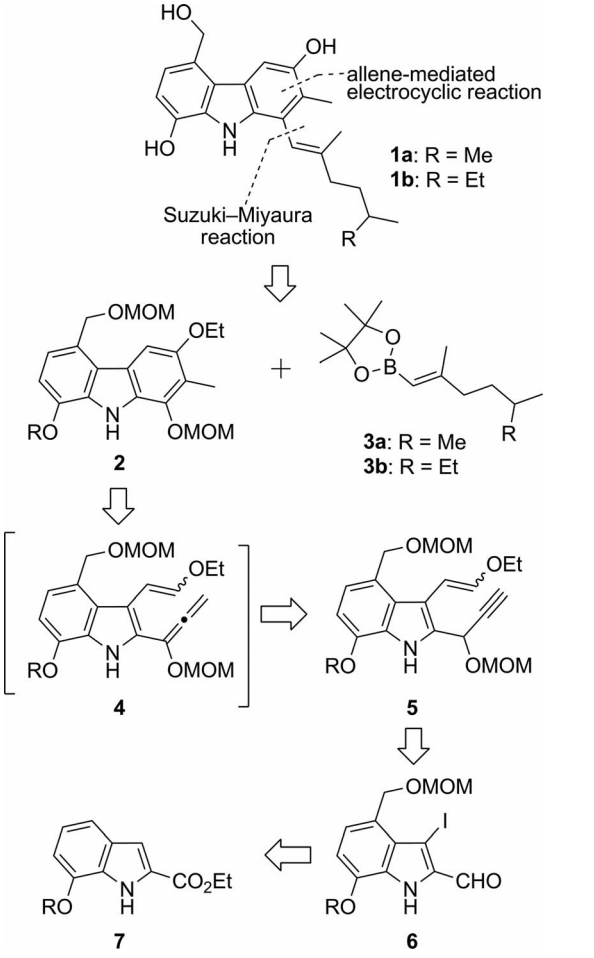
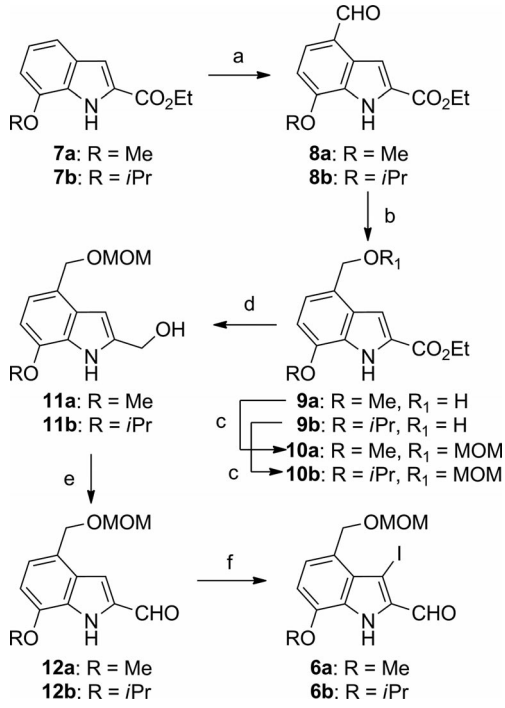
figuration at the C-1 position of **1** through a Suzuki–Miyaura reaction[13] with alkenyl pinacol borates **3**.



Scheme 1. Retrosynthetic analysis of carbazomadurines A and B (MOM = methoxymethyl).

Results and Discussion

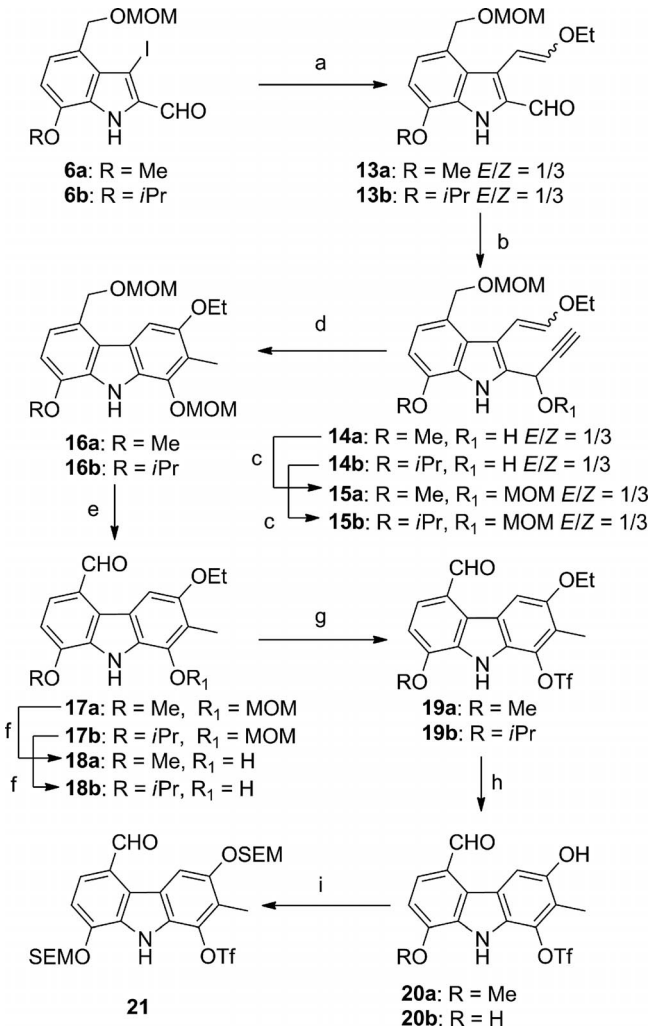
To synthesize the initially required 7-oxygenated 2,3,4,7-tetrasubstituted indoles **6a** and **6b**, we chose known ethyl 7-alkoxyindole-2-carboxylates **7a** and **7b**[14] as the starting materials (see Scheme 2). The treatment of **7a** or **7b** with α,α-dichloromethyl methyl ether in the presence of $TiCl_4$[15] gave 4-formylindoles **8a** and **8b**, respectively. The formyl groups of **8a** and **8b** were subsequently reduced with $NaBH_4$ to give the hydroxymethyl groups of **9a** and **9b**, which were treated with chloromethyl methyl ether (MOMCl) in the presence of *N*,*N*-diisopropylethylamine (*i*Pr_2NEt) to yield MOM ethers **10a** and **10b**. The reduction of the ester groups of **10a** and **10b** by treatment with Red-Al in toluene followed by oxidation of the resulting alcohols **11a** and **11b** with MnO_2 afforded indole-2-carbaldehydes **12a** and **12b**. Further treatment of **12a** or **12b** with I_2 gave the two required 7-oxygenated-2,3,4,7-tetrasubstituted indoles **6a** (67% yield from **7a**) and **6b** (57% yield from **7b**), respectively.



Scheme 2. Reagents and conditions: (a) Cl_2CHOCH_3, $TiCl_4$ (1 M), CH_2Cl_2, –10 °C, 4 h, **8a** (89%), **8b** (86%); (b) $NaBH_4$, EtOH, 0 °C, 3 h, **9a** (99%), **9b** (99%); (c) MOMCl, *i*Pr_2NEt, CH_2Cl_2, 0 °C to room temp., 5 h, **10a** (97%), **10b** (86%); (d) 65% Red-Al, toluene, 0 °C, 3 h, **11a** (99%), **11b** (99%); (e) MnO_2, CH_2Cl_2, room temp., 12 h, **12a** (87%), **12b** (84%); (f) KOH, I_2, *N*,*N*-dimethylformamide (DMF), 0 °C, 12 h, **6a** (91%), **6b** (94%).

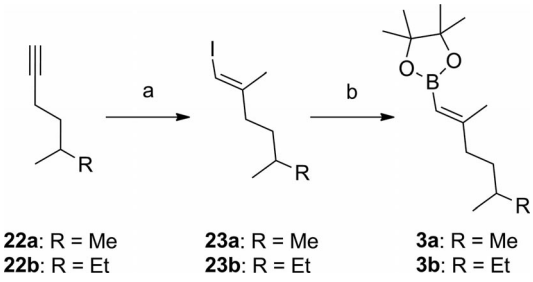
We then synthesized 1,3,8-trioxygenated 1,2,3,5,8-pentasubstituted carbazoles **19a** and **19b** from 2,3,4,7-tetrasubstituted indoles **6a** and **6b** (see Scheme 3). The Stille coupling reaction of 3-iodoindoles **6a** and **6b** with tributyl(2-ethoxyvinyl)stannane[16] in the presence of $PdCl_2(PPh_3)_2$ gave 3-alkenylindoles **13a** (*E*/*Z*, 1:3) and **13b** (*E*/*Z*, 1:3), respectively. The Grignard reaction of **13a** and **13b** with ethynylmagnesium bromide followed by treatment of the resulting alcohols **14a** and **14b** with MOMCl and *i*Pr_2NEt produced MOM propargyl ethers **15a** (*E*/*Z*, 1:3) and **15b** (*E*/*Z*, 1:3) corresponding to **5**. We subjected **15a** and **15b** to an allene-mediated thermal electrocyclic reaction[6–12] using tetra-*n*-butylammonium fluoride (TBAF) in tetrahydrofuran (THF) according to our reported method[8b] to provide the desired carbazoles **16a** and **16b** corresponding to **2**, respectively, in somewhat low yields. The oxidation of **16a** and **16b** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) afforded 5-formylcarbazoles **17a** and **17b**, which were treated with 4 M HCl in THF to yield the 1-hydroxycarbazoles **18a** and **18b**. The sequential treatment of **18a** and **18b** with *N*-phenyl-bis(trifluoromethanesulfonimide) ($PhNTf_2$) and NaH gave the corresponding triflates **19a** (10.4% yield from **7a** in 13 steps) and **19b** (8.5% from **7b** in 13 steps). To prepare the 3,8-dihydroxycarbazole at the next stage, we attempted a cleavage of the 3,8-dialkoxy groups of **19a** and **19b**. Although treatment of **19a** with

BBr_3 in CH_2Cl_2 gave only 3-hydroxycarbazole **20a** (60%), the treatment of **19b** with BBr_3 successfully gave 3,8-dihydroxycarbazole **20b**. The hydroxy groups of compound **20b** were immediately protected by using 2-(trimethylsilyl)-ethoxymethyl chloride (SEMCl) and iPr$_2$NEt to produce 3,8-bis(OSEM)-carbazole **21** (97% from **19b**).



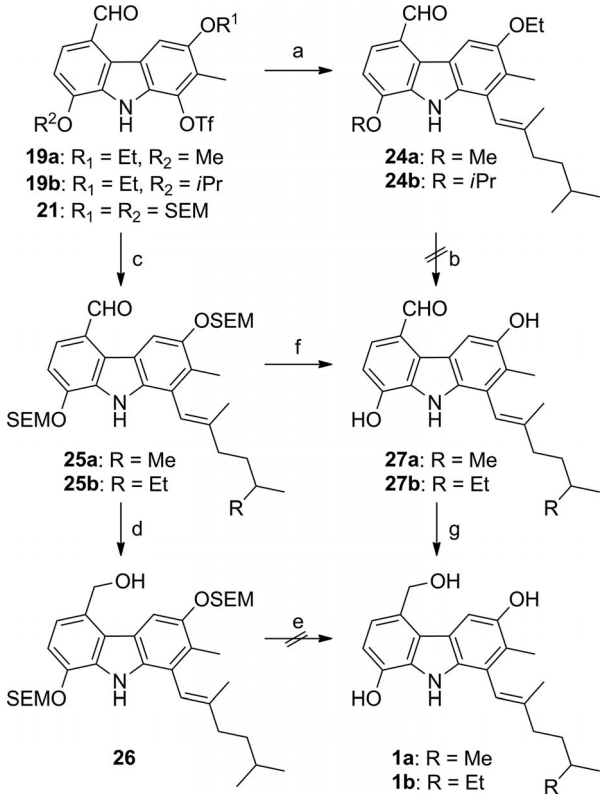
Scheme 3. Reagents and conditions: (a) tributyl(2-ethoxyvinyl)-stannane, $PdCl_2(PPh_3)_2$, Et_4NCl, DMF, 80 °C, 2 h, **13a** (77%), **13b** (86%); (b) ethynylmagnesium bromide, THF, 0 °C or –30 °C, 1 h, **14a** (97%), **14b** (81%); (c) MOMCl, iPr$_2$NEt, CH_2Cl_2, 50 °C, 12 h, **15a** (80%), **15b** (81%); (d) TBAF, THF, 80 °C, 6 h, **16a** (40%), **16b** (40%); (e) DDQ, CH_2Cl_2, room temp., 20 min, **17a** (95%), **17b** (73%); (f) HCl (4 M), ethylene glycol, THF, 50 °C, 30 min, **18a** (89%), **18b** (91%); (g) $PhNTf_2$, NaH, THF, 0 °C, 30 min, **19a** (77%), **19b** (99%); (h) BBr_3, CH_2Cl_2, –78 °C to room temp., 3 h, **20a** (60%), **20b** (99%); (i) SEMCl, iPr$_2$NEt, CH_2Cl_2, 0 °C to room temp., 12 h, 98%.

However, to introduce the (*E*)-alkenyl side chain, which is found at the C-1 position of carbazomadurins A (**1a**) and B (**1b**), pinacol borates **3a** and **3b** were prepared from commercially available 5-methyl-1-hexyne (**22a**) and known (*S*)-(+)-5-methyl-1-heptyne (**22b**), respectively, {$[\alpha]_D$ = +15.3 ($CHCl_3$)}[5,17] in two steps (see Scheme 4). The zirconium-catalyzed carboalumination of **22a** and **22b** by treatment with trimethylaluminum in the presence of zirconocene dichloride, according to the reported procedure by Negishi,[18] followed by the addition of I_2 afforded (*E*)-alkenyl iodides **23a** (78%) and **23b** (58%).[4,5] A subsequent Suzuki–Miyaura reaction[13] of **23a** and **23b** with bis(pinacolato)-diboron in the presence of $PdCl_2$(dppf) afforded pinacol borates **3a** (48%) and **3b** (53%, $[\alpha]_D$ = +26.5), respectively.



Scheme 4. Reagents and conditions: (a) (1) Me_3Al, Cp_2ZrCl_2 (Cp = cyclopentadienyl), 1,2-dichloroethane, room temp., 12 h; (2) I_2, THF, 0 °C to room temp., 1 h, **23a** (79%), **23b** (58%); (b) bis-(pinacolato)diboron, KOAc, $PdCl_2$(dppf), dimethyl sulfoxide (DMSO), 80 °C, 2 h, **3a** (48%), **3b** (53%).

As shown in Scheme 5, triflates **19a** and **19b** were subjected to a Suzuki–Miyaura cross-coupling reaction[13] with alkenyl pinacol borates **3a** in the presence of $Pd(PPh_3)_4$ and Na_2CO_3 to give 1-alkenylcarbazoles **24a** (96%) and **24b** (99%), respectively, in excellent yields. The treatment of **24a** or **24b** with BBr_3 to cleave the two ether bonds, however, did not provide the expected 3,8-dihydroxycarbazole **27a**. On the other hand, the cross-coupling reaction of the triflate **21** with **3a** or **3b** in the presence of Na_2CO_3 and $Pd(PPh_3)_4$ gave the corresponding 1-alkenylcarbazoles **25a** (86%) and **25b** (83%, $[\alpha]_D$ = +7.1), respectively. Although reduction of the formyl group of **25a** afforded alcohol **26**, the sequential treatment with TBAF did not provide carbazomadurin A (**1a**) as had been previously reported.[12] As a result, the cleavage of both SEM groups of **25a** and **25b** by using TBAF in hexamethylphosphoramide (HMPA) produced the expected 3,8-dihydroxycarbazole **27a** (71%) and **27b** (67%, $[\alpha]_D$ = +20.0), respectively. Finally, the reduction of **27a** and **27b** with $NaBH_4$ in MeOH provided the corresponding carbazomadurin A (**1a**, 70%) and (*S*)-(+)-carbazomadurin B (**1b**, 78%). The spectral and physical data of synthetic carbazomadurin A (**1a**) and (+)-carbazomadurin B (**1b**) were identical with those of the reported data.[3–5] The value for the specific rotation of our synthetic (+)-carbazomadurin B (**1b**) was $[\alpha]_D$ = +13.1 (c = 0.05, MeOH), which is consistent with the value $[\alpha]_D$ = +13.0 (c = 0.05, MeOH) that was reported by the Knölker group.[5] This value of specific rotation was higher than that of natural (+)-carbazomadurin B {**1b**, $[\alpha]_D$ = +4 (c = 0.05, MeOH)}.[3] The absolute configuration of **1b** was *S*, as it was derived from known (*S*)-(+)-5-methyl-1-heptyne (**22b**).[17] The Knölker group[5] also assigned the *S* configuration to the stereogenic center of **1b**.



Scheme 5. Reagents and conditions: (a) **3a**, $Pd(PPh_3)_4$, Na_2CO_3, DMF, 80 °C, 5 h, **24a** (96%), **24b** (99%); (b) BBr_3, CH_2Cl_2, –78 °C, 3 h; (c) **3a** or **3b**, $Pd(PPh_3)_4$, Na_2CO_3 (3 M aqueous solution), DMF, 70 °C, 2 h, **25a** (86%), **25b** (83%); (d) diisobutylaluminum hydride (DIBAL-H), toluene, 0 °C, 1 h, 90%; (e) TBAF, THF, 80 °C, 1 h; (f) TBAF, HMPA, 100 °C, 1 h, **27a** (71%), **27b** (67%); (g) $NaBH_4$, MeOH, room temp., 5 min, **1a** (70%), **1b** (78%).

Conclusions

On the basis of these results, the known ethyl 7-isopropoxyindole-2-carboxylate (**7b**)[14] was a convenient starting material to realize our total syntheses of carbazomadurins A (**1a**) and B (**1b**). The 2,3,4,7-tetrasubstituted indole **6b** was prepared from the indole **7b** in six steps. The synthesis of functionalized carbazole **19b** was achieved in seven steps from **6b** through an allene-mediated electrocyclic reaction of the 6π-electron system that involved the indole 2,3-bond. Carbazole **19b** was converted into 3,8-bis(OSEM)-carbazole **21**, which was subjected to a Suzuki–Miyaura cross-coupling reaction by treatment with alkenyl pinacol borates **3a** or **3b** to yield 1-alkenylcarbazoles **25a** and (+)-**25b**, respectively, The treatment of either **25a** or (+)-**25b** with TBAF gave the desired 3,8-dihydroxycarbazoles **27a** and (+)-**27b**, which were then reduced with $NaBH_4$ to provide carbazomadurin A (**1a**; 3.5% overall yields in 18 steps from **7b**) and (*S*)-(+)-carbazomadurin B (**1b**; 3.3% overall yields in same number of steps from **7b**), respectively. The physical and spectroscopic data of synthetic carbazomadurin A (**1a**) and (*S*)-(+)-carbazomadurin B (**1b**) were consistent with natural and synthetic carbazomadurins A (**1a**) and B (**1b**) in all respects.[3–5]

Experimental Section

General Methods: All nonaqueous reactions were carried out under 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 60N (63-210 μm, Kanto Chemical Co. Ltd.). All melting points were determined with a Yanagimoto micro melting point apparatus. The proton nuclear magnetic resonance (^1H NMR) spectroscopic data were recorded with a JEOL AL-300 at 300 MHz and a JEOL JMN-LA500 at 500 MHz. Chemical shifts are reported relative to Me_4Si (δ = 0.00 ppm). The NMR spectroscopic data were recorded using $CDCl_3$, unless otherwise noted. Multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br. (broad). The carbon nuclear magnetic resonance (^{13}C NMR) spectroscopic data were recorded with a JEOL AL-300 at 75 MHz and JEOL JMN-LA500 at 125 MHz. Chemical shifts are reported relative to $CDCl_3$ (δ = 77.0 ppm) and $[D_6]$DMSO (δ = 39.7 ppm). Infrared spectra were recorded using the attenuated total reflectance (ATR) method with a Shimadzu FTIR-8000 spectrophotometer and Technologies DuraScop. Low and high resolution mass spectra were recorded with JEOL JMS-700 spectrometers by using a direct inlet system. Optical rotations were measured with a JASCO P-2200 polarimeter.

Ethyl 4-Formyl-7-methoxyindole-2-carboxylate (8a): To a solution of ethyl 7-methoxyindole-2-carboxylate (**7a**[14], 1.0 g, 4.54 mmol) and α,α-dichloromethyl methyl ether (1.24 mL, 13.62 mmol) in dry CH_2Cl_2 (30 mL) was added dropwise $TiCl_4$ (1.5 mL, 13.62 mmol) at –10 °C. The mixture was stirred at the same temperature for 4 h and then was poured into ice water. The mixture was extracted with CH_2Cl_2. The CH_2Cl_2 phase was washed with water and brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 10 g; EtOAc/hexane, 1:5 v/v) to give 4-formylindole **8a** (1.0 g, 89%) as a pale yellow solid; m.p. 165–167 °C (acetone/hexane). IR (ATR): $\tilde{\nu}$ = 1710, 1650 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.42 (t, J = 7.2 Hz, 3 H), 4.07 (s, 3 H), 4.42 (q, J = 7.2 Hz, 2 H), 6.83 (d, J = 7.9 Hz, 1 H), 7.63 (d, J = 7.9 Hz, 1 H), 7.94 (d, J = 2.2 Hz, 1 H), 9.29 (br. s, 1 H), 10.06 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.4, 55.9, 61.3, 103.5, 109.1, 124.2, 125.9, 127.9, 129.6, 132.1, 151.5, 161.7, 191.2 ppm. MS (EI): m/z = 247 $[M]^+$. HRMS (EI): calcd for $C_{13}H_{13}NO_4$ 247.0845; found 247.0849.

Ethyl 4-Formyl-7-isopropoxyindole-2-carboxylate (8b): The same procedure as above was carried out using ethyl 7-isopropoxyindole-2-carboxylate (**7b**[14], 240 mg, 1.03 mmol), α,α-dichloromethyl methyl ether (0.28 mL, 3.11 mmol), and $TiCl_4$ (0.34 mL, 3.11 mmol) in dry CH_2Cl_2 (30 mL) to give 4-formylindole **8b** (230 mg, 86%) as a pale yellow solid; m.p. 134–137 °C (EtOAc). IR (ATR): $\tilde{\nu}$ = 1706, 1654 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.42 (t, J = 7.2 Hz, 3 H), 1.47 (d, J = 6.1 Hz, 6 H), 4.42 (q, J = 7.2 Hz, 2 H), 4.81–4.93 (m, 1 H), 6.80 (d, J = 8.1 Hz, 1 H), 7.60 (d, J = 8.1 Hz, 1 H), 7.92 (d, J = 2.4 Hz, 1 H), 9.31 (br. s, 1 H), 10.04 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.4, 22.0 (2×), 61.3, 71.2, 104.7, 109.1, 123.6, 126.0, 128.6, 129.4, 132.2, 150.0, 161.8, 191.1 ppm. MS (EI): m/z = 275 $[M]^+$. HRMS (EI): calcd. for $C_{15}H_{17}NO_4$ 275.1158; found 275.1159.

Ethyl 4-Hydroxymethyl-7-methoxyindole-2-carboxylate (9a): To a solution of 4-formylindole **8a** (100 mg, 0.40 mmol) in EtOH (4 mL) was added $NaBH_4$ (18.3 mg, 0.48 mmol) at 0 °C. The mixture was stirred at room temperature for 3 h and then was concentrated under reduced pressure. Water was added to the residue, and then the mixture was extracted with EtOAc. The EtOAc phase was washed

with water and brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 10 g; EtOAc/hexane, 1:4 v/v) to give the 4-hydroxymethylindole **9a** (101 mg, 99%) as a white solid; m.p. 106–107 °C (EtOAc/hexane). IR (ATR): $\tilde{\nu}$ = 3320, 1700 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.42 (t, J = 7.2 Hz, 3 H), 3.98 (s, 3 H), 4.41 (q, J = 7.2 Hz, 2 H), 4.92 (s, 1 H), 6.68 (d, J = 7.7 Hz, 1 H), 7.04 (d, J = 7.7 Hz, 1 H), 7.35 (d, J = 2.2 Hz, 1 H), 9.13 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.4, 55.5, 61.1, 63.7, 103.7, 107.2, 120.1, 126.7, 127.2, 127.3, 128.1, 146.4, 161.8 ppm. MS (EI): m/z = 249 $[M]^+$. HRMS (EI): calcd. for $C_{13}H_{15}NO_4$ 249.1001, found 249.1015.

Ethyl 4-Hydroxymethyl-7-isopropoxyindole-2-carboxylate (9b): The same procedure as above was carried out using 4-formylindole **8b** (224 mg, 0.81 mmol) and $NaBH_4$ (37 mg, 0.98 mmol) in EtOH (8 mL) to give 4-hydroxymethylindole **9b** (224 mg, 99%) as a white solid; m.p. 132–134 °C (EtOAc). IR (ATR): $\tilde{\nu}$ = 3460, 1680 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.39–1.44 (m, 9 H), 4.40 (q, J = 7.2 Hz, 2 H), 4.66–4.79 (m, 1 H), 4.90 (s, 2 H), 6.66 (d, J = 7.7 Hz, 1 H), 7.01 (d, J = 7.7 Hz, 1 H), 7.33 (d, J = 2.5 Hz, 1 H), 9.16 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.4, 22.1 (2×), 61.1, 63.6, 70.5, 105.7, 107.2, 120.1, 126.4, 127.2, 127.3, 129.1, 144.5, 161.9 ppm. MS (EI): m/z = 277 $[M]^+$. HRMS (EI): calcd. for $C_{15}H_{19}NO_4$ 277.1314; found 277.1284.

Ethyl 7-Methoxy-4-(methoxymethyloxy)methylindole-2-carboxylate (10a): To a solution of 4-hydroxymethylindole **9a** (94 mg, 0.377 mmol) and MOMCl (0.03 mL, 0.45 mmol) in dry CH_2Cl_2 (30 mL) was added dropwise iPr$_2$NEt (0.33 mL, 1.89 mmol) with cooling by an ice-water bath. The mixture was stirred at room temperature for 5 h and then was quenched with aqueous NH_4Cl. The resulting mixture was extracted with CH_2Cl_2. The CH_2Cl_2 phase was washed with water and brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 10 g; EtOAc/hexane, 1:4 v/v) to give MOM ether **10a** (127 mg, 97%) as a pale yellow solid; m.p. 82–83 °C (Et_2O). IR (ATR): $\tilde{\nu}$ = 1710 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.41 (t, J = 7.2 Hz, 3 H), 3.44 (s, 3 H), 3.97 (s, 3 H), 4.40 (q, J = 7.2 Hz, 2 H), 4.72 (s, 2 H), 4.82 (s, 2 H), 6.67 (d, J = 7.7 Hz, 1 H), 7.04 (d, J = 7.7 Hz, 1 H), 7.32 (d, J = 2.2 Hz, 1 H), 9.13 (br. s, 1 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$): δ = 14.4, 55.4, 55.5, 61.0, 67.3, 95.4, 103.7, 107.5, 121.4, 123.5, 127.3, 127.8, 128.1, 146.5, 161.8 ppm. MS (EI): m/z = 293 $[M]^+$. HRMS (EI): calcd. for $C_{15}H_{19}NO_5$ 293.1263; found 293.1277.

Ethyl 7-Isopropoxy-4-(methoxymethyloxy)methylindole-2-carboxylate (10b): The same procedure as above was carried out using 4-hydroxymethylindole **9b** (750 mg, 2.70 mmol), MOMCl (0.25 mL, 3.24 mmol), and iPr$_2$NEt (2.34 mL, 13.52 mmol) in dry CH_2Cl_2 (30 mL) to give the oily MOM ether **10b** (720 mg, 86%). IR (ATR): $\tilde{\nu}$ = 1700 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.39–1.44 (m, 9 H), 3.45 (s, 3 H), 4.41 (q, J = 7.0 Hz, 2 H), 4.66–4.76 (m, 3 H), 4.82 (s, 2 H), 6.66 (d, J = 7.9 Hz, 1 H), 7.01 (d, J = 7.9 Hz, 1 H), 7.31 (d, J = 2.2 Hz, 1 H), 9.15 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.4, 22.1 (2×), 55.4, 61.0, 67.3, 70.4, 95.4, 105.7, 107.4, 121.5, 123.1, 127.1, 128.0, 129.1, 144.6, 161.9 ppm. MS (EI): m/z = 321 $[M]^+$. HRMS (EI): calcd. for $C_{17}H_{23}NO_5$ 321.1576; found 321.1570.

2-Hydroxymethyl-7-methoxy-4-(methoxymethyloxy)methylindole (11a): To a solution of MOM ether **10a** (500 mg, 1.70 mmol) in dry toluene (10 mL) was added dropwise Red-Al (65% in toluene, 1.27 g, 4.09 mmol) with cooling by an ice-water bath. The mixture was stirred at room temperature for 2 h and then was poured into ice water. The mixture was filtered through a pad of Celite. The filtrate was extracted with EtOAc. The EtOAc phase was washed with water and brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 30 g; EtOAc/hexane, 1:1 v/v) to give the oily alcohol **11a** (417 mg, 99%). IR (ATR): $\tilde{\nu}$ = 3290 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 3.44 (s, 3 H), 3.95 (s, 3 H), 4.71 (s, 2 H), 4.80 (br. s, 2 H), 4.81 (br. s, 2 H), 6.50 (d, J = 2.2 Hz, 1 H), 6.59 (d, J = 7.7 Hz, 1 H), 7.00 (d, J = 7.7 Hz, 1 H), 8.69 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.3, 55.4, 58.7, 67.5, 95.2, 99.4, 101.6, 120.8, 121.8, 126.8, 128.5, 137.4, 146.0 ppm. MS (EI): m/z = 251 $[M]^+$. HRMS (EI): calcd. for $C_{13}H_{17}NO_4$ 251.1158; found 251.1171.

2-Hydroxymethyl-7-isopropoxy-4-(methoxymethyloxy)methylindole (11b): The same procedure as above was carried out using MOM ether **10b** (2.2 g, 6.69 mmol) and Red-Al (65% in toluene, 4.99 g, 16.06 mmol) in dry toluene (50 mL) to give the oily alcohol **11b** (2.2 g, 99%). IR (ATR): $\tilde{\nu}$ = 3200 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.40 (d, J = 5.9 Hz, 6 H), 3.44 (s, 3 H), 4.66–4.81 (m, 7 H), 6.48 (d, J = 2.6 Hz, 1 H), 6.59 (d, J = 7.7 Hz, 1 H), 6.97 (d, J = 7.7 Hz, 1 H), 8.72 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.2 (2×), 55.3, 58.7, 67.6, 70.2, 95.2, 99.4, 103.8, 120.9, 121.4, 127.8, 128.7, 137.3, 144.1 ppm. MS (EI): m/z = 279 $[M]^+$. HRMS (EI): calcd. for $C_{15}H_{21}NO_4$ 279.1471; found 249.1459.

7-Methoxy-4-(methoxymethyloxy)methylindole-2-carbaldehyde (12a): A mixture of the alcohol **11a** (400 mg, 1.69 mmol) and activated MnO_2 (733 mg, 8.44 mmol) in dry CH_2Cl_2 (40 mL) was stirred at room temperature for 12 h. The reaction mixture was filtered through a pad of Celite, and then the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 40 g; EtOAc/hexane, 2:8 v/v) to give aldehyde **12a** (344 mg, 87%) as a pale yellow solid; m.p. 94–96 °C (Et_2O/hexane). IR (ATR): $\tilde{\nu}$ = 1660 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 3.45 (s, 3 H), 3.97 (s, 3 H), 4.72 (s, 2 H), 4.84 (s, 2 H), 6.72 (d, J = 7.7 Hz, 1 H), 7.06 (d, J = 7.7 Hz, 1 H), 7.37 (d, J = 2.2 Hz, 1 H), 9.24 (br. s, 1 H), 9.84 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.5, 55.6, 67.2, 95.4, 105.3, 113.4, 121.8, 124.2, 127.7, 129.5, 135.6, 146.8, 181.9 ppm. MS (EI): m/z = 249 $[M]^+$. HRMS (EI): calcd. for $C_{13}H_{13}NO_4$ 249.1001; found 249.1014.

7-Isopropoxy-4-(methoxymethyloxy)methylindole-2-carbaldehyde (12b): The same procedure as above was carried out using alcohol **11b** (2.3 g, 8.23 mmol) and activated MnO_2 (3.58 g, 41.13 mmol) in dry CH_2Cl_2 (40 mL) to give aldehyde **12b** (1.9 g, 84%) as a pale yellow solid; m.p. 78–80 °C (Et_2O). IR (ATR): $\tilde{\nu}$ = 1670 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.40 (d, J = 6.1 Hz, 6 H), 3.45 (s, 3 H), 4.67–4.75 (m, 3 H), 4.83 (s, 2 H), 6.71 (d, J = 7.7 Hz, 1 H), 7.03 (d, J = 7.7 Hz, 1 H), 7.36 (d, J = 2.2 Hz, 1 H), 9.38 (br. s, 1 H), 9.83 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.1 (2×), 55.5, 67.2, 70.6, 95.4, 107.3, 113.4, 121.9, 123.8, 127.8, 130.5, 135.5, 144.9, 182.0 ppm. MS (EI): m/z = 277 $[M]^+$. HRMS (EI): calcd for $C_{15}H_{19}NO_4$ 277.1314; found 277.1291.

3-Iodo-7-methoxy-4-(methoxymethyloxy)methylindole-2-carbaldehyde (6a): To a mixture of aldehyde **12a** (300 mg, 1.20 mmol) and KOH powder (81 mg, 1.44 mmol) in DMF (10 mL) was added a solution of I_2 (229 mg, 1.81 mmol) in DMF (10 mL) with cooling by an ice-water bath. The mixture was stirred at room temperature for 12 h and then was poured into a solution of $NaHSO_3$ (140 mg, 1.33 mmol), 28% NH_3 (10 mL), and water (10 mL). The mixture was extracted with EtOAc. The EtOAc phase was washed with water and brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 10 g; EtOAc/hexane, 1:5 v/v) to give 3-iodoindole

6a (362 mg, 91%) as a pale yellow solid; m.p. 112–113 °C (EtOAc/hexane). IR (ATR): $\tilde{\nu}$ = 1660 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 3.45 (s, 3 H), 3.96 (s, 3 H), 4.81 (s, 2 H), 5.11 (s, 2 H), 6.72 (d, J = 7.9 Hz, 1 H), 7.13 (d, J = 7.9 Hz, 1 H), 9.48 (br. s, 1 H), 9.85 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.7, 55.7, 65.1, 67.6, 95.5, 105.4, 124.2, 124.4, 127.5, 129.6, 133.4, 146.9, 183.5 ppm. MS (EI): m/z = 375 $[M]^+$. HRMS (EI): calcd. for $C_{13}H_{14}NO_4I$ 374.9968; found 374.9951.

3-Iodo-7-isopropoxy-4-(methoxymethyloxy)methylindole-2-carbaldehyde (6b): The same procedure as above was carried out using aldehyde **12b** (2.5 g, 8.83 mmol), KOH powder (594 mg, 10.60 mmol), and I_2 (3.36 g, 13.25 mmol) to give 3-iodoindole **6b** (3.3 g, 94%) as a pale yellow solid; m.p. 88–89 °C (EtOAc). IR (ATR): $\tilde{\nu}$ = 1670 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.40 (d, J = 6.2 Hz, 6 H), 3.46 (s, 3 H), 4.66–4.78 (m, 1 H), 4.81 (s, 2 H), 5.10 (s, 2 H), 6.71 (d, J = 7.7 Hz, 1 H), 7.10 (d, J = 7.7 Hz, 1 H), 9.47 (br. s, 1 H), 9.85 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.0 (2×), 55.6, 65.1, 67.7, 70.8, 95.5, 107.3, 123.9, 124.3, 127.6, 130.5, 133.3, 145.0, 183.6 ppm. MS (EI): m/z = 403 $[M]^+$. HRMS (EI): calcd. for $C_{15}H_{18}NO_4I$ 403.0281; found 403.0266.

3-Ethoxyvinyl-7-methoxy-4-(methoxymethyloxy)methylindole-2-carbaldehyde (13a): A solution of tributyl(2-ethoxyvinyl)stannane (458 mg, 1.27 mmol) in dry DMF (20 mL) was added to a stirred suspension of 3-iodoindole **6a** (350 mg, 1.06 mmol), Et_4NCl (200 mg, 1.27 mmol), and $PdCl_2(PPh_3)_2$ (6 mg, 0.0093 mmol) in dry DMF (10 mL) at the room temperature, and then the mixture was heated at 80 °C for 2 h. After cooling the reaction to an ambient temperature, the mixture was quenched with aqueous 30% KF. The mixture was stirred at the same temperature for 30 min and then was filtered through a pad of Celite. The filtrate was extracted with EtOAc. The EtOAc phase was washed with water and brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 5 g; EtOAc/hexane, 2:8 v/v) to give the oily 3-alkenylindole **13a** (310 mg, 77%). IR (ATR): $\tilde{\nu}$ = 1650 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.26 (t, J = 7.0 Hz, 9/4 H), 1.39 (t, J = 7.0 Hz, 3/4 H), 3.43 (s, 3 H), 3.88–4.04 (m, 5 H), 4.70 (s, 6/4 H), 4.71 (s, 2/4 H), 4.87 (s, 2/4 H), 4.87 (s, 6/4 H), 5.89 (d, J = 7.0 Hz, 3/4 H), 6.36 (d, J = 12.5 Hz, 1/4 H), 6.42 (d, J = 7.0 Hz, 3/4 H), 6.62–6.71 (m, 5/4 H), 6.98–7.03 (m, 1 H), 9.04 (br. s, 1 H), 9.81 (s, 1/4 H), 10.0 (s, 3/4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.7, 15.1, 55.4, 65.8, 66.7, 66.7, 68.5, 94.6, 94.8, 96.3, 96.5, 104.5, 105.1, 121.2, 123.0, 123.0, 124.3, 124.6, 125.3, 126.1, 126.5, 129.1, 129.2, 130.9, 131.9, 146.6, 146.7, 147.2, 151.6, 181.7, 183.8 ppm. MS (EI): m/z = 319 $[M]^+$. HRMS (EI): calcd. for $C_{17}H_{21}NO_5$ 319.1420; found 319.1402.

3-Ethoxyvinyl-7-isopropoxy-4-(methoxymethyloxy)methylindole-2-carbaldehyde (13b): The same procedure as above was carried out using 3-iodoindole **6b** (606 mg, 1.50 mmol), Et_4NCl (373 mg, 2.25 mmol), and $PdCl_2(PPh_3)_2$ (10 mg, 0.015 mmol) in dry DMF (10 mL) along with tributyl(2-ethoxyvinyl)stannane (814 mg, 2.25 mmol) in dry DMF (20 mL) to give the oily 3-alkenylindole **13b** (451 mg, 86%). IR (ATR): $\tilde{\nu}$ = 1650 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.25 (t, J = 7.0 Hz, 9/4 H), 1.36–1.42 (m, 27/4 H), 3.43 (s, 3 H), 3.91 (q, J = 7.0 Hz, 6/4 H), 4.01 (q, J = 7.0 Hz, 2/4 H), 4.65–4.73 (m, 3 H), 4.87 (s, 2 H), 5.89 (d, J = 7.2 Hz, 3/4 H), 6.36 (d, J = 12.5 Hz, 1/4 H), 6.41 (d, J = 7.2 Hz, 3/4 H), 6.62–6.70 (m, 5/4 H), 6.96–7.01 (m, 1 H), 9.09 (br. s, 1 H), 9.81 (s, 1/4 H), 10.04 (s, 3/4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.7, 15.0, 21.9 (2×), 55.4, 65.8, 66.7, 66.7, 68.5, 70.3, 70.3, 94.6, 94.8, 96.4, 96.6, 106.5, 107.0, 121.3, 123.1, 123.1, 123.9, 124.1, 125.4, 126.3, 126.6, 130.1, 130.2, 130.8, 131.8, 144.7, 144.8, 147.2, 151.5, 181.7, 183.9 ppm. MS (EI): m/z = 347 $[M]^+$. HRMS (EI): calcd. for $C_{19}H_{25}NO_5$ 347.1733; found 347.1756.

3-Ethoxyvinyl-2-(1-hydroxyprop-2-yn-1-yl)-7-methoxy-4-(methoxymethyloxy)methylindole (14a): To a solution of 3-alkenylindole **13a** (4.7 g, 14.6 mmol) in dry THF (30 mL) was gradually added ethynylmagnesium bromide (0.5 M in THF, 87.6 mL, 43.8 mmol) at 0 °C. After stirring the reaction at 0 °C for 1 h, the mixture was quenched with aqueous NH_4Cl solution. The resulting mixture was extracted with EtOAc. The EtOAc phase was washed with brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 20 g; EtOAc/hexane, 3:17 v/v) to give the oily 2-propargyl alcohol **14a** (4.9 g, 97%). IR (ATR): $\tilde{\nu}$ = 3280 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.28 (t, J = 7.0 Hz, 9/4 H), 1.36 (t, J = 7.0 Hz, 3/4 H), 2.65–2.67 (m, 1 H), 3.43 (s, 3 H), 3.85–4.01 (m, 5 H), 4.66–4.99 (m, 4 H), 5.69–5.73 (m, 1 H), 5.81 (d, J = 7.0 Hz, 3/4 H), 6.17 (d, J = 12.8 Hz, 1/4 H), 6.26 (d, J = 7.0 Hz, 3/4 H), 6.57–6.65 (m, 5/4 H), 6.97–7.05 (m, 1 H), 8.84 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.8, 14.9, 55.3, 55.3, 57.3, 65.1, 66.9, 67.0, 68.6, 74.4, 74.5, 81.3, 82.4, 94.5, 94.8, 97.5, 99.0, 101.9, 101.9, 108.3, 110.9, 122.3, 122.4, 122.6, 122.7, 126.3, 126.5, 126.9, 127.2, 133.4, 145.1, 146.2, 146.3 ppm. MS (EI): m/z = 345 $[M]^+$. HRMS (EI): calcd. for $C_{19}H_{23}NO_5$ 345.1576; found 345.1588.

3-Ethoxyvinyl-2-(1-hydroxyprop-2-yn-1-yl)-7-isopropoxy-4-(methoxymethyloxy)methylindole (14b): The same procedure as above was carried out using 3-alkenylindole **13b** (1.1 g, 3.17 mmol) and ethynylmagnesium bromide (0.5 M in THF, 18.9 mL, 9.49 mmol), which was added at –30 °C. The reaction mixture was then stirred at 0 °C for 1 h to give the oily 2-propargyl alcohol **14b** (960 mg, 81%). IR (ATR): $\tilde{\nu}$ = 3280 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.28 (t, J = 7.0 Hz, 9/4 H), 1.36–1.42 (m, 27/4 H), 2.67 (d, J = 2.2 Hz, 3/4 H), 2.69 (d, J = 2.2 Hz, 1/4 H), 3.42 (s, 3 H), 3.84–3.97 (m, 2 H), 4.65–4.78 (m, 5 H), 5.72 (t, J = 2.6 Hz, 1 H), 5.81 (d, J = 7.0 Hz, 3/4 H), 6.16 (d, J = 12.8 Hz, 1/4 H), 6.26 (d, J = 7.0 Hz, 3/4 H), 6.57–6.63 (m, 5/4 H), 6.95 (d, J = 7.0 Hz, 1 H), 8.71 (br. s, 1/4 H), 8.75 (br. s, 3/4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.8, 14.9, 22.1 (2×), 22.2 (2×), 55.2, 55.4, 57.2, 66.9, 68.7, 70.2, 70.3, 74.4, 74.5, 81.2, 82.4, 94.6, 94.9, 97.5, 99.1, 104.0, 105.5, 108.3, 110.8, 121.9, 122.7, 126.9, 127.3, 127.4, 133.1, 144.3, 144.4, 144.9, 145.0 ppm. MS (EI): m/z = 373 $[M]^+$. HRMS (EI): calcd. for $C_{21}H_{27}NO_5$ 373.1889; found 373.1873.

3-Ethoxyvinyl-7-methoxy-2-{[1-(methoxymethyloxy)prop-2-yn-1-yl]}-4-(methoxymethyloxy)methylindole (15a): To a mixture of propargyl alcohol **14a** (546 mg, 1.56 mmol) and iPr$_2$NEt (1.35 mL, 7.82 mmol) in dry CH_2Cl_2 (30 mL) was added chloromethyl methyl ether (0.35 mL, 4.69 mmol) with cooling by an ice-water bath, and then the mixture was heated at 50 °C for 12 h. After cooling the reaction to an ambient temperature, the mixture was quenched with aqueous NH_4Cl. The resulting mixture was extracted with CH_2Cl_2. The CH_2Cl_2 phase was washed with water and brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 10 g; EtOAc/hexane, 3:17 v/v) to give the oily propargyl ether **15a** (492 mg, 80%). IR (ATR): $\tilde{\nu}$ = 3274 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.30 (t, J = 7.0 Hz, 9/4 H), 1.37 (t, J = 7.0 Hz, 3/4 H), 2.56 (d, J = 2.2 Hz, 3/4 H), 2.63–2.66 (m, 1/4 H), 3.40 (s, 3 H), 3.43 (s, 3 H), 3.88–3.98 (m, 5 H), 4.63–5.03 (m, 6 H), 5.73 (d, J = 7.0 Hz, 3/4 H), 5.85 (d, J = 2.2 Hz, 3/4 H), 6.13 (d, J = 12.7 Hz, 1/4 H), 6.23 (d, J = 7.0 Hz, 3/4 H), 6.55–6.61 (m, 5/4 H), 6.95–7.02 (m, 1 H), 8.65 (br. s, 1/4 H), 8.69 (br. s, 3/4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.8, 15.2, 55.4, 55.8, 56.0, 56.4, 59.6, 60.3, 65.1, 66.9, 67.0, 68.3, 74.1, 75.4, 80.3, 80.7, 93.6, 93.6, 94.7, 95.0, 97.2, 97.7, 101.7, 102.0, 109.6, 111.8, 122.3, 122.6, 122.8, 126.6, 126.8, 127.1, 129.8, 130.6, 145.1, 146.2, 149.3 ppm. MS (EI): m/z = 389 $[M]^+$. HRMS (EI): calcd. for $C_{21}H_{27}NO_6$ 389.1838; found 389.1841.

3-Ethoxyvinyl-7-isopropoxy-2-{[1-(methoxymethyloxy)prop-2-yn-1-yl]}-4-(methoxymethyloxy)methylindole (15b): The same procedure as above was carried out using propargyl alcohol **14b** (2.6 g, 6.88 mmol), iPr$_2$NEt (5.96 mL, 34.41 mmol), and MOMCl (1.57 mL, 20.64 mmol) to give the oily propargyl ether **15b** (2.4 g, 81%). IR (ATR): $\tilde{\nu}$ = 3280 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.31 (t, J = 7.0 Hz, 9/4 H), 1.38–1.46 (m, 27/4 H), 2.59 (d, J = 2.2 Hz, 3/4 H), 2.66 (d, J = 2.2 Hz, 1/4 H), 3.41–3.43 (m, 6 H), 3.88–3.98 (m, 2 H), 4.65–4.97 (m, 7 H), 5.72–5.75 (m, 1 H), 5.86 (d, J = 2.2 Hz, 3/4 H), 6.14 (d, J = 12.8 Hz, 1/4 H), 6.23 (d, J = 7.0 Hz, 3/4 H), 6.55–6.61 (m, 5/4 H), 6.94–7.00 (m, 1 H), 8.63 (s, 1/4 H), 8.67 (s, 3/4 H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 14.8, 15.2, 22.1 (2×), 22.1 (2×), 55.3, 55.7, 56.0, 59.6, 60.3, 65.0, 66.9, 67.0, 68.2, 70.0, 70.1, 74.1, 75.3, 80.4, 80.7, 93.6, 93.6, 94.7, 95.0, 97.3, 97.8, 103.8, 104.0, 109.5, 111.7, 122.1, 122.3, 122.3, 126.9, 127.2, 127.5, 127.8, 129.7, 130.5, 144.2, 144.3, 145.0 ppm. MS (EI): m/z = 417 [M]$^+$. HRMS (EI): calcd. for C$_{23}$H$_{31}$NO$_6$ 417.2151; found 417.2140.

3-Ethoxy-8-methoxy-1-methoxymethyloxy-5-(methoxymethyloxy)-methyl-2-methylcarbazole (16a): To a solution of propargyl ether **15a** (120 mg, 0.31 mmol) in dry THF (1 mL) was added TBAF (1 M in THF, 0.92 mL, 0.924 mmol) at room temperature, and then the mixture was heated at 80 °C for 6 h. After cooling the reaction to an ambient temperature, the mixture was quenched with water. The resulting mixture was extracted with EtOAc. The EtOAc phase was washed with water and brine, dried with Na$_2$SO$_4$, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 30 g; EtOAc/hexane, 1:9 v/v) to give carbazole **16a** (40 mg, 40%) as a yellow solid; m.p. 105–106 °C (EtOAc/hexane). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.48 (t, J = 7.0 Hz, 3 H), 2.33 (s, 3 H), 3.44 (s, 3 H), 3.75 (s, 3 H), 4.01 (s, 3 H), 4.15 (q, J = 7.0 Hz, 2 H), 4.76 (s, 2 H), 5.08 (s, 2 H), 5.23 (s, 2 H), 6.79 (d, J = 7.9 Hz, 1 H), 7.06 (d, J = 7.9 Hz, 1 H), 7.50 (s, 1 H), 9.25 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 9.8, 15.1, 55.5, 55.6, 57.1, 64.9, 67.9, 95.1, 98.6, 101.4, 104.5, 117.5, 120.6, 122.0, 123.1, 123.7, 127.1, 130.2, 142.0, 146.0, 151.9 ppm. MS (EI): m/z = 389 [M]$^+$. HRMS (EI): calcd. for C$_{21}$H$_{27}$NO$_6$ 389.1838; found 389.1827.

3-Ethoxy-8-isopropoxy-1-methoxymethyloxy-5-(methoxymethyloxy)-methyl-2-methylcarbazole (16b): The same procedure as above was carried out using propargyl ether **15b** (2.4 g, 5.63 mmol) and TBAF (1 M in THF, 16.9 mL, 16.9 mmol) to give carbazole **16b** (930 mg, 40%) as a pale yellow solid; m.p. 69–71 °C (Et$_2$O). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.44 (d, J = 6.1 Hz, 6 H), 1.49 (t, J = 7.0 Hz, 3 H), 2.34 (s, 3 H), 3.46 (s, 3 H), 3.75 (s, 3 H), 4.15 (q, J = 7.0 Hz, 2 H), 4.67–4.75 (m, 1 H), 4.78 (s, 2 H), 5.08 (s, 2 H), 5.23 (s, 2 H), 6.82 (d, J = 7.9 Hz, 1 H), 7.04 (d, J = 7.9 Hz, 1 H), 7.49 (s, 1 H), 9.28 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 9.8, 15.1, 22.3 (2×), 55.6, 57.0, 64.9, 67.9, 71.2, 95.1, 98.7, 101.5, 108.0, 117.5, 120.6, 122.0, 123.3, 123.7, 127.2, 131.6, 141.9, 144.1, 151.8 ppm. MS (EI): m/z = 417 [M]$^+$. HRMS (EI): calcd. for C$_{23}$H$_{31}$NO$_6$ 417.2151; found 417.2151.

3-Ethoxy-8-methoxy-1-methoxymethyloxy-2-methylcarbazole-5-carbaldehyde (17a): To a solution of carbazole **16a** (1.2 g, 3.08 mmol) in CH$_2$Cl$_2$ (30 mL) was added DDQ (839 mg, 3.70 mmol) at room temperature, and the resulting mixture was stirred at that temperature for 20 min. The reaction mixture was filtered through a pad of Celite. The filtrate was concentrated under reduced pressure, and the resulting residue was purified by column chromatography (silica gel, 40 g; EtOAc/hexane, 2:8 v/v) to give carbazole-5-carbaldehyde **17a** (1.0 g, 95%) as a pale yellow solid; m.p. 102–103 °C (EtOAc/hexane). IR (ATR): $\tilde{\nu}$ = 1650 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.50 (t, J = 7.0 Hz, 3 H), 2.35 (s, 3 H), 3.76 (s, 3 H), 4.11 (s, 3 H), 4.25 (q, J = 7.0 Hz, 2 H), 5.23 (s, 2 H), 6.96 (d, J = 8.0 Hz, 1 H), 7.68 (d, J = 8.0 Hz, 1 H), 8.49 (s, 1 H), 9.55 (br. s, 1 H), 10.20 (s, 1 H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 9.9, 15.0, 55.9, 57.1, 64.5, 98.7, 103.5, 104.1, 119.1, 121.9, 122.4, 125.7, 127.8, 130.1, 131.0, 141.7, 150.8, 151.7, 192.0 ppm. MS (EI): m/z = 343 [M]$^+$. HRMS (EI): calcd. for C$_{19}$H$_{21}$NO$_5$ 343.1420; found 343.1419.

3-Ethoxy-8-isopropoxy-1-methoxymethyloxy-2-methylcarbazole-5-carbaldehyde (17b): The same procedure as above was carried out using carbazole **16b** (2.3 g, 5.51 mmol) and DDQ (1.5 g, 6.61 mmol) to give carbazole-5-carbaldehyde **17b** (1.5 g, 73%) as a pale yellow solid; m.p. 130–131 °C (EtOAc). IR (ATR): $\tilde{\nu}$ = 1670 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.48–1.53 (m, 9 H), 2.35 (s, 3 H), 3.75 (s, 3 H), 4.25 (q, J = 7.0 Hz, 2 H), 4.82–4.94 (m, 1 H), 5.22 (s, 2 H), 6.93 (d, J = 8.3 Hz, 1 H), 7.63 (d, J = 8.3 Hz, 1 H), 8.48 (s, 1 H), 9.55 (br. s, 1 H), 10.18 (s, 1 H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 9.9, 15.1, 22.2 (2×), 57.0, 64.5, 71.2, 98.9, 103.6, 105.9, 119.2, 121.9, 122.5, 125.3, 128.0, 131.0, 141.7, 149.3, 151.6, 191.9 ppm. MS (EI): m/z = 371 [M]$^+$. HRMS (EI): calcd. for C$_{21}$H$_{25}$NO$_5$ 371.1733; found 371.1720.

3-Ethoxy-1-hydroxy-8-methoxy-2-methylcarbazole-5-carbaldehyde (18a): To a mixture of 5-formylcarbazole **17a** (940 mg, 2.74 mmol) and ethylene glycol (2 mL) in THF (20 mL) was added HCl (4 M solution, 2 mL) at room temperature. After stirring the reaction at 50 °C for 30 min, the mixture was cooled to an ambient temperature and then extracted with EtOAc. The EtOAc phase was washed with water and brine, dried with Na$_2$SO$_4$, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 10 g; EtOAc/hexane, 4:6 v/v) to give 1-hydroxycarbazole **18a** (730 mg, 89%) as a pale yellow solid; m.p. 234–236 °C (EtOAc/hexane). IR (ATR): $\tilde{\nu}$ = 3367, 1646 cm^{-1}. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 1.42 (t, J = 7.0 Hz, 3 H), 2.19 (s, 3 H), 4.06–4.11 (m, 5 H), 7.17 (d, J = 8.1 Hz, 1 H), 7.78 (d, J = 8.1 Hz, 1 H), 8.12 (s, 1 H), 8.99 (s, 1 H), 10.13 (s, 1 H), 10.85 (br. s, 1 H) ppm. ^{13}C NMR (300 MHz, [D$_6$]DMSO): δ = 9.2, 14.9, 55.9, 63.6, 98.4, 104.6, 111.6, 120.2, 121.1, 125.0, 125.3, 129.3, 131.0, 140.0, 150.7, 151.1, 192.0 ppm. MS (EI): m/z = 299 [M]$^+$. HRMS (EI): calcd. for C$_{17}$H$_{17}$NO$_4$ 299.1158; found 299.1153.

3-Ethoxy-1-hydroxy-8-isopropoxy-2-methylcarbazole-5-carbaldehyde (18b): The same procedure as above was carried out using 5-formylcarbazole **17b** (411 mg, 1.11 mmol) and HCl (4 M solution, 2 mL) to give 1-hydroxycarbazole **18b** (329 mg, 91%) as a pale yellow solid; m.p. 207–209 °C (EtOAc). IR (ATR): $\tilde{\nu}$ = 3320, 1650 cm^{-1}. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 1.38–1.46 (m, 9 H), 2.18 (s, 3 H), 4.08 (q, J = 7.0 Hz, 2 H), 4.97–5.05 (m, 1 H), 7.16 (d, J = 8.1 Hz, 1 H), 7.72 (d, J = 8.1 Hz, 1 H), 8.12 (br. s, 1 H), 9.08 (br. s, 1 H), 10.10 (s, 1 H), 10.65 (s, 1 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 9.6, 15.3, 22.2, 31.0, 64.1, 71.2, 99.0, 106.5, 112.1, 120.7, 121.6, 124.9, 125.4, 130.3, 131.8, 140.2, 149.4, 151.5, 192.5 ppm. MS (EI): m/z = 327 [M]$^+$. HRMS (EI): calcd. for C$_{19}$H$_{21}$NO$_4$ 327.1471; found 327.1484.

3-Ethoxy-8-methoxy-2-methyl-1-(trifluoromethylsulfonyloxy)carbazole-5-carbaldehyde (19a): To a stirred mixture of NaH (60%, 240 mg, 6.01 mmol) in THF (20 mL) was added 1-hydroxycarbazole **18a** (720 mg, 2.41 mmol) in THF (5 mL) with cooling by an ice-water bath. After stirring the resulting mixture at 0 °C for 10 min, Tf$_2$NPh (992 mg, 2.65 mmol) was added to the reaction mixture at the same temperature. The stirring was continued at the same temperature for an additional 30 min, and then the mixture was quenched with aqueous NH$_4$Cl. The resulting soluton was extracted with EtOAc. The EtOAc phase was washed with water and

brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 10 g; EtOAc/hexane, 1:9 v/v) to give triflate **19a** (800 mg, 77%) as a pale yellow solid; m.p. 165–167 °C (EtOAc/hexane). IR (ATR): $\tilde{\nu}$ = 1680, 1400, 1210 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.52 (t, J = 7.0 Hz, 3 H), 2.42 (s, 3 H), 4.13 (s, 3 H), 4.29 (q, J = 7.0 Hz, 2 H), 7.02 (d, J = 8.3 Hz, 1 H), 7.73 (d, J = 8.3 Hz, 1 H), 8.59 (br. s, 1 H), 8.82 (s, 1 H), 10.14 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.3, 14.9, 56.0, 64.9, 105.1, 108.1, 116.6, 121.4, 121.6, 123.4, 125.7, 127.0, 130.6, 131.4, 132.5, 150.9, 151.6, 191.9 ppm. MS (EI): m/z = 431 $[M]^+$. HRMS (EI): calcd. for $C_{18}H_{16}F_3NO_6S$ 431.0650; found 431.0658.

3-Ethoxy-8-isopropoxy-2-methyl-1-(trifluoromethylsulfonyloxy)carbazole-5-carbaldehyde (19b): The same procedure as above was carried out using NaH (60%, 37 mg, 0.92 mmol), 1-hydroxycarbazole **18b** (200 mg, 0.68 mmol) in THF (5 mL), and Tf_2NPh (254 mg, 0.68 mmol) to give triflate **19b** (310 mg, 99%) as a pale yellow solid; m.p. 131–133 °C (EtOAc). IR (ATR): $\tilde{\nu}$ = 1680, 1400, 1210 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.50–1.54 (m, 9 H), 2.42 (s, 3 H), 4.28 (q, J = 7.0 Hz, 2 H), 4.87–4.95 (m, 1 H), 7.01 (d, J = 8.3 Hz, 1 H), 7.70 (d, J = 8.3 Hz, 1 H), 8.59 (br. s, 1 H), 8.82 (s, 1 H), 10.12 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.4, 14.9, 22.1 (2×), 64.8, 71.6, 106.6, 108.1, 121.2, 121.8, 123.4, 125.2, 126.9, 131.3, 131.5, 132.5, 149.4, 151.5, 191.9 ppm. MS (EI): m/z = 459 $[M]^+$. HRMS (EI): calcd. for $C_{20}H_{20}F_3NO_6S$ 459.0963; found 459.0966.

3-Hydroxy-8-methoxy-2-methyl-1-(trifluoromethylsulfonyloxy)carbazole-5-carbaldehyde (20a): To a solution of triflate **19a** (50 mg, 0.12 mmol) in CH_2Cl_2 (10 mL) was added BBr_3 (57 µL, 0.58 mmol) at –78 °C. After stirring at room temperature for 3 h, the reaction mixture was poured into ice water. The mixture was extracted with EtOAc. The EtOAc phase was washed with water and brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 10 g; EtOAc/hexane, 2:8 v/v) to give 3-hydroxycarbazole **20a** (28 mg, 60%) as a pale yellow solid; m.p. 280–284 °C (EtOAc/hexane). IR (ATR): $\tilde{\nu}$ = 3200, 1650 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.29 (s, 3 H), 4.11 (s, 3 H), 7.25 (d, J = 8.3 Hz, 1 H), 7.85 (d, J = 8.3 Hz, 1 H), 8.65 (s, 1 H), 9.78 (s, 1 H), 10.09 (s, 1 H), 11.61 (s, 1 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$): δ = 11.0, 56.3, 106.2, 110.0, 116.1, 118.9, 120.3, 123.3, 125.2, 126.9, 127.0, 131.0, 132.7, 148.9, 151.3, 192.4 ppm. MS (EI): m/z = 403 $[M]^+$. HRMS (EI): calcd. for $C_{16}H_{12}F_3NO_6S$ 403.0337; found 403.0331.

3,8-Dihydroxy-2-methyl-1-(trifluoromethylsulfonyloxy)carbazole-5-carbaldehyde (20b): To a solution of triflate **19b** (64 mg, 0.14 mmol) in CH_2Cl_2 (10 mL) was added BBr_3 (136 µL, 1.39 mmol) at –78 °C. After stirring at room temperature for 5 h, the reaction mixture was poured into ice water. The mixture was extracted with EtOAc. The EtOAc phase was washed with water and brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 10 g; EtOAc/hexane, 4:6 v/v) to give 3-hydroxycarbazole **20b** (54 mg, 99%) as a pale yellow solid; m.p. 266–268 °C (EtOAc/hexane). IR (ATR): $\tilde{\nu}$ = 3200, 1650 cm^{-1}. ^1H NMR (300 MHz, [D$_6$]DMSO): δ = 2.28 (s, 3 H), 7.02 (d, J = 8.1 Hz, 1 H), 7.72 (d, J = 8.1 Hz, 1 H), 8.65 (s, 1 H), 10.00 (s, 1 H), 11.35 (s, 1 H), 11.39 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 11.1, 110.2, 110.4, 116.3, 119.0, 121.2, 123.6, 124.1, 127.1, 130.9, 132.7, 133.2, 149.0, 150.3, 192.1 ppm. MS (EI): m/z = 389 $[M]^+$. HRMS (EI): calcd. for $C_{15}H_{10}F_3NO_6S$ 389.0181; found 389.0179.

2-Methyl-1-trifluoromethylsulfonyloxy-3,8-bis[(2-trimethylsilyl)ethoxymethyloxy]carbazole-5-carbaldehyde (21): To a solution of 3,8-dihydroxycarbazole **20b** (115 mg, 0.30 mmol) in CH_2Cl_2 (10 mL) was added SEMCl (157 µL, 0.89 mmol) and iPr$_2$NEt (256 µL, 1.48 mmol) with cooling by an ice-water bath. After stirring at room temperature for 12 h, the reaction mixture was quenched with aqueous NH_4Cl. The resulting mixture was extracted with CH_2Cl_2. The organic layer was washed with water and brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 10 g; EtOAc/hexane, 1:19 v/v) to give the oily SEM ether **21** (187 mg, 97%). IR (ATR): $\tilde{\nu}$ = 1690, 1400, 1210, 1040 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 0.01 (s, 9 H), 0.01 (s, 9 H), 0.99–1.08 (m, 4 H), 2.44 (s, 3 H), 3.88 (t, J = 8.3 Hz, 4 H), 5.43 (s, 2 H), 5.51 (s, 2 H), 7.29 (d, J = 8.1 Hz, 1 H), 7.72 (d, J = 8.1 Hz, 1 H), 8.77 (br. s, 1 H), 8.98 (s, 1 H), 10.18 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –1.5 (3×), –1.4 (3×), 10.6, 18.1, 18.1, 66.7, 67.4, 93.6, 94.4, 109.3, 111.8, 116.5, 120.8, 122.2, 123.5, 126.3, 128.0, 131.0, 131.2, 131.6, 148.5, 149.6, 191.7 ppm. MS (EI): m/z = 649 $[M]^+$. HRMS (EI): calcd. for $C_{27}H_{38}NO_8SSi_2$ 649.1809; found 649.1779.

1-Iodo-2,5-dimethylhex-1-ene (23a): To a solution of Cp_2ZrCl_2 (608 mg, 2.08 mmol) in dry 1,2-dichloroethane (4 mL) was added Me_3Al (15% in hexane, 4.46 mL, 6.24 mmol) at room temperature, and the resulting mixture was stirred at the same temperature for 20 min. A solution of 5-methyl-1-hexyne (**22a**, 0.274 mL, 2.08 mmol) in dry 1,2-dichloroethane (2 mL) was added, and the mixture was stirred at the same temperature for 12 h and then cooled to 0 °C. A solution of I_2 (633 mg, 2.50 mmol) in dry THF (4 mL) was added dropwise. After stirring at room temperature for 1 h, the reaction was poured into ice water, and the resulting mixture was filtered through a pad of Celite. The filtrate was extracted with EtOAc. The organic layer was washed with water and brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 20 g; hexane) to give the oily alkenyl iodide **23a** (390 mg, 79%). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.89 (d, J = 6.6 Hz, 6 H), 1.26–1.35 (m, 3 H), 1.45–1.55 (m, 1 H), 1.83 (d, J = 1.1 Hz, 3 H), 2.20 (dt, J = 1.1, 7.7 Hz, 2 H), 5.86 (q, J = 1.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.4 (2×), 23.9, 27.5, 36.9, 37.5, 74.2, 148.5 ppm. MS (EI): m/z = 238 $[M]^+$. HRMS (EI): calcd. for $C_8H_{15}I$ 238.0218; found 238.0222.

1-Iodo-2,5-dimethylhept-1-ene (23b): The same procedure as above was carried out using (*S*)-(+)-5-methyl-1-heptyne (**22b**,[5,17] 300 mg, 2.72 mmol), Cp_2ZrCl_2 (796 mg, 2.72 mmol), Me_3Al (15% in hexane, 5.8 mL, 8.17 mmol), and I_2 (829 mg, 3.27 mmol) to give the oily alkenyl iodide **23b** (400 mg, 58%). $[a]_D^{20}$ = +13.1 (c = 0.05, MeOH). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.84–0.88 (m, 6 H), 1.07–1.49 (m, 5 H), 1.83 (d, J = 1.1 Hz, 3 H), 2.14–2.23 (m, 2 H), 5.86 (q, J = 1.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.3, 19.0, 23.9, 29.3, 33.9, 34.5, 37.2, 74.2, 148.6 ppm. MS (EI): m/z = 252 $[M]^+$. HRMS (EI): calcd. for $C_9H_{17}I$ 252.0375; found 252.0372.

Pinacol (2,5-Dimethylhex-1-en-1-yl)boronate (3a): A solution of alkenyl iodide **23b** (100 mg, 0.42 mmol) in dry DMSO (20 mL) was added to a stirred suspension of bis(pinacolato)diboron (106 mg, 0.42 mmol), KOAc (124 mg, 1.26 mmol), and $PdCl_2$(dppf) [3 mg, 0.0042 mmol, dppf = 1,1′-bis(diphenylphosphanyl)ferrocene] in dry DMSO (20 mL) at room temperature, and then the mixture was heated at 80 °C for 1 h. After cooling to an ambient temperature, the reaction was quenched with aqueous NH_4Cl, and the resulting mixture was stirred at the same temperature for 30 min. After filtering the mixture through a pad of Celite, the filtrate was extracted with EtOAc. The EtOAc layer was washed with water and brine, dried with Na_2SO_4, and concentrated under reduced pressure. The

residue was purified by column chromatography (silica gel, 20 g; EtOAc/hexane, 1:19 v/v) to give the oily pinacol 1-alkenylboronate **3a** (48 mg, 48%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.87 (d, J = 6.6 Hz, 6 H), 1.19–1.36 (m, 14 H), 1.49–1.57 (m, 1 H), 1.97 (s, 1 H), 2.09 (t, J = 7.7 Hz, 2 H), 5.11 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.2, 22.6 (2×), 24.9 (4×), 27.7, 36.9, 40.0, 82.6 (2×), 163.6 ppm. The carbon signal adjacent to boron was not observed because of low intensity.[19] MS (EI): m/z = 238 $[M]^+$. HRMS (EI): calcd. for $C_{14}H_{27}BO_2$ 238.2104; found 238.2100.

Pinacol (2,5-Dimethylhept-1-en-1-yl)boronate (3b): The same procedure as above was carried out using alkenyl iodide **23b** (200 mg, 0.79 mmol), bis(pinacolato)diboron (201 mg, 0.79 mmol), KOAc (234 mg, 2.38 mmol), and $PdCl_2$(dppf) (6 mg, 0.0079 mmol) to give the oily pinacol 1-alkenylboronate **3b** (101 mg, 53%). $[\alpha]_D^{20}$ = +26.5 (c = 0.05, MeOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83–0.87 (m, 6 H), 1.05–1.52 (m, 17 H), 1.98 (d, J = 1.1 Hz, 1 H), 2.01–2.12 (m, 2 H), 5.12 (d, J = 1.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.3, 19.1, 21.2, 24.9 (4×), 29.37, 34.1, 34.5, 39.7, 82.6 (2×), 163.7 ppm. The carbon signal adjacent to boron was not observed because of low intensity.[19] MS (EI): m/z = 252 $[M]^+$. HRMS (EI): calcd. for $C_{15}H_{29}BO_2$ 252.2261; found 252.2258.

3-Ethoxy-1-(2,5-dimethylhex-1-en-1-yl)-8-methoxy-2-methylcarbazole-5-carbaldehyde (24a): To a stirred mixture of triflate **19a** (100 mg, 0.23 mmol), Na_2CO_3 (74 mg, 0.70 mmol), and $Pd(PPh_3)_4$ (3 mg, 0.0023 mmol) in dry DMF (5 mL) was added a solution of pinacol 1-alkenylboronate **3a** (166 mg, 0.70 mmol) in dry DMF (15 mL) at room temperature. The mixture was heated at 80 °C for 3 h and then was cooled to an ambient temperature. The mixture was quenched with aqueous NH_4Cl, and the resulting mixture was stirred at the same temperature for 30 min. After filtration through a pad of Celite, the filtrate was extracted with EtOAc. The EtOAc phase was washed with water and brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 5 g; EtOAc/hexane, 1:14 v/v) to give 1-alkenylcarbazole **24a** (88 mg, 96%) as a pale yellow solid; m.p. 130–132 °C (Et_2O/hexane). IR (ATR): $\tilde{\nu}$ = 1660 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.01 (d, J = 6.6 Hz, 6 H), 1.49–1.57 (m, 9 H), 1.64–1.75 (m, 1 H), 2.28 (s, 3 H), 2.35 (t, J = 7.0 Hz, 2 H), 4.11 (s, 3 H), 4.26 (q, J = 7.0 Hz, 2 H), 6.33 (s, 1 H), 6.95 (d, J = 8.1 Hz, 1 H), 7.68 (d, J = 8.1 Hz, 1 H), 8.11 (br. s, 1 H), 8.58 (s, 1 H), 10.22 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.5, 15.1, 17.8, 22.6 (2×), 27.9, 37.2, 37.4, 55.8, 64.3, 103.9, 106.0, 118.9, 119.8, 121.6, 125.7, 126.5, 129.8, 130.7, 130.7, 133.6, 143.2, 150.4, 151.7, 192.0 ppm. MS (EI): m/z = 393 $[M]^+$. HRMS (EI): calcd. for $C_{25}H_{31}NO_3$ 393.2304; found 393.2302.

3-Ethoxy-8-isopropoxy-1-(2,5-dimethylhex-1-en-1-yl)-2-methylcarbazole-5-carbaldehyde (24b): The same procedure as above was carried out using triflate **19b** (20 mg, 0.44 mmol), Na_2CO_3 (14 mg, 0.131 mmol), $Pd(PPh_3)_4$ (5 mg, 0.0044 mmol), and pinacol 1-alkenylboronate **3a** (31 mg, 0.131 mmol) to give 1-alkenylcarbazole **24b** (18 mg, 99%) as a pale yellow solid; m.p. 84–86 °C (EtOAc/hexane). IR (ATR): $\tilde{\nu}$ = 1670 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.02 (d, J = 6.6 Hz, 6 H), 1.49–1.55 (m, 9 H), 1.68–1.76 (m, 1 H), 2.29 (s, 3 H), 2.37 (t, J = 7.9 Hz, 1 H), 4.26 (q, J = 7.0 Hz, 2 H), 4.86–4.94 (m, 1 H), 6.35 (s, 1 H), 6.93 (d, J = 8.0 Hz, 1 H), 7.64 (d, J = 8.0 Hz, 1 H), 8.06 (br. s, 1 H), 8.58 (s, 1 H), 10.20 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.5, 15.1, 17.7, 22.2 (2×), 22.7 (2×), 27.8, 37.3, 37.4, 64.3, 71.1, 105.5, 106.1, 119.3, 119.9, 121.5, 122.8, 125.2, 126.5, 130.6, 130.7, 133.5, 143.0, 148.9, 151.7, 191.9 ppm. MS (EI): m/z = 421 $[M]^+$. HRMS (EI): calcd. for $C_{27}H_{35}NO_3$ 421.2617; found 421.2600.

1-(2,5-Dimethylhex-1-en-1-yl)-2-methyl-3,8-bis[(2-trimethylsilyl)ethoxymethyloxy]carbazole-5-carbaldehyde (25a): The same procedure as above was carried out using SEM ether **21** (75 mg, 0.12 mmol), Na_2CO_3 (3 M solution, 115 μL, 0.35 mmol), $Pd(PPh_3)_4$ (1.39 mg, 0.0012 mmol), and pinacol 1-alkenylboronate **3a** (72 mg, 0.35 mmol) to give the oily 3,8-bis(OSEM)-1-alkenylcarbazole **25a** (61 mg, 86%). IR (ATR): $\tilde{\nu}$ = 1680, 1060 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.01 (s, 9 H), 0.02 (s, 9 H), 0.88–0.94 (m, 1 H), 0.99–1.10 (m, 10 H), 1.53 (s, 3 H), 1.64–1.76 (m, 2 H), 2.32 (s, 3 H), 2.36 (t, J = 7.3 Hz, 1 H), 3.88 (q, J = 8.4 Hz, 4 H), 5.42 (s, 2 H), 5.49 (s, 2 H), 6.34 (s, 1 H), 7.19 (d, J = 7.2 Hz, 1 H), 7.66 (d, J = 7.2 Hz, 1 H), 8.33 (br. s, 1 H), 8.70 (s, 1 H), 10.28 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –1.4 (6×), 13.7, 17.8, 18.1, 18.1, 22.6 (2×), 27.9, 37.2, 37.3, 66.3, 67.1, 93.5, 94.4, 108.2, 109.7, 118.9, 119.8, 121.5, 123.2, 126.3, 127.3, 129.5, 130.3, 134.4, 143.2, 148.0, 149.8, 191.7 ppm. MS (EI): m/z = 611 $[M]^+$. HRMS (EI): calcd. for $C_{34}H_{53}NO_5SSi_2$ 611.3462; found 611.3470.

1-(2,5-Dimethylhept-1-en-1-yl)-2-methyl-3,8-bis[(2-trimethylsilyl)ethoxymethyloxy]carbazole-5-carbaldehyde (25b): The same procedure as above was carried out using SEM ether **21** (75 mg, 0.12 mmol), Na_2CO_3 (3 M solution, 115 μL, 0.35 mmol), $Pd(PPh_3)_4$ (1 mg, 0.0012 mmol), and pinacol 1-alkenylboronate **3b** (87 mg, 0.346 mmol) to give the oily 3,8-bis(OSEM)-1-alkenylcarbazole **25b** (60 mg, 83%). $[\alpha]_D^{20}$ = +7.1 (c = 0.05, MeOH). IR (ATR): $\tilde{\nu}$ = 1680, 1080 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.01 (s, 9 H), 0.02 (s, 9 H), 0.83–0.90 (m, 1 H), 0.94–1.09 (m, 10 H), 1.22–1.31 (m, 1 H), 1.41–1.51 (m, 2 H), 1.53 (d, J = 0.7 Hz, 3 H), 1.62–1.71 (m, 1 H), 2.31 (s, 3 H), 2.37 (t, J = 6.6 Hz, 1 H), 3.88 (q, J = 8.4 Hz, 4 H), 5.41 (s, 2 H), 5.49 (s, 2 H), 6.34 (s, 1 H), 7.20 (d, J = 8.1 Hz, 1 H), 7.66 (d, J = 8.1 Hz, 1 H), 8.29 (br. s, 1 H), 8.68 (s, 1 H), 10.29 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –1.5 (3×), –1.4 (3×), 11.5, 13.7, 17.8, 18.1, 18.1, 19.2, 29.4, 34.2, 34.9, 36.9, 66.3, 67.1, 93.4, 94.4, 108.1, 109.7, 119.0, 119.9, 121.5, 123.2, 126.3, 127.3, 129.5, 130.3, 134.4, 143.1, 148.0, 149.8, 191.6 ppm. MS (EI): m/z = 625 $[M]^+$. HRMS (EI): calcd. for $C_{35}H_{55}NO_5SSi_2$ 625.3619; found 625.3621.

1-(2,5-Dimethylhex-1-en-1-yl)-5-hydroxymethyl-2-methyl-3,8-bis[(2-trimethylsilyl)ethoxymethyloxy]carbazole (26): To a solution of 3,8-bis(OSEM)-1-alkenylcarbazole **25a** (75 mg, 0.12 mmol) in dry toluene (1 mL) was added DIBAL-H (0.99 M in toluene, 247 μL, 0.25 mmol) with cooling by an ice-water bath. After stirring at room temperature for 20 min, the reaction mixture was poured into ice water. The mixture was filtered through a pad of Celite, and then the filtrate was extracted with EtOAc. The EtOAc phase was washed with water and brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 5 g; EtOAc/hexane, 3:7 v/v) to give the oily 5-hydroxymethylcarbazole **26** (68 mg, 90%). IR (ATR): $\tilde{\nu}$ = 3460, 1060 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.02 (s, 9 H), 0.02 (s, 9 H), 1.00–1.06 (m, 10 H), 1.54 (t, J = 10.0 Hz, 5 H), 1.66–1.75 (m, 1 H), 2.29 (s, 3 H), 2.34 (t, J = 7.7 Hz, 2 H), 3.86 (t, J = 8.1 Hz, 4 H), 5.18 (s, 2 H), 5.34 (s, 2 H), 5.38 (s, 2 H), 6.33 (s, 1 H), 7.01–7.07 (m, 2 H), 7.82 (s, 1 H), 8.36 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –1.4 (3×), –1.4 (3×), 13.5, 17.9, 18.1, 18.2, 22.6, 27.9, 37.3, 37.4, 64.1, 66.1, 66.7, 94.1, 94.6, 107.1, 109.9, 118.7, 119.1, 119.7, 121.9, 123.0, 125.3, 128.6, 130.6, 133.7, 142.9, 143.2, 150.2 ppm. MS (EI): m/z = 613 $[M]^+$. HRMS (EI): calcd. for $C_{34}H_{53}NO_5SSi_2$ 613.3619; found 613.3614.

3,8-Dihydroxy-2-methyl-1-(2,5-dimethylhex-1-en-1-yl)carbazole-5-carbaldehyde (27a): To a solution of 3,8-bis(OSEM)-1-alkenylcarbazole **25a** (83 mg, 0.14 mmol) in dry HMPA (2 mL) was added TBAF (1 M in THF, 678 μL, 0.68 mmol) at room temperature. The mixture was heated at 100 °C for 1 h and then was cooled to an ambient temperature. The mixture was quenched with water, and

the resulting mixture was extracted with EtOAc. The EtOAc phase was washed with water and brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 5 g; EtOAc/hexane, 1:1 v/v) to give 3,8-dihydroxycarbazole **27a** (34 mg, 71%) as a pale yellow solid; m.p. 248–250 °C (EtOAc/hexane). IR (ATR): $\tilde{\nu}$ = 3430, 1650 cm^{-1}. ^1H NMR (300 MHz, [D_6]DMSO): δ = 0.97 (d, J = 6.2 Hz, 6 H), 1.44 (s, 3 H), 1.51 (t, J = 7.7 Hz, 2 H), 1.60–1.69 (m, 1 H), 2.13 (s, 3 H), 2.28–2.33 (m, 2 H), 6.38 (s, 1 H), 6.91 (d, J = 8.1 Hz, 1 H), 7.61 (d, J = 8.1 Hz, 1 H), 8.39 (s, 1 H), 8.99 (s, 1 H), 10.03 (s, 1 H), 10.27 (s, 1 H), 10.78 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.7, 17.8, 22.6, 27.5 (2×), 36.74 (2×), 107.7, 109.0, 119.2, 119.6, 121.5, 121.8, 123.8, 123.8, 129.3, 131.3, 133.4, 141.5, 148.7, 149.3, 191.4 ppm. MS (EI): m/z = 351 $[M]^+$. HRMS (EI): calcd. for $C_{22}H_{25}NO_3$ 351.1834; found 351.1804.

3,8-Dihydroxy-2-methyl-1-(2,5-dimethylhept-1-en-1-yl)carbazole-5-carbaldehyde (27b): To a solution of 3,8-bis(OSEM)-1-alkenylcarbazole **25b** (50 mg, 0.08 mmol) in dry HMPA (2 mL) was added TBAF (1 M in THF, 399 μL, 0.39 mmol) at room temperature. The mixture was heated at 100 °C for 1 h and then was cooled to an ambient temperature. The mixture was quenched with water, and the resulting mixture was extracted with EtOAc. The EtOAc phase was washed with water and brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 5 g; EtOAc/hexane, 1:4 v/v) to give 3,8-dihydroxycarbazole **27b** (20 mg, 67%) as a pale yellow solid; m.p. 222–224 °C (EtOAc/hexane). $[\alpha]_D^{20}$ = +20.0 (c = 0.05, MeOH). IR (ATR): $\tilde{\nu}$ = 3420, 1640 cm^{-1}. ^1H NMR (300 MHz, [D_6]DMSO): δ = 0.91 (t, J = 7.2 Hz, 3 H), 0.96 (d, J = 6.1 Hz, 3 H), 1.18–1.27 (m, 1 H), 1.42–1.48 (m, 6 H), 1.61–1.68 (m, 1 H), 2.15 (s, 3 H), 2.27–2.35 (m, 2 H), 6.39 (s, 1 H), 6.92 (d, J = 7.9 Hz, 1 H), 7.62 (d, J = 7.9 Hz, 1 H), 8.39 (s, 1 H), 8.98 (s, 1 H), 10.04 (s, 1 H), 10.24 (s, 1 H), 10.77 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, [D_6]-DMSO): δ = 11.3, 13.7, 17.8, 19.1, 28.9, 33.7, 34.3, 36.4, 107.7, 109.0, 119.3, 119.6, 121.5, 121.9, 123.8, 123.8, 129.3, 131.2, 133.3, 141.5, 148.7, 149.2, 191.4 ppm. MS (EI): m/z = 365 $[M]^+$. HRMS (EI): calcd. for $C_{23}H_{27}NO_3$ 365.1991; found 365.1989.

Carbazomadurin A (1a): To a solution of 3,8-dihydroxycarbazole **27a** (62 mg, 0.18 mmol) in MeOH was added $NaBH_4$ (8 mg, 0.22 mmol) at room temperature. After stirring at that temperature for 5 min, the reaction mixture was concentrated under reduced pressure. Water was added, and the resulting mixture was extracted with EtOAc. The organic layer was washed with water and brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was recrystallized with chloroform/hexane to give carbazomadurin A (**1a**, 44 mg, 70%) as a pale yellow solid; m.p. 167–169 °C ($CHCl_3$/hexane). IR (ATR): $\tilde{\nu}$ = 3480, 3420, 1640, 1580, 1430, 1370 cm^{-1}. ^1H NMR (300 MHz, CD_3COCD_3): δ = 0.99 (d, J = 6.2 Hz, 6 H), 1.55 (s, 3 H), 1.63–1.73 (m, 1 H), 2.25 (s, 3 H), 2.34 (t, J = 7.7 Hz, 2 H), 3.89 (t, J = 5.5 Hz, 1 H), 5.00 (d, J = 5.9 Hz, 2 H), 6.42 (s, 1 H), 6.71 (d, J = 7.7 Hz, 1 H), 6.90 (d, J = 7.7 Hz, 1 H), 7.57 (s, 1 H), 7.78 (br. s, 1 H), 8.35 (br. s, 1 H), 8.88 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, CD_3COCD_3): δ = 13.6, 18.0, 22.9, 28.6, 37.8, 38.0, 63.9, 107.1, 109.7, 118.9, 120.4, 121.5, 122.4, 122.5, 123.7, 128.5, 130.6, 133.6, 133.7, 142.8, 143.0, 150.0 ppm. MS (EI): m/z = 353 $[M]^+$. HRMS (EI): calcd. for $C_{22}H_{27}NO_3$ 353.1991; found 353.1975.

(*S*)-(+)-Carbazomadurin B (1b): To a solution of 3,8-dihydroxycarbazole **27b** (70 mg, 0.19 mmol) in MeOH (4 mL) was added $NaBH_4$ (9 mg, 0.23 mmol) at room temperature. After stirring at that temperature for 5 min, the reaction mixture was concentrated under reduced pressure. Water was added, and the resulting mixture was extracted with EtOAc. The organic layer was washed with water and brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was recrystallized with $CHCl_3$/hexane to give carbazomadurin B (**1b**, 55 mg, 78%) as a pale yellow solid, m.p. 166–167 °C ($CHCl_3$/hexane); ref.[3] m.p. 108–110 °C; ref.[5] m.p. 165 °C. $[\alpha]_D^{20}$ = +13.1 (c = 0.05, MeOH). IR (ATR): $\tilde{\nu}$ = 3480, 3430, 1630, 1580, 1430, 1370 cm^{-1}. ^1H NMR (500 MHz, CD_3COCD_3): δ = 0.95 (t, J = 7.3 Hz, 3 H), 1.00 (d, J = 6.1 Hz, 3 H), 1.22–1.29 (m, 1 H), 1.44–1.52 (m, 3 H), 1.57 (d, J = 1.2 Hz, 3 H), 1.68–1.74 (m, 1 H), 2.27 (s, 3 H), 2.32–2.43 (m, 2 H), 3.90 (t, J = 5.5 Hz, 1 H), 5.02 (d, J = 5.2 Hz, 2 H), 6.44 (s, 1 H), 6.74 (d, J = 7.6 Hz, 1 H), 6.93 (d, J = 7.6 Hz, 1 H), 7.60 (s, 1 H), 7.78 (br. s, 1 H), 8.37 (br. s, 1 H), 8.86 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz, CD_3COCD_3): δ = 11.4, 13.2, 17.6, 19.1, 29.8, 34.7, 35.4, 37.2, 63.5, 106.8, 109.4, 118.6, 120.1, 121.2, 122.1, 122.2, 123.3, 128.2, 130.3, 133.4, 142.5, 142.6, 149.7 ppm. MS (EI): m/z = 367 $[M]^+$. HRMS (EI): calcd. for $C_{23}H_{29}NO_3$ 367.2147; found 367.2154.

Supporting Information (see footnote on the first page of this article): Copies of the ^1H and ^{13}C NMR spectra of all compounds.

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