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Total Syntheses of Murrayamine E, I, and K

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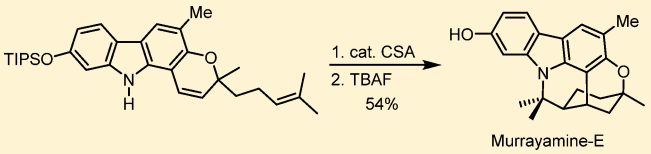
Supporting Information

ABSTRACT: We describe efficient synthetic routes to murrayamine A (mukoenine C), *O*-methylmurrayamine A, mahanine, *O*-methylmahanine, and murrayamine D and the first total syntheses of murrayamine E, I, and K. Key steps are a palladium-catalyzed construction of the carbazole framework and an annulation of the pyran ring, which is either catalyzed by phenylboronic acid or promoted by a Lewis acid.



INTRODUCTION

Pyranocarbazole alkaloids have been mainly isolated from terrestrial plants of the genera *Murraya* and *Clausena*, which are applied in traditional Asian medicine.[1] It is assumed that carbazole alkaloids play a pivotal role in the beneficial effects of those plants. Murrayamine A (**1**) was first isolated in 1991 by Wu[2] from *Murraya euchrestifolia* (Figure 1). Two years later, Furukawa and co-workers[3] obtained the same alkaloid from *Murraya koenigii* and named it mukoenine C (**1**). In the course of the structural elucidation, Wu[2] described the O-methylation of **1** to provide *O*-methylmurrayamine A (**2**), which was isolated as a natural product in 2003 by Nakatani and co-workers[4] from the leaves of *M. koenigii*. The geranyl-derived pyranocarbazole mahanine (**3**) has been isolated from the same natural sources as **1**. In 1991, Wu[2] isolated (+)-**3** from the leaves of *M. euchrestifolia* and assigned an (*S*)-configuration based on the Cotton effect.[5] (−)-Mahanine [(−)-**3**] had been isolated already in 1970 by Narasimhan et al.[6] from the leaves of *M. koenigii*. More than 30 years later, Nakatani and co-workers[7] obtained the enantiomer (+)-**3** from the same species. The corresponding O-methyl derivative (±)-**4** was first described as a synthetic compound by Kapil and co-workers in 1972.[8] In 2003, Nakatani and co-workers[4] obtained (+)-*O*-methylmahanine [(+)-**4**] from the leaves of *M. koenigii*. However, the value for the optical rotation was very small ($[\alpha]_D^{25}$ = +3.0, *c* 0.10, $CHCl_3$) and the authors did not comment on the absolute configuration. Murrayamine D (**5**) and murrayamine E (**6**) were first isolated in 1995 by Wu et al.[9] from the leaves of *M. euchrestifolia*. Compound **6** was reported to be optically active ($[\alpha]_D$ = +39.68, *c* 0.133, $CHCl_3$). The authors did not comment on the optical activity of **5**. According to our previous findings,[10] both alkaloids may derive from a Brønsted acid-catalyzed cyclization of mahanine (**3**).[10] The acetoxy-substituted alkaloids murrayamine I (**7**) and murrayamine K (**8**) were also isolated in 1996 by Wu et al.[11] from *M. euchrestifolia*. The authors did not report whether **7** and **8** were optically active. Herein, we describe our route to the pyrano[3,2-*a*]carbazoles **1**−**5** and the first synthetic access to the pyranocarbazoles **6**−**8** (Figure 1).

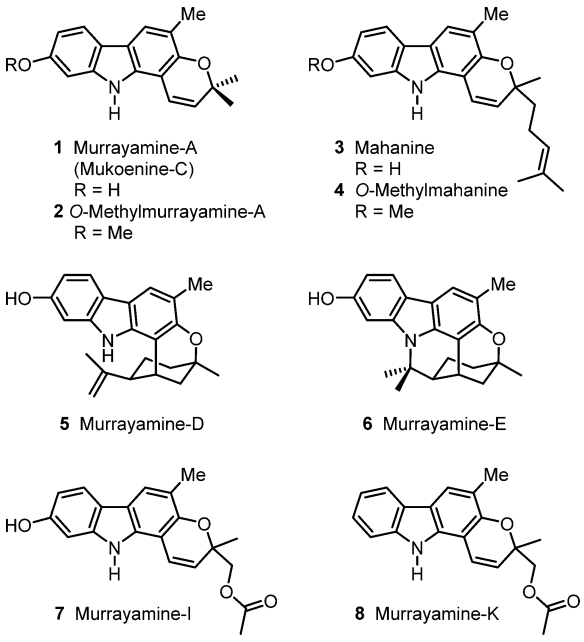


Figure 1. Naturally occurring 7-oxygenated pyrano[3,2-*a*]carbazole alkaloids **1**−**7** and murrayamine K (**8**).

RESULTS AND DISCUSSION

Our approach to the natural products **1**−**7** relies on a late-stage pyran ring annulation at the protected 2-hydroxycarbazole **13**, which is readily available via our palladium-catalyzed construction of the carbazole skeleton (Scheme 1).[12] Buchwald−Hartwig amination[13] of the silyl-protected bromophenol **9** with the aniline **10a**,[10] using catalytic amounts of palladium(II) acetate and racemic 2,2′-bis(diphenylphosphino)-1,1′-bi-

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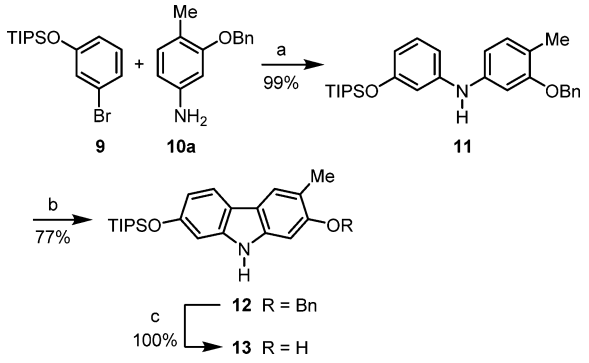
Scheme 1. Synthesis of the 2-Hydroxycarbazole 13[a]



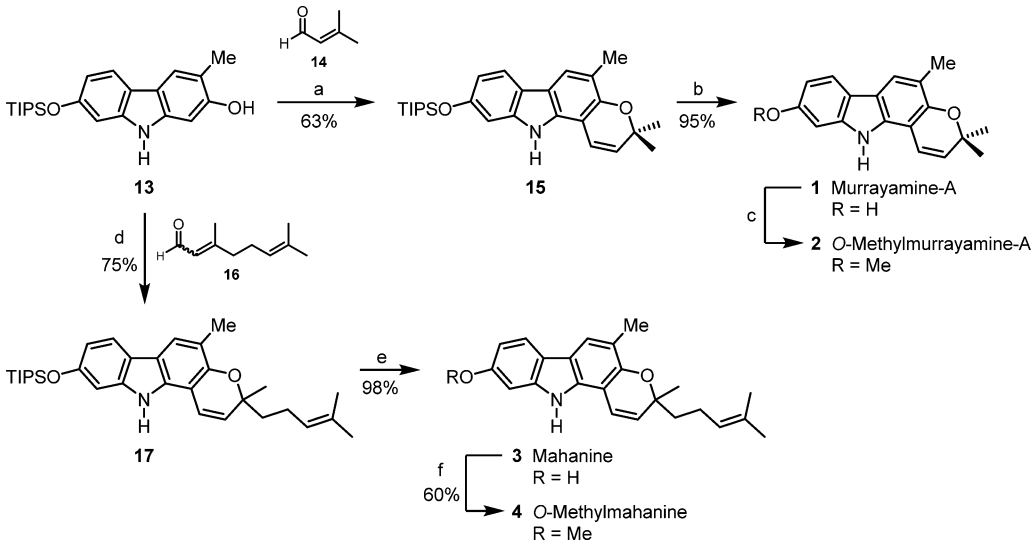
[a]Reagents and conditions: (a) 1.0 equiv of **9**, 1.2 equiv of **10a**, 6 mol % $Pd(OAc)_2$, 6 mol % *rac*-BINAP, 1.5 equiv of Cs_2CO_3, PhMe, reflux, 23.5 h. (b) 10 mol % $Pd(OAc)_2$, 2.5 equiv of $Cu(OAc)_2$, AcOH, microwave, 300 W, 130 °C, 2 h. (c) 20 wt % Pd/C, H_2 (1 atm), MeOH−CH_2Cl_2 (5:2), rt, 24 h.

naphthyl (*rac*-BINAP), provided the diarylamine **11** almost quantitatively. Microwave heating of **11** in the presence of catalytic amounts of palladium(II) acetate and copper(II) acetate as reoxidant led to the protected carbazole **12**. The desired annulation precursor **13** was finally obtained by hydrogenolytic cleavage of the benzyl ether.

Various methods have been developed for the annulation of pyran rings to hydroxyarenes, notably those described by the groups of Iwai and Ide, Godfrey, Casiraghi, and Dufresne.[14] Treatment of hydroxycarbazole **13** with prenal (**14**), propionic acid, and catalytic amounts of phenylboronic acid in toluene at reflux provided the pyrano[3,2-*a*]carbazole **15** (Scheme 2).[15] Subsequent cleavage of the silyl ether with tetra-*n*-butylammonium fluoride (TBAF) transformed **15** into murrayamine A (**1**), which was obtained in five steps and 46% overall yield based on the protected 3-bromophenol **9**. *O*-Methylmurrayamine A (**2**) is available from **1** following the procedure of Wu.[2] The prenylated analogues mahanine (**3**) and *O*-methylmahanine (**4**) have been synthesized following a similar route. Phenylboronic acid-catalyzed reaction of the 2-hydroxycarbazole **13** and citral (**16**) in toluene provided the silyl-protected mahanine **17** in 75% yield.[15] The transformation of 2-hydroxy-3-methylcarbazole into cyclomahanimbine, which corresponds to the transformation of **13** into **17**, is known to proceed only in moderate yield with citral in pyridine (35%).[16] Cleavage of the silyl ether provided mahanine (**3**) in five steps and 56% overall yield based on the protected 3-bromophenol **9**. Methyl ether formation by treatment of **3** with sodium hydride and methyl iodide afforded *O*-methylmahanine (**4**). Thus, our present route provides the hydroxycarbazole alkaloids **1** and **3** and their corresponding methyl ethers **2** and **4** (Scheme 2). Synthetic access to the latter compounds, *O*-methylmurrayamine A (**2**) and *O*-methylmahanine (**4**), by pyran annulation at 2-hydroxy-7-methoxy-3-methylcarbazole has been described by us previously.[17] The improved palladium-catalyzed approach is superior to both, our iron-mediated synthesis of **2**[18] and also to our first palladium-catalyzed route to **2**, which did not afford the hydroxycarbazoles **1** and **3**.[17]

On the basis of our studies on the synthesis of cyclized monoterpenoid pyrano[3,2-*a*]carbazole alkaloids, such as cyclomahanimbine (curryanin, murrayazolidine), mahanimbidine (curryangin, murrayazoline),[10] murrayamine G, and isomurrayazoline,[19] we envisaged the total synthesis of murrayamine D (**5**) and murrayamine E (**6**) by proton-catalyzed cyclization of the protected mahanine **17** (Scheme 3). Treatment of **17** with 0.5 equiv of trifluoroacetic acid (TFA) in toluene led to the triisopropylsilyl (TIPS)-protected murrayamine D **18** in 80% yield. Cleavage of the silyl ether with TBAF provided murrayamine D (**5**).[15] On the other hand, cyclization in the presence of 5 mol % camphorsulfonic acid (CSA) in *n*-hexane afforded, after flash chromatography, a mixture of **18** and the silyl-protected murrayamine E **19** in a ratio of 1:2.38 (94% yield). Under these conditions, precipitation of **19** from the solvent prevents further proton-catalyzed isomerization of **19** to **18** (cf. ref 10 for the corresponding proton-catalyzed transformation of mahanimbidine to cyclomahanimbine). After

Scheme 2. Synthesis of Pyrano[3,2-*a*]carbazole Alkaloids 1−4[a]



[a]Reagents and conditions: (a) 1.5 equiv of prenal (**14**), 20 mol % $PhB(OH)_2$, 110 equiv of propanoic acid, PhMe, reflux, 36 h. (b) 1.5 equiv of TBAF, DMF, 0 °C, 5 min. (c) See ref 2. (d) 1.5 equiv of citral (**16**), 20 mol % $PhB(OH)_2$, PhMe, reflux, 3 days. (e) 1.6 equiv of TBAF, DMF, 0 °C, 30 min. (f) 1.3 equiv of NaH, 1.0 equiv of MeI, THF, rt, 24 h.

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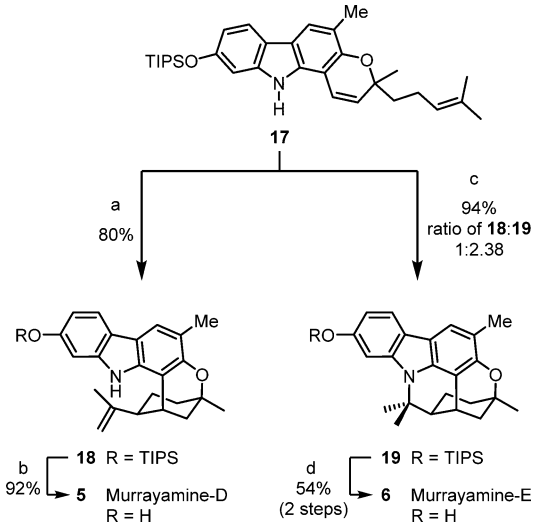
Scheme 3. Syntheses of Murrayamine D (5) and Murrayamine E (6)[a]



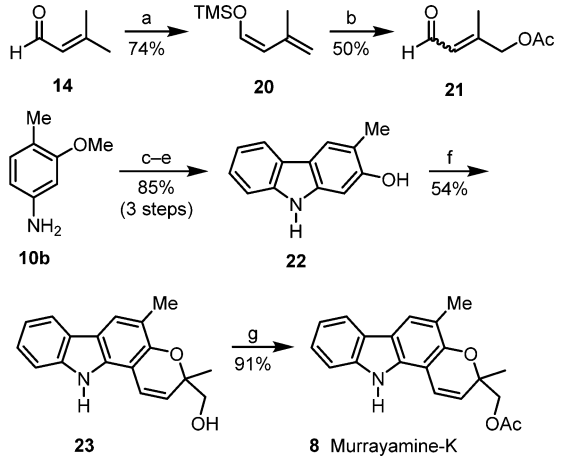
[a]Reagents and conditions: (a) 0.5 equiv of TFA, PhMe, rt, 16.5 h. (b) 1.4 equiv of TBAF, DMF, 0 °C, 30 min. (c) 5 mol % CSA, *n*-hexane, rt, 22 h (ratio of **18**:**19** = 1:2.38); (d) 1.5 equiv of TBAF, THF, 0 °C, 5 min.

cleavage of the silyl ether, isomers **5** and **6** could be separated and pure murrayamine E (**6**) was obtained in 54% yield based on **17**. The structure of murrayamine E (**6**) has been unequivocally confirmed by single-crystal X-ray analysis (see Supporting Information, Figure S1). On the basis of our previous studies,[10] it can be assumed that the proton-catalyzed isomerization of **17** rapidly leads to **19**, accompanied by a slow direct formation of **18**. In a further proton-catalyzed isomerization, **19** is then converted to **18**. With *n*-hexane as solvent, the latter process is retarded due to precipitation of the cyclization products.

For the syntheses of murrayamine K (**8**) and murrayamine I (**7**), we required the known acetoxy-substituted prenal derivative **21** (Scheme 4). Treatment of prenal (**14**) with chlorotrimethylsilane and triethylamine in the presence of zinc chloride provided the silyl dienolate **20**.[20] Oxidation of **20** with stoichiometric amounts of palladium(II) acetate in the presence of sodium acetate afforded 4-acetoxyprenal (**21**).[21] 2-Hydroxy-3-methylcarbazole (**22**) was prepared from the arylamine **10b** by our well-established palladium-catalyzed route.[10] Buchwald–Hartwig coupling[13] of iodobenzene and **10b**, followed by palladium(II)-catalyzed oxidative cyclization, provided 2-methoxy-3-methylcarbazole that has been isolated from natural sources by Bhattacharyya et al.[22] Cleavage of the methyl ether afforded 2-hydroxy-3-methylcarbazole (**22**), which has been isolated from natural sources as well.[23] On the basis of our previous syntheses of non-oxygenated pyrano[3,2-*a*]-carbazoles,[10] the pyran ring was annulated at **22** by a modification of Casiraghi's method.[10,14e,17] Reaction of **22** and 4-acetoxyprenal (**21**) in the presence of titanium(IV) isopropoxide provided a mixture of murrayamine K (**8**) and the carbazole **23**. This mixture was immediately treated with methanolic potassium carbonate to provide exclusively **23**. Esterification of **23** with acetic anhydride afforded murrayamine K (**8**) in five steps and 42% overall yield.

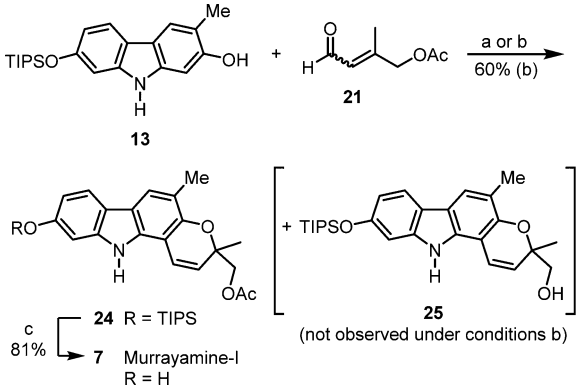
Analogously, murrayamine I (**7**) was obtained by pyran annulation at the monoprotected 2,7-dioxygenated carbazole

Scheme 4. Synthesis of Murrayamine K (8)[a]



[a]Reagents and conditions: (a) 1.1 equiv of TMSCl, 1.9 equiv of NEt_3, 0.9 mol % $ZnCl_2$, reflux, 25 h (ref 20). (b) 0.85 equiv of $Pd(OAc)_2$, 0.85 equiv of NaOAc, MeCN, 40 °C, 3 h (ref 21). (c) 1.2 equiv of **10b**, 1.0 equiv of PhI, 5 mol % $Pd(OAc)_2$, 10 mol % SPhos, 1.4 equiv of Cs_2CO_3, PhMe, 100 °C, 26 h, 96%. (d) 5 mol % $Pd(OAc)_2$, 5 mol % K_2CO_3, PivOH, air, 100 °C, 24 h, 90%. (e) 1.6 equiv of BBr_3, CH_2Cl_2, −78 °C to rt, 15.5 h, 98%. (f) (1) 1.5 equiv of **21**, 2.7 equiv of $Ti(OiPr)_4$, PhMe, −78 °C to rt, 19.5 h; (2) 0.5 equiv of K_2CO_3, MeOH, rt, 19 h. (g) 1.2 equiv of Ac_2O, 1.5 equiv of NEt_3, 5 mol % DMAP, CH_2Cl_2, rt, 1 h.

Scheme 5. Synthesis of Murrayamine I (7)[a]



[a]Reagents and conditions: (a) 1.5 equiv of **21**, 4.0 equiv of $Ti(OiPr)_4$, PhMe, rt, 22.5 h, 24% [mixture of **24** (7%) and **25** (17%)]. (b) 2.0 equiv of **21**, 20 mol % $PhB(OH)_2$, 110 equiv of propanoic acid, PhMe, reflux, 17 h, 60% (only **24**). (c) 1.5 equiv of TBAF, THF, 0 °C, 5 min.

13 (Scheme 5). Reaction of the carbazole **13** and 4-acetoxyprenal (**21**) in the presence of titanium(IV) isopropoxide afforded a mixture of the silyl-protected murrayamine I **24** and the corresponding deacetyl derivative **25** in only low yield. However, treatment of **13** and **21** with substoichiometric amounts of phenylboronic acid and an excess of propionic acid (cf. ref 15) provided selectively the silyl-protected murrayamine I **24**. Finally, cleavage of the silyl ether with TBAF afforded murrayamine I (**7**) in five steps and 37% overall yield.

■ CONCLUSIONS

We have achieved the total syntheses of eight pyrano[3,2-*a*]carbazole alkaloids. Synthetic strategies previously developed on simple derivatives have been applied successfully to more complex structures. Thus, murrayamine A (**1**) has been

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obtained in five steps and 46% overall yield, mahanine (**3**) in five steps and 56% overall yield, *O*-methylmahanine (**4**) in six steps and 34% overall yield, and murrayamine D (**5**) in six steps and 42% overall yield. We have shown that titanium(IV)-mediated and phenylboronic acid-catalyzed pyran ring annulation methodologies can be applied to the synthesis of acetoxymethyl-substituted pyrano[3,2-*a*]carbazoles. Our studies led to the first total syntheses of murrayamine E (**6**) (six steps, 31% overall yield), murrayamine I (**7**) (five steps, 37% overall yield), and murrayamine K (**8**) (five steps, 42% overall yield). The spectroscopic data of all synthetic compounds match those reported for the natural products and thus confirm the original structural assignments.

EXPERIMENTAL SECTION

General Information. All reactions were carried out in oven-dried glassware with dry solvents under an argon atmosphere unless stated otherwise. Acetonitrile, dichloromethane, tetrahydrofuran, and toluene were dried by use of a solvent purification system. Palladium acetate was recrystallized from acetic acid. Other chemicals were used as received from commercial sources. Microwave irradiations were carried out in a CEM Discover microwave apparatus with maximum power of 300 W and maximum pressure of 20 bar. Flash chromatography was performed with silica gel (0.035−0.070 mm). UV spectra were recorded on a UV/vis spectrometer. IR spectra were recorded on a Fourier transform infrared (FT-IR) spectrometer by the ATR method (attenuated total reflectance). NMR spectra were recorded on 500 and 600 MHz spectrometers. Chemical shifts δ are reported in parts per million with the nondeuterated solvent as internal standard. The following abbreviations have been used: s, singlet; d, doublet; t, triplet; m, multiplet; br, broad. Mass spectra and high-resolution mass spectra (HRMS) were obtained from a double-focusing sector field analyzer, electron impact, 70 eV. Elemental analyses were measured on a CHNS-elemental analyzer. X-ray crystal structure analyses were performed with a charge-coupled device (CCD) that was equipped with a low-temperature device. SHELXS-97,[24] SADABS version 2.10,[25] SHELXL-97,[26] POV-Ray for Windows version 3.6.2.msvc9.win64, and ORTEP-3 for Windows[27] were used as software.

Synthesis of Murrayamine A (1). *3-(Triisopropylsilyloxy)-bromobenzene (**9**).* 3-Bromophenol (1.00 g, 5.78 mmol) was added to a stirred solution of imidazole (0.79 g, 12 mmol) in *N*,*N*-dimethylformamide (DMF, 25 mL). Subsequently, triisopropylsilyl chloride (1.79 g, 9.28 mmol) was added dropwise. After 2 h of stirring at room temperature, water (30 mL) was added and the mixture was extracted with diethyl ether (3 × 50 mL). The combined organic layers were washed with water (3 × 20 mL) and then with a saturated aqueous solution of NaCl (20 mL) and dried over $MgSO_4$. Removal of the solvent and purification of the crude product by flash chromatography (silica gel, petroleum ether−ethyl acetate 9:1) afforded 3-(triisopropylsilyloxy)bromobenzene (**9**) (1.79 g, 94%) as a colorless oil. IR (ATR) ν 2944, 2892, 2867, 1587, 1566, 1473, 1294, 1270, 1235, 995, 929, 881, 772, 743, 680, 662 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ) 1.09 (d, J = 7.4 Hz, 18H), 1.21−1.28 (m, 3H), 6.79−6.81 (m, 1H), 7.04−7.09 (m, 3H). ^{13}C NMR and distortionless enhancement by polarization transfer (DEPT) (125 MHz, $CDCl_3$, δ) 12.6 (3CH), 17.9 ($6CH_3$), 118.6 (CH), 122.4 (C), 123.3 (CH), 124.1 (CH), 130.4 (CH), 156.9 (C). EIMS (70 eV) m/z 330 (16), 328 (16) $[M]^+$, 287 (100), 285 (98), 259 (29), 257 (29), 231 (55), 229 (54), 217 (26), 215 (30), 201 (18), 199 (17), 157 (12), 135 (14). HRMS m/z $[M^+]$ calcd for $C_{15}H_{25}BrOSi$, 328.0858; found, 328.0855. Anal. Calcd for $C_{15}H_{25}BrOSi$: C, 54.70; H, 7.65. Found: C, 54.87; H, 7.73.

*3-Benzyloxy-4-methyl-N-[3-(triisopropylsilyloxy)phenyl]aniline (**11**).* A solution of 3-(triisopropylsilyloxy)bromobenzene (**9**) (277 mg, 0.844 mmol) in toluene (5 mL) was added via syringe pump over a period of 3.5 h to a solution of 3-benzyloxy-4-methylaniline (**10a**) (216 mg, 1.01 mmol), cesium carbonate (416 mg, 1.28 mmol), palladium acetate (11.3 mg, 50.3 μmol), and *rac*-BINAP (31.4 mg, 50.4 μmol) in toluene (15 mL) at reflux temperature. After 20 h of heating at reflux, the reaction mixture was allowed to cool to room temperature and the solvent was removed in vacuo. Purification of the crude product by flash chromatography (silica gel, petroleum ether−ethyl acetate 9:1) afforded diarylamine **11** (387 mg, 99%) as a brownish oil. IR (ATR) ν 3396, 3062, 3029, 2943, 2865, 1593, 1508, 1489, 1460, 1383, 1275, 1186, 1153, 1125, 998, 881, 832, 766, 685 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ) 1.09 (d, J = 7.4 Hz, 18H), 1.19−1.27 (m, 3H), 2.23 (s, 3H), 5.02 (s, 2H), 5.57 (br s, 1H), 6.42 (dd, J = 8.0, 2.0 Hz, 1H), 6.54 (dd, J = 8.0, 2.0 Hz, 1H), 6.57 (t, J = 2.0 Hz, 1H), 6.60 (dd, J = 8.0, 2.0 Hz, 1H), 6.67 (d, J = 2.0 Hz, 1H), 7.04 (t, J = 8.0 Hz, 2H), 7.32 (m, 1H), 7.37−7.43 (m, 4H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$, δ) 12.7 (3CH), 15.8 (CH_3), 17.9 ($6CH_3$), 69.8 (CH_2), 103.0 (CH), 108.7 (CH), 110.0 (CH), 110.7 (CH), 112.1 (CH), 120.0 (C), 127.8 (2 CH), 127.7 (CH), 128.5 (2CH), 129.8 (CH), 131.0 (CH), 137.3 (C), 141.7 (C), 144.9 (C), 157.1 (C), 157.4 (C). EIMS (70 eV) m/z 461 (100) $[M]^+$, 418 (16), 326 (22), 91 (50). HRMS m/z $[M]^+$ calcd for $C_{29}H_{39}NO_2Si$, 461.2750; found, 461.2761. Anal. Calcd for $C_{29}H_{39}NO_2Si$: C, 75.44; H, 8.51; N, 3.03. Found: C, 75.52; H, 8.58; N, 3.15.

*2-Benzyloxy-3-methyl-7-(triisopropylsilyloxy)carbazole (**12**).* A 10 mL microwave tube was charged with diarylamine **11** (317 mg, 0.687 mmol), palladium acetate (15.4 mg, 68.6 μmol), cupric acetate (312 mg, 1.72 mmol), and glacial acetic acid (3 mL). The tube was irradiated in the microwave reactor at 130 °C and 300 W for 2 h. Removal of the solvent and purification of the crude product by flash chromatography (silica gel, petroleum ether−ethyl acetate 9:1) provided 2-benzyloxy-3-methyl-7-(triisopropylsilyloxy)carbazole (**12**) (242 mg, 77%) as a light brown solid; mp 123−125 °C. UV (MeOH) λ_{max} 211 (sh), 237, 263, 308, 322 nm. Fluorescence (MeOH) λ_{ex} 287 nm, λ_{em} 352 nm. IR (ATR) ν 3385, 3349, 3062, 3034, 2943, 2865, 1614, 1474, 1461, 1381, 1341, 1269, 1229, 1157, 1140, 1027, 998, 961, 880, 833, 739, 677, 631 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ) 1.11 (d, J = 7.4 Hz, 18H), 1.23−1.32 (m, 3H), 2.41 (s, 3H), 5.15 (s, 2H), 6.76 (dd, J = 8.4, 2.1 Hz, 1H), 6.85 (d, J = 2.1 Hz, 1H), 6.86 (s, 1H), 7.32 (m, 1H), 7.36−7.40 (m, 2H), 7.48 (m, 2H), 7.69 (s, 1H), 7.71 (br s, 1H), 7.73 (d, J = 8.4 Hz, 1H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$, δ) 12.7 (CH_3), 16.9 (3CH), 18.0 ($6CH_3$), 70.2 (CH_2), 94.2 (CH), 101.4 (CH), 112.9 (CH), 116.8 (C), 117.7 (C), 119.5 (C), 119.7 (CH), 120.9 (CH), 127.0 (2CH), 127.7 (CH), 128.5 (2CH), 137.6 (C), 138.9 (C), 140.5 (C), 153.9 (C), 155.4 (C). EIMS (70 eV) m/z 459 (44) $[M]^+$, 369 (46), 368 (100), 91 (12). HRMS m/z $[M]^+$ calcd for $C_{29}H_{37}NO_2Si$, 459.2594; found, 459.2587. Anal. Calcd for $C_{29}H_{37}NO_2Si$: C, 75.77; H, 8.11; N, 3.05. Found: C, 75.82; H, 8.23; N, 3.04.

*2-Hydroxy-3-methyl-7-(triisopropylsilyloxy)carbazole (**13**).* A mixture of carbazole **12** (231 mg, 0.504 mmol) and palladium on activated carbon (10 wt % Pd, 46 mg) in a mixture of dichloromethane (4 mL) and methanol (10 mL) was stirred at room temperature for 24 h under a hydrogen atmosphere at normal pressure. The reaction mixture was filtered over Celite (diethyl ether). Removal of the solvent from the combined filtrates and purification of the crude product by flash chromatography (silica gel, petroleum ether−ethyl acetate 2:1) afforded 2-hydroxy-3-methyl-7-(triisopropylsilyloxy)carbazole (**13**) (186 mg, 100%) as a colorless solid; mp 126 °C. UV (MeOH) λ_{max} 231, 237, 264, 315, 322 nm. Fluorescence (MeOH) λ_{ex} 286 nm, λ_{em} 352 nm. IR (ATR) ν 3554, 3404, 2942, 2865, 1614, 1473, 1380, 1342, 1273, 1236, 1221, 1156, 1131, 1072, 1010, 994, 964, 920, 881, 854, 833, 813, 765, 707, 682, 642, 613 cm^{-1}. ^1H NMR (500 MHz, acetone-d_6, δ) 1.17 (d, J = 7.5 Hz, 18H), 1.30−1.39 (m, 3H), 2.36 (s, 3H), 6.76 (dd, J = 8.4, 2.2 Hz, 1H), 6.94 (s, 1H), 6.97 (d, J = 2.2 Hz, 1H), 7.71 (s, 1H), 7.80 (d, J = 8.4 Hz, 1H), 8.15 (s, 1H), 9.81 (br s, 1H). ^{13}C NMR and DEPT (125 MHz, acetone-d_6, δ) 13.4 (3CH), 16.7 (CH_3), 18.3 ($6CH_3$), 97.1 (CH), 102.1 (CH), 112.6 (CH), 117.1 (C), 117.3 (C), 118.9 (C), 120.0 (CH), 121.5 (CH), 140.9 (C), 142.0 (C), 154.3 (C), 154.6 (C). EIMS (70 eV) m/z 369 (100) $[M]^+$, 326 (59), 298 (22), 284 (15), 270 (12), 256 (14), 224 (32), 196 (15), 135 (57), 128 (19). Anal. Calcd for $C_{22}H_{31}NO_2Si$: C, 71.50; H, 8.46; N, 3.79. Found: C, 71.76; H, 8.43; N, 3.82.

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*O-(Triisopropylsilyl)murrayamine A (**15**).* Propanoic acid (1.89 mL, 25.3 mmol) and 3-methyl-2-butenal (prenal, **14**) (35.9 μL, 0.345 mmol) were added to a solution of the 2-hydroxycarbazole **13** (83.6 mg, 0.227 mmol) and phenylboronic acid (5.5 mg, 0.045 mmol) in toluene (8 mL). The reaction mixture was heated at reflux for 36 h. Removal of the solvent and purification of the crude product by flash chromatography (silica gel, petroleum ether−ethyl acetate 9:1) provided *O*-(triisopropylsilyl)murrayamine A (**15**) (63.0 mg, 63%) as a light brown oil. UV (MeOH) λ_{max} 219, 241, 269, 294, 311, 361 nm. Fluorescence (MeOH) λ_{ex} 240 nm, λ_{em} 357 nm. IR (ATR) ν 2940, 2865, 1720, 1608, 1494, 1458, 1379, 1275, 1243, 1207, 1155, 1127, 1058, 969, 882, 833, 804, 684, 644 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ) 1.12 (d, J = 7.4 Hz, 18H), 1.25−1.32 (m, 3H), 1.46 (s, 6H), 2.31 (s, 3H), 5.68 (d, J = 9.7 Hz, 1H), 6.58 (d, J = 9.7 Hz, 1H), 6.75 (dd, J = 8.3, 2.1 Hz, 1H), 6.88 (d, J = 2.1 Hz, 1H), 7.55 (s, 1H), 7.70 (d, J = 8.3 Hz, 1H), 7.74 (br s, 1H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$, δ) 12.7 (3CH), 16.0 (CH_3), 18.0 ($6CH_3$), 27.5 ($2CH_3$), 75.7 (C), 101.5 (CH), 104.5 (C), 113.0 (CH), 116.9 (C), 117.3 (CH), 118.1 (C), 118.4 (C), 119.6 (CH), 120.4 (CH), 129.5 (CH), 134.7 (C), 140.6 (C), 148.8 (C), 154.0 (C). EIMS (70 eV) m/z 435 (100) $[M]^+$, 420 (56), 392 (13), 161 (30), 154 (14). HRMS m/z: $[M]^+$ calcd for $C_{27}H_{37}NO_2Si$, 435.2594; found, 435.2588.

*Murrayamine A (Mukoenine C, 7-Hydroxygirinimbine, **1**).* Tetrabutylammonium fluoride (110 μL, 110 μmol; 1 M in tetrahydrofuran) was added dropwise at 0 °C to a solution of *O*-(triisopropylsilyl)murrayamine A (**15**) (31.0 mg, 0.071 mmol) in DMF (5 mL), and the mixture was stirred at 0 °C for 5 min. After addition of water (10 mL), the mixture was extracted with diethyl ether (3 × 50 mL). The combined organic layers were washed with water (50 mL) and then with a saturated aqueous solution of NaCl (50 mL) and dried over magnesium sulfate. Removal of the solvent and purification of the crude product by flash chromatography (silica gel, petroleum ether−ethyl acetate 2:1) provided murrayamine A (**1**) (18.5 mg, 95%) as a yellow oil (lit.[2] mp 162−163 °C). UV (MeOH) λ_{max} 220, 240, 285 (sh), 294, 324, 362 nm. Fluorescence (MeOH) λ_{ex} 280 nm, λ_{em} 371 nm. IR (ATR) ν 3417, 2955, 2923, 2854, 1625, 1456, 1439, 1376, 1317, 1267, 1206, 1156, 1128, 1058, 1024, 958, 804, 777, 720, 669 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ) 1.46 (s, 6H), 2.30 (d, J = 0.4 Hz, 3H), 5.67 (d, J = 9.7 Hz, 1H), 6.56 (d, J = 9.7 Hz, 1H), 6.66 (dd, J = 8.3, 2.0 Hz, 1H), 6.77 (d, J = 2.0 Hz, 1H), 7.54 (s, 1H), 7.70 (d, J = 8.3 Hz, 1H), 7.74 (br s, 1H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$, δ) 16.0 (CH_3), 27.5 ($2CH_3$), 75.7 (C), 96.9 (CH), 104.5 (C), 108.3 (CH), 116.8 (C), 117.2 (CH), 118.0 (C), 118.4 (C), 120.0 (CH), 120.3 (CH), 129.6 (CH), 134.7 (C), 140.7 (C), 148.8 (C), 153.6 (C). EIMS (70 eV) m/z 279 (36) $[M]^+$, 264 (100). HRMS m/z $[M]^+$ calcd for $C_{18}H_{17}NO_2$, 279.1259; found, 279.1258.

Syntheses of Murrayamine D (5) and Murrayamine E (6). *O-(Triisopropylsilyl)mahanine (**17**).* Citral (**16**) (164 μL, 0.948 mmol) was added to a solution of the 2-hydroxycarbazole **13** (233 mg, 0.632 mmol) and phenylboronic acid (15.4 mg, 0.126 mmol) in toluene (10 mL). The solution was heated at reflux for 3 days and then allowed to cool to room temperature. Removal of the solvent and purification of the crude product by flash chromatography (silica gel, petroleum ether−ethyl acetate 9:1) provided *O*-(triisopropylsilyl)mahanine (**17**) (238 mg, 75%) as a light yellow oil. UV (MeOH) λ_{max} 242, 283 (sh), 294, 325, 359 (sh) nm. Fluorescence (MeOH) λ_{ex} 325 nm, λ_{em} 369 nm. IR (ATR) ν 3425, 2937, 2925, 2865, 1697, 1621, 1494, 1456, 1436, 1397, 1346, 1276, 1242, 1210, 1159, 1058, 1014, 969, 918, 882, 833, 804, 714, 681, 589 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ) 1.12 (d, J = 7.6 Hz, 18H), 1.24−1.34 (m, 3H), 1.43 (s, 3H), 1.57 (s, 3H), 1.65 (s, 3H), 1.72−1.78 (m, 2H), 2.12−2.18 (m, 2H), 2.31 (s, 3H), 5.08−5.11 (m, 1H), 5.64 (d, J = 9.8 Hz, 1H), 6.60 (d, J = 9.8 Hz, 1H), 6.75 (dd, J = 8.4, 2.1 Hz, 1H), 6.88 (d, J = 2.1 Hz, 1H), 7.54 (s, 1H), 7.69 (d, J = 8.4 Hz, 1H), 7.72 (br s, 1H). ^1H NMR (500 MHz, acetone-d_6, δ) 1.17 (d, J = 7.4 Hz, 18H), 1.31−1.39 (m, 3H), 1.47 (s, 3H), 1.60 (s, 3H), 1.67 (d, J = 0.7 Hz, 3H), 1.78−1.81 (m, 2H), 2.19−2.25 (m, 2H), 2.33 (d, J = 0.7 Hz, 3H), 5.15−5.18 (m, 1H), 5.78 (d, J = 9.8 Hz, 1H), 6.78 (dd, J = 8.4, 2.1 Hz, 1H), 6.94 (d, J = 9.8 Hz, 1H), 6.98 (d, J = 2.1 Hz, 1H), 7.65 (s, 1H), 7.82 (d, J = 8.4 Hz, 1H), 10.13 (br s, 1H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$, δ) 12.7 (3CH), 16.0 (CH_3), 17.6 (CH_3), 18.0 ($6CH_3$), 22.7 (CH_2), 25.7 ($2CH_3$), 40.6 (CH_2), 77.9 (C), 101.5 (CH), 104.3 (C), 113.0 (CH), 116.8 (C), 117.5 (CH), 118.2 (C), 119.6 (CH), 120.4 (CH), 124.2 (CH), 128.7 (CH), 131.6 (C), 134.8 (C), 137.8 (C), 140.6 (C), 148.9 (C), 153.9 (C). ^{13}C NMR and DEPT (125 MHz, acetone-d_6, δ) 13.4 (3CH), 16.2 (CH_3), 17.6 (CH_3), 18.3 ($6CH_3$), 23.4 (CH_2), 25.8 (CH_3), 26.1 (CH_3), 41.4 (CH_2), 78.7 (C), 102.2 (CH), 105.2 (C), 113.1 (CH), 117.6 (C), 117.9 (C), 118.9 (C), 118.9 (CH), 120.3 (CH), 121.1 (CH), 125.1 (CH), 129.1 (CH), 131.8 (C), 136.2 (C), 142.1 (C), 149.7 (C), 154.6 (C). EIMS (70 eV) m/z 503 (100) $[M]^+$.

*Mahanine (**3**).* Tetrabutylammonium fluoride (241 μL, 0.241 mmol; 1 M in THF) was added slowly at 0 °C to a solution of *O*-(triisopropylsilyl)mahanine (**17**) (75.8 mg, 0.151 mmol) in DMF (7 mL), and the solution was stirred at 0 °C for 30 min. After addition of water at 0 °C, the mixture was extracted with diethyl ether and the organic layer was dried over magnesium sulfate. Removal of the solvent and purification of the crude product by flash chromatography (silica gel, petroleum ether−ethyl acetate, 2:1) provided mahanine (**3**) (51.0 mg, 98%) as a light yellow solid, mp 110−115 °C [lit.[6a] mp 100 °C for (−)-**3**; lit.[2] mp 95−96 °C for (+)-**3**]. UV (MeOH) λ_{max} 219, 241, 296, 327, 362 (sh) nm. Fluorescence (MeOH) λ_{ex} 327 nm, λ_{em} 357 nm. IR (ATR) ν 3416, 2967, 2919, 2853, 1624, 1486, 1456, 1439, 1377, 1316, 1293, 1241, 1205, 1155, 1108, 1081, 1057, 1029, 979, 957, 907, 866, 803, 776, 748, 718, 676 cm^{-1}. ^1H NMR (500 MHz, acetone-d_6, δ) 1.46 (s, 3H), 1.60 (s, 3H), 1.67 (s, 3H), 1.77−1.81 (m, 2H), 2.19−2.25 (m, 2H), 2.33 (s, 3H), 5.17 (m, 1H), 5.76 (d, J = 9.8 Hz, 1H), 6.72 (dd, J = 8.4, 2.1 Hz, 1H), 6.90 (d, J = 2.1 Hz, 1H), 6.95 (d, J = 9.8 Hz, 1H), 7.60 (s, 1H), 7.76 (d, J = 8.4 Hz, 1H), 8.02 (br s, 1H), 8.28 (br s, 1H). ^{13}C NMR and DEPT (125 MHz, acetone-d_6, δ) 16.2 (CH_3), 17.6 (CH_3), 23.4 (CH_2), 25.7 (CH_3), 26.1 (CH_3), 41.4 (CH_2), 75.5 (C), 97.5 (CH), 105.2 (C), 108.9 (CH), 117.5 (C), 117.6 (C), 117.9 (C), 119.0 (CH), 120.4 (CH), 120.8 (CH), 125.1 (CH), 128.9 (CH), 131.8 (C), 136.1 (C), 142.5 (C), 149.3 (C), 156.3 (C). EIMS (70 eV) m/z 347 (80) $[M]^+$, 328 (24), 264 (100). HRMS m/z $[M]^+$ calcd for $C_{23}H_{25}NO_2$, 347.1885; found, 347.1891.

*O-Methylmahanine (**4**).* Sodium hydride (19.2 mg, 0.489 mmol; 60% in oil) was added at 0 °C to a solution of mahanine (**3**) (130 mg, 0.376 mmol) in THF (8 mL). After 10 min of stirring, methyl iodide (23.4 μL, 0.376 mmol) was added. The reaction mixture was stirred at room temperature for 24 h. Water was added and the mixture was extracted three times with diethyl ether. The combined organic layers were dried over magnesium sulfate. Removal of the solvent and purification of the crude product by flash chromatography (silica gel, petroleum ether−ethyl acetate 4:1) provided *O*-methylmahanine (**4**) (79.8 mg, 60%) as a colorless solid, mp 179−183 °C (lit.[8] mp 180 °C). UV (MeOH) λ_{max} 221, 242, 284 (sh), 294, 341, 361 (sh) nm. Fluorescence (MeOH) λ_{ex} 300 nm, λ_{em} 371 nm. IR (ATR) ν 3404, 2962, 2922, 2852, 1698, 1623, 1495, 1455, 1402, 1376, 1310, 1270, 1243, 1210, 1194, 1156, 1105, 1080, 1058, 1030, 979, 913, 873, 828, 807, 777, 721, 678 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ) 1.43 (s, 3H), 1.57 (s, 3H), 1.65 (s, 3H), 1.75 (t, J = 8.4 Hz, 2H), 2.12−2.19 (m, 2H), 2.31 (s, 3H), 3.87 (s, 3H), 5.09−5.12 (m, 1H), 5.64 (d, J = 9.8 Hz, 1H), 6.61 (d, J = 9.8 Hz, 1H), 6.79 (dd, J = 8.5, 2.2 Hz, 1H), 6.87 (d, J = 2.2 Hz, 1H), 7.55 (s, 1H), 7.76 (d, J = 8.5 Hz, 1H, and br s, 1H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$, δ) 16.0 (CH_3), 17.6 (CH_3), 22.7 (CH_2), 25.66 (CH_3), 25.74 (CH_3), 40.7 (CH_2), 55.6 (CH_3), 78.0 (C), 95.1 (CH), 104.3 (C), 107.6 (CH), 116.7 (C), 117.5 (CH), 117.9 (C), 118.2 (C), 119.9 (CH), 120.4 (CH), 124.2 (CH), 128.7 (CH), 131.7 (C), 134.7 (C), 140.6 (C), 148.9 (C), 157.9 (C). EIMS (70 eV) m/z 361 (72) $[M]^+$, 278 (34), 239 (100), 224 (31). Anal. Calcd for $C_{24}H_{27}NO_2$: C, 79.74; H, 7.53; N, 3.87. Found: C, 79.42; H, 7.59; N, 3.91.

*O-(Triisopropylsilyl)murrayamine D (**18**).* Trifluoroacetic acid (7.0 μL, 0.094 mmol) was added to a solution of *O*-(triisopropylsilyl)-mahanine (**17**) (88.1 mg, 0.175 mmol) in toluene (7 mL), and the mixture was stirred at room temperature for 16.5 h. Removal of the solvent and purification of the crude product by flash chromatography (silica gel, petroleum ether−ethyl acetate 9:1) provided *O*-(triisopropylsilyl)murrayamine D (**18**) (70.5 mg, 80%) as colorless crystals, mp 105−110 °C. UV (MeOH) λ_{max} 214, 241, 266, 315 nm.

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J. Org. Chem. 2015, 80, 5666−5673

Fluorescence (MeOH) λ_{ex} 315 nm, λ_{em} 353 nm. IR (ATR) ν 3433, 2942, 2926, 2865, 1697, 1613, 1494, 1450, 1375, 1347, 1275, 1233, 1211, 1156, 1102, 1056, 997, 970, 918, 882, 833, 800, 713, 682, 601 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ) 1.12 (d, J = 7.3 Hz, 18H), 1.21−1.36 (m, 3H), 1.42 (s, 3H), 1.47 (m, 1H), 1.48 (s, 3H), 1.59−1.63 (m, 2H), 1.85−1.88 (m, 1H), 2.00 (dd, J = 12.8, 2.7 Hz, 1H), 2.07 (dt, J = 8.9, 2.3 Hz, 1H), 2.30 (s, 3H), 2.55−2.57 (m, 1H), 3.36 (d, J = 2.7 Hz, 1H), 4.73 (s, 1H), 4.81 (s, 1H), 6.71 (dd, J = 8.3, 2.1 Hz, 1H), 6.81 (d, J = 2.1 Hz, 1H), 7.51 (s, 1H), 7.55 (br s, 1H), 7.66 (d, J = 8.3 Hz, 1H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$, δ) 12.7 (3CH), 16.7 (CH_3), 18.0 ($6CH_3$), 21.6 (CH_3), 23.1 (CH_2), 29.0 (CH_3), 36.3 (CH), 37.4 (CH_2), 39.9 (CH_2), 48.7 (CH), 73.7 (C), 101.4 (CH), 105.3 (C), 112.0 (CH_2), 112.4 (CH), 114.7 (C), 117.3 (C), 118.5 (C), 118.8 (CH), 119.2 (CH), 138.3 (C), 140.6 (C), 150.2 (C), 152.7 (C), 153.4 (C). EIMS (70 eV) m/z 503 (100) $[M]^+$, 420 (13), 161 (23). HRMS m/z $[M]^+$ calcd for $C_{32}H_{45}NO_2Si$, 503.3220; found, 503.3208.

*Murrayamine D (**5**).* Tetrabutylammonium fluoride (175 μL, 0.175 mmol; 1 M in THF) was added slowly at 0 °C to a solution of *O*-(triisopropylsilyl)murrayamine D (**18**) (62.9 mg, 0.125 mmol) in DMF (10 mL), and the mixture was stirred at 0 °C for 30 min. After addition of water, the reaction mixture was extracted with diethyl ether and the combined organic layers were dried over magnesium sulfate. Removal of the solvent and purification of the crude product by flash chromatography (silica gel, petroleum ether−ethyl acetate 2:1) provided murrayamine D (**5**) (39.9 mg, 92%) as a light yellow solid, mp 105−109 °C (lit.[9] oil). UV (MeOH) λ_{max} 246, 275 (sh), 318 nm. Fluorescence (MeOH) λ_{ex} 318 nm, λ_{em} 384 nm. IR (ATR) ν 3425, 2965, 2923, 2846, 1709, 1613, 1495, 1443, 1374, 1314, 1275, 1231, 1208, 1153, 1102, 1053, 958, 869, 826, 800, 672, 604 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ) 1.42 (s, 3H), 1.44−1.47 (m, 1H), 1.48 (s, 3H), 1.53−1.61 (m, 2H), 1.85−1.89 (m, 1H), 2.00 (dd, J = 12.8, 2.0 Hz, 1H), 2.05−2.10 (m, 1H), 2.30 (s, 3H), 2.55−2.57 (m, 1H), 3.36 (m, 1H), 4.73 (s, 1H), 4.80 (t, J = 1.4 Hz, 1H), 6.64 (dd, J = 8.3, 2.2 Hz, 1H), 6.77 (d, J = 2.2 Hz, 1H), 7.52 (s, 1H), 7.60 (br s, 1H), 7.68 (d, J = 8.3 Hz, 1H). ^1H NMR (500 MHz, acetone-d_6, δ) 1.43 (s, 3H), 1.64 (s, 3H), 1.62−1.68 (m, 1H), 1.74 (dt, J = 4.7, 13.3 Hz, 1H), 1.85−1.89 (m, 2H), 2.13−2.16 (m, 2H), 2.31 (s, 3H), 2.59 (dt, J = 12.5, 2.9 Hz, 1H), 3.60 (m, 1H), 4.49 (s, 1H), 4.66 (t, J = 1.5 Hz, 1H), 6.67 (dd, J = 8.4, 2.2 Hz, 1H), 6.87 (d, J = 2.2 Hz, 1H), 7.54 (s, 1H), 7.70 (d, J = 8.4 Hz, 1H), 8.14 (s, 1H), 8.91 (br s, 1H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$, δ) 16.7 (CH_3), 21.1 (CH_3), 21.6 (CH_2), 29.0 (CH_3), 36.2 (CH), 37.4 (CH_2), 39.9 (CH_2), 48.7 (CH), 73.8 (C), 96.8 (CH), 105.3 (C), 107.9 (CH), 112.0 (CH_2), 114.6 (C), 117.4 (C), 118.4 (C), 118.7 (CH), 119.7 (CH), 138.2 (C), 140.6 (C), 150.1 (C), 153.06 (C), 153.11 (C). ^{13}C NMR and DEPT (125 MHz, acetone-d_6, δ) 16.9 (CH_3), 22.2 (CH_3), 24.2 (CH_2), 29.3 (CH_3), 35.3 (CH), 37.8 (CH_2), 40.7 (CH_2), 49.5 (CH), 74.4 (C), 97.5 (CH), 106.0 (C), 108.5 (CH), 111.8 (CH_2), 115.8 (C), 116.6 (C), 117.9 (C), 119.2 (CH), 120.0 (CH), 139.1 (C), 142.1 (C), 149.2 (C), 153.2 (C), 155.8 (C). EIMS (70 eV) m/z 347 (100) $[M]^+$, 332 (61), 264 (46). HRMS m/z: $[M]^+$ calcd for $C_{23}H_{25}NO_2$, 347.1885; found, 347.1877.

*Murrayamine E (**6**).* Camphorsulfonic acid (1 mg, 0.004 mmol) was added to a solution of *O*-(triisopropylsilyl)mahanine (**17**) (42 mg, 0.083 mmol) in *n*-hexane (0.6 mL), and the mixture was stirred at room temperature for 22 h. A small portion of sodium hydrogen carbonate was added and the solvent was evaporated. Purification of the residue by flash chromatography (silica gel, isohexane−ethyl acetate 30:1) provided an inseparable mixture of *O*-(triisopropylsilyl)-murrayamine D (**18**) and *O*-(triisopropylsilyl)murrayamine E (**19**) as a yellow solid [39.5 mg, 94%; ratio of **18**:**19** = 1:2.38 as determined by integration of the signals in the ^1H NMR spectrum (see Supporting Information)].

TBAF (1 M in THF, 0.13 mL, 0.133 mmol) was added at 0 °C to a solution of the mixture of pyrano[3,2-*a*]carbazoles **18** and **19** (45 mg, 0.089 mmol, ratio of **18**:**19** = 1:2) in THF (2 mL), and the mixture was stirred at 0 °C for 5 min. After addition of water, the mixture was diluted with diethyl ether, and the organic layer was separated. The organic layer was washed with water and the aqueous layer was extracted once with diethyl ether. The combined organic layers were dried over magnesium sulfate and the solvent was evaporated. Purification of the residue by flash chromatography (silica gel, isohexane−ethyl acetate 4:1) provided murrayamine E (**6**) (16.8 mg, 54%), murrayamine D (**5**) (5.6 mg, 18%), and a fraction containing both compounds (8.5 mg, 27%).

Spectroscopic data for **6**: light yellow solid, mp >260 °C (decomp) (lit.[9] 275−276 °C decomp). UV (MeOH) λ_{max} 216, 244, 273, 316, 336 (sh) nm. Fluorescence (MeOH) λ_{ex} 273 nm, λ_{em} 379 nm. IR (ATR) ν 3340, 2973, 2939, 2913, 1697, 1621, 1571, 1504, 1453, 1430, 1396, 1374, 1346, 1304, 1262, 1203, 1146, 1075, 1058, 1036, 1011, 995, 975, 915, 863, 837, 799, 784, 743, 699, 649, 618 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ) 0.14−0.23 (m, 1H), 1.27 (s, 3H), 1.28−1.33 (m, 1H), 1.45 (s, 3H), 1.50−1.64 (m, 2H), 1.86 (s, 3H), 1.89 (d, J = 13.2 Hz, 1H), 1.94−1.97 (m, 1H), 2.31 (s, 3H), 2.37 (ddd, J = 13.2, 5.2, 3.3 Hz, 1H), 3.27 (d, J = 5.2 Hz, 1H), 6.65 (dd, J = 8.3, 2.0 Hz, 1H), 6.95 (d, J = 2.0 Hz, 1H), 7.36 (s, 1H), 7.69 (d, J = 8.3 Hz, 1H). ^1H NMR (500 MHz, DMSO-d_6, δ) −0.08−0.00 (m, 1H), 1.16 (s, 3H), 1.22−1.27 (m, 1H), 1.38 (s, 3H), 1.42−1.47 (m, 1H), 1.50−1.57 (m, 1H), 1.80 (s, 3H), 1.95 (d, J = 13.0 Hz, 1H), 2.01 (ddd, J = 10.9, 5.3, 2.0 Hz, 1H), 2.20 (s, 3H), 2.20−2.24 (m, 1H), 3.20 (d, J = 4.3 Hz, 1H), 6.58 (dd, J = 8.3, 2.0 Hz, 1H), 6.90 (d, J = 2.0 Hz, 1H), 7.29 (s, 1H), 7.61 (d, J = 8.3 Hz, 1H), 9.17 (s, 1H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$, δ) 15.5 (CH_3), 22.0 (CH_2), 22.9 (CH_3), 28.4 (CH), 29.4 (CH_3), 30.1 (CH_3), 36.3 (CH_2), 36.9 (CH_2), 48.9 (CH), 60.6 (C), 76.1 (C), 100.7 (CH), 107.6 (C), 107.8 (CH), 114.2 (C), 118.4 (C), 118.6 (CH), 120.2 (CH), 121.6 (C), 142.0 (C), 142.6 (C), 152.2 (C), 154.3 (C). ^{13}C NMR and DEPT (125 MHz, DMSO-d_6, δ) 15.2 (CH_3), 21.4 (CH_2), 22.2 (CH_3), 27.6 (CH), 29.0 (CH_3), 29.4 (CH_3), 35.3 (CH_2), 36.1 (CH_2), 47.5 (CH), 60.1 (C), 75.9 (C), 100.4 (CH), 107.4 (C), 108.9 (CH), 113.8 (C), 116.6 (C), 118.1 (CH), 119.2 (C), 119.9 (CH), 141.7 (C), 141.8 (C), 153.2 (C), 154.1 (C). EIMS (70 eV) m/z 347 $[M]^+$ (100), 332 (68), 304 (17), 264 (59). Anal. Calcd for $C_{23}H_{25}NO_2$: C, 79.51; H, 7.25; N, 4.03. Found: C, 79.72; H, 7.35; N, 3.65.

Crystallographic data for murrayamine E (**6**): $C_{23}H_{25}NO_2$, M = 347.44 g·mol^{-1}, crystal size 0.39 × 0.18 × 0.09 mm^3, monoclinic, space group $P2_1/c$, a = 10.845(3) Å, b = 11.246(2) Å, c = 15.472(3) Å, β = 107.92(2)°, V = 1795.5(7) Å^3, Z = 4, ρ_{calcd} = 1.285 g·cm^{-3}, μ = 0.081 mm^{-1}, λ = 0.710 73 Å, T = 198(2) K, θ range = 3.28−25.40°, reflections collected 44 140, independent reflections 3298 (R_{int} = 0.0551), 240 parameters. The structure was solved by direct methods and refined by full-matrix least-squares on F^2; final R indices [$I > 2\sigma(I)$] R_1 = 0.0490 and wR_2 = 0.1010; maximal residual electron density 0.190 e·Å^{-3}. CCDC-1055185 contains the supplementary crystallographic data for this structure. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Synthesis of Murrayamine K (8). *(3,5-Dimethyl-3,11-dihydropyrano[3,2-a]carbazol-3-yl)methanol (**23**).* 4-Acetoxy-3-methylbut-2-enal (**21**) (143 mg, 1.01 mmol) was added to a solution of 2-hydroxy-3-methylcarbazole (**22**)[10] (132 mg, 0.669 mmol) in toluene (20 mL), and the mixture was cooled to −78 °C. Titanium(IV) isopropoxide (0.80 mL, 0.77 g, 2.70 mmol) was added slowly and the reaction mixture was stirred for 19.5 h under warming to room temperature. The mixture was diluted with ethyl acetate and washed several times with water, diluted hydrochloric acid, and brine. The aqueous layers were extracted with ethyl acetate, the combined organic layers were dried over sodium sulfate, the solvent was evaporated, and the residue was dried in high vacuum. The crude material was dissolved in methanol (20 mL), potassium carbonate (46.2 mg, 0.334 mmol) was added, and the solution was stirred for 19 h at room temperature. The mixture was diluted with diethyl ether and washed several times with water, a saturated aqueous solution of ammonium chloride, and brine. The aqueous layers were extracted with diethyl ether, the combined organic layers were dried over sodium sulfate, and the solvent was evaporated. Purification by column chromatography (silica gel, pentane−dichloromethane−ethyl acetate, gradient from 10:5:1 to 7:5:1) provided (3,5-dimethyl-3,11-dihydropyrano[3,2-*a*]carbazol-3-yl)methanol (**23**) (100 mg, 54%) as a slightly yellow solid, mp 140 °C. UV (MeOH) λ_{max} 222, 237, 277

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J. Org. Chem. 2015, 80, 5666−5673

(sh), 287, 326, 342, 358 nm. Fluorescence (MeOH) λ_{ex} 287 nm; λ_{em} 371, 381 nm. IR (ATR) ν 3418, 2959, 2919, 2856, 1734, 1699, 1642, 1606, 1491, 1456, 1443, 1403, 1373, 1308, 1215, 1159, 1108, 1037, 978, 928, 886, 859, 829, 782, 748, 720, 698, 677, 617 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ) 1.43 (s, 3H), 2.00 (t, J = 6.2 Hz, 1H), 2.34 (d, J = 0.7 Hz, 3H), 3.70 (dd, J = 11.6, 5.4 Hz, 1H), 3.77 (dd, J = 11.6, 6.2 Hz, 1H), 5.70 (d, J = 9.8 Hz, 1H), 6.77 (d, J = 9.8 Hz, 1H), 7.19 (ddd, J = 8.0, 7.0, 1.0 Hz, 1H), 7.33 (ddd, J = 8.1, 7.0, 1.1 Hz, 1H), 7.39 (d, J = 8.1 Hz, 1H), 7.69 (s, 1H), 7.92 (br s, 1H), 7.93 (d, J = 7.4 Hz, 1H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$, δ) 16.2 (CH_3), 22.4 (CH_3), 68.7 (CH_2), 79.3 (C), 104.3 (C), 110.6 (CH), 117.4 (C), 118.4 (C), 119.6 (CH), 119.8 (2CH), 121.8 (CH), 123.9 (C), 124.7 (CH), 125.7 (CH), 135.0 (C), 139.6 (C), 149.1 (C). ^1H NMR (600 MHz, acetone-d_6, δ) 1.43 (s, 3H), 2.30 (s, 3H), 3.68 (dd, J = 11.3, 6.2 Hz, 1H), 3.73 (dd, J = 11.3, 6.2 Hz, 1H), 4.02 (t, J = 6.2 Hz, 1H), 5.79 (d, J = 9.8 Hz, 1H), 7.00 (d, J = 9.8 Hz, 1H), 7.11 (t, J = 7.7 Hz, 1H), 7.26 (br t, J = 7.7 Hz, 1H), 7.41 (d, J = 8.0 Hz, 1H), 7.71 (s, 1H), 7.94 (d, J = 7.7 Hz, 1H), 10.28 (br s, 1H). ^{13}C NMR and DEPT (150 MHz, acetone-d_6, δ) 16.2 (CH_3), 23.0 (CH_3), 68.3 (CH_2), 79.8 (C), 105.3 (C), 111.4 (CH), 117.6 (C), 118.3 (C), 119.7 (CH), 119.9 (CH), 120.0 (CH), 121.8 (CH), 124.4 (C), 124.9 (CH), 127.0 (CH), 136.4 (C), 141.0 (C), 150.3 (C). EIMS (70 eV) m/z 279 (16) $[M]^+$, 248 (100), 217 (4), 204 (4). HRMS m/z $[M]^+$ calcd for $C_{18}H_{17}NO_2$, 279.1259; found, 279.1258. Anal. Calcd for $C_{18}H_{17}NO_2$: C, 77.40; H, 6.13; N, 5.01. Found: C, 77.24; H, 6.27; N, 4.99.

*Murrayamine K (**8**).* Triethylamine (60 μL, 44 mg, 0.43 mmol), acetic anhydride (33 μL, 36 mg, 0.35 mmol), and 4-dimethylaminopyridine (DMAP; 1.8 mg, 0.015 mmol) were added to a solution of (3,5-dimethyl-3,11-dihydropyrano[3,2-*a*]carbazol-3-yl)methanol (**23**) (81.3 mg, 0.291 mmol) in dichloromethane (9 mL), and the mixture was stirred for 1 h at room temperature. The mixture was diluted with diethyl ether and washed several times with water, saturated aqueous solution of ammonium chloride, and brine. The aqueous layers were extracted with diethyl ether, the combined organic layers were dried over sodium sulfate, and the solvent was evaporated. Purification by column chromatography (silica gel, pentane−dichloromethane−ethyl acetate, gradient from 20:5:1 to 16:5:1) provided murrayamine K (**8**) (85.4 mg, 91%) as a colorless solid, mp 137 °C (lit.[11] mp 127−128 °C). UV (MeOH) λ_{max} 222, 237, 278, 288, 326, 329, 344, 359 nm. Fluorescence (MeOH) λ_{ex} 237 nm, λ_{em} 358 nm. IR (ATR) ν 3372, 3335, 3055, 2988, 2939, 1719, 1685, 1643, 1611, 1495, 1457, 1373, 1323, 1255, 1213, 1147, 1124, 1060, 1027, 979, 940, 896, 840, 783, 742, 721, 703, 678, 639 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ) 1.51 (s, 3H), 2.02 (s, 3H), 2.32 (s, 3H), 4.18 (d, J = 11.5 Hz, 1H), 4.27 (d, J = 11.5 Hz, 1H), 5.63 (d, J = 9.8 Hz, 1H), 6.77 (d, J = 9.8 Hz, 1H), 7.19 (ddd, J = 7.9, 7.0, 0.9 Hz, 1H), 7.32 (ddd, J = 8.1, 7.0, 1.1 Hz, 1H), 7.38 (d, J = 8.1 Hz, 1H), 7.67 (s, 1H), 7.91 (d, J = 7.9 Hz, 1H), 7.94 (br s, 1H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$, δ) 16.1 (CH_3), 21.0 (CH_3), 23.4 (CH_3), 68.0 (CH_2), 76.9 (C), 104.1 (C), 110.6 (CH), 117.3 (C), 118.5 (C), 119.5 (CH), 119.7 (CH), 120.0 (CH), 121.9 (CH), 123.9 (C), 124.5 (CH), 124.6 (CH), 134.9 (C), 139.6 (C), 149.4 (C), 171.1 (C═O). EIMS (70 eV) m/z 321 (8) $[M]^+$, 248 (100), 233 (3), 217 (5), 204 (6). Anal. Calcd for $C_{20}H_{19}NO_3$: C, 74.75; H, 5.96; N, 4.36. Found: C, 74.93; H, 5.98; N, 4.55.

Synthesis of Murrayamine I (7). *O-(Triisopropylsilyl)-murrayamine I (**24**) and [3,5-dimethyl-9-(triisopropylsilyloxy)-3,11-dihydropyrano[3,2-a]carbazol-3-yl]methanol (**25**). Method A.* 4-Acetoxy-3-methylbut-2-enal (**21**) (123 mg, 0.865 mmol) was added to a solution of the 2-hydroxycarbazole **13** (213 mg, 0.576 mmol) in toluene (10 mL). Titanium(IV) isopropoxide (0.69 mL, 0.66 g, 2.33 mmol) was added slowly, and the reaction mixture was stirred at room temperature for 22.5 h. The mixture was diluted with dichloromethane, the solvent was evaporated, and the residue was purified by column chromatography (silica gel, isohexane−ethyl acetate 5:1). Pyranocarbazolylmethanol **25** was obtained from the more polar fraction (44.8 mg, 17%) as a light yellow oil. UV (MeOH) λ_{max} 221, 241, 284 (sh), 293, 324, 359 nm. Fluorescence (MeOH) λ_{ex} 293 nm, λ_{em} 378 nm. IR (ATR) ν 3332, 2942, 2865, 1732, 1697, 1623, 1495, 1453, 1400, 1311, 1277, 1241, 1210, 1159, 1057, 1017, 969, 884, 838, 803, 714, 682 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ) 1.13 (d, J = 7.4 Hz, 18H), 1.26−1.33 (m, 3H), 1.41 (s, 3H), 2.32 (s, 3H), 3.68 (dd, J = 11.5, 3.9 Hz, 1H), 3.75 (dd, J = 11.5, 4.8 Hz, 1H), 5.67 (d, J = 9.8 Hz, 1H), 6.73 (d, J = 9.8 Hz, 1H), 6.77 (dd, J = 8.4, 2.1 Hz, 1H), 6.89 (d, J = 2.1 Hz, 1H), 7.57 (s, 1H), 7.71 (d, J = 8.4 Hz, 1H), 7.82 (br s, 1H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$, δ) 12.8 (3CH), 16.2 (CH_3), 18.1 (6CH_3), 22.3 (CH_3), 68.6 (CH_2), 79.1 (C), 101.7 (CH), 104.3 (C), 113.3 (CH), 117.6 (C), 118.08 (C), 118.11 (C), 119.8 (CH), 119.9 (CH), 121.0 (CH), 125.8 (CH), 135.0 (C), 140.9 (C), 148.1 (C), 154.3 (C). ESIMS (+10 V) m/z 452 $[M + H]^+$. Anal. Calcd for $C_{27}H_{37}NO_3Si$: C, 71.80; H, 8.26; N, 3.10. Found: C, 71.84; H, 8.52; N, 2.93.

O-(Triisopropylsilyl)murrayamine I (**24**) was obtained from the less polar fraction (19.5 mg, 7%) as a brownish solid; see spectroscopic data below.

Method B. A 25 mL round-bottom flask was charged with the 2-hydroxycarbazole **13** (197 mg, 0.533 mmol) and phenylboronic acid (13 mg, 0.11 mmol) under an argon atmosphere. Toluene (4.7 mL), propanoic acid (4.4 mL, 59 mmol), and 4-acetoxy-3-methyl-but-2-enal (**21**) (152 mg, 1.07 mmol) were added, and the mixture was stirred at reflux for 17 h and then cooled to room temperature. Diethyl ether was added, and the mixture was washed with saturated aqueous potassium carbonate and water. The combined aqueous layers were extracted with ether once, the combined organic layers were dried over magnesium sulfate, and the solvent was evaporated. Purification of the residue by flash chromatography (silica gel, isohexane−ethyl acetate 8:1) provided **24** (158 mg, 60%) as a brownish solid, mp 62−65 °C. UV (MeOH) λ_{max} 220, 240, 284 (sh), 294, 324, 360 nm. Fluorescence (MeOH) λ_{ex} 294 nm, λ_{em} 370 nm. IR (ATR) ν 3379, 2943, 2865, 1725, 1623, 1560, 1496, 1439, 1370, 1311, 1276, 1241, 1211, 1157, 1043, 969, 883, 837, 801, 778, 748, 714, 680, 641 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ) 1.12 (d, J = 7.4 Hz, 18H), 1.24−1.35 (m, 3H), 1.50 (s, 3H), 2.03 (s, 3H), 2.30 (d, J = 0.4 Hz, 3H), 4.17 (d, J = 11.5 Hz, 1H), 4.26 (d, J = 11.5 Hz, 1H), 5.63 (d, J = 9.8 Hz, 1H), 6.73 (d, J = 9.8 Hz, 1H), 6.76 (dd, J = 8.4, 2.1 Hz, 1H), 6.88 (d, J = 2.1 Hz, 1H), 7.56 (s, 1H), 7.70 (d, J = 8.4 Hz, 1H), 7.77 (br s, 1H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$, δ) 12.9 (3CH), 16.1 (CH_3), 18.1 (6CH_3), 21.0 (CH_3), 23.3 (CH_3), 67.9 (CH_2), 76.7 (C), 101.7 (CH), 104.2 (C), 113.3 (CH), 117.5 (C), 118.1 (C), 118.3 (C), 119.9 (CH), 120.0 (CH), 121.1 (CH), 124.7 (CH), 134.9 (C), 140.8 (C), 148.4 (C), 154.3 (C), 171.1 (C═O). ESIMS (+10 V) m/z = 494 $[M + H]^+$. Anal. Calcd for $C_{29}H_{39}NO_4Si$: C, 70.55; H, 7.96; N, 2.84. Found: C, 70.46; H, 7.98; N, 2.94.

*Murrayamine I (**7**).* TBAF (1 M in THF, 0.38 mL, 0.38 mmol) was added slowly at 0 °C to a solution of the pyrano[3,2-*a*]carbazole **24** (125 mg, 0.253 mmol) in THF (5 mL). The mixture was stirred for 5 min at 0 °C and water was added. The mixture was diluted with diethyl ether and washed with water. The aqueous layer was extracted with diethyl ether. The combined organic layers were dried over magnesium sulfate and the solvent was evaporated. Purification of the residue by column chromatography (silica gel, isohexane−ethyl acetate 2:1) provided murrayamine I (**7**) (69 mg, 81%) as a light yellow solid, mp 182−185 °C (lit.[11] oil). UV (MeOH) λ_{max} 218, 239, 285 (sh), 295, 327, 359 nm. Fluorescence (MeOH) λ_{ex} 295 nm, λ_{em} 359 nm. IR (ATR) ν 3405, 3286, 2982, 2930, 1844, 1709, 1652, 1627, 1486, 1474, 1438, 1388, 1287, 1249, 1210, 1153, 1126, 1024, 981, 957, 913, 874, 829, 802, 776, 749, 721, 676, 638 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ) 1.50 (s, 3H), 2.02 (s, 3H), 2.30 (s, 3H), 4.17 (d, J = 11.5 Hz, 1H), 4.26 (d, J = 11.5 Hz, 1H), 4.90 (br s, 1H), 5.63 (d, J = 9.8 Hz, 1H), 6.69 (dd, J = 8.4, 2.2 Hz, 1H), 6.73 (d, J = 9.8 Hz, 1H), 6.83 (d, J = 2.2 Hz, 1H), 7.56 (s, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.79 (br s, 1H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$, δ) 16.1 (CH_3), 21.0 (CH_3), 23.4 (CH_3), 68.0 (CH_2), 76.7 (C), 97.1 (CH), 104.2 (C), 108.6 (CH), 117.4 (C), 118.1 (C), 118.4 (C), 120.0 (CH), 120.3 (CH), 121.1 (CH), 124.8 (CH), 134.8 (C), 140.9 (C), 148.5 (C), 153.9 (C), 171.1 (C═O). EIMS (70 eV) m/z 337 (6) $[M]^+$, 264 (100), 234 (6), 220 (5), 43 (11). Anal. Calcd for $C_{20}H_{19}NO_4$: C, 71.20; H, 5.68; N, 4.15. Found: C, 71.13; H, 6.02; N, 4.14.

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■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra of **1**, **3**−**9**, **11**−**13**, **15**, **17**, **18**, and **23**−**25**, ^{1}H NMR spectrum of the mixture of **18** and **19**, and 2D NMR spectra of **6**, **7**, and **23**; one figure and three tables describing X-ray crystal structure determination of **6** (PDF). Crystallographic structure file for **6** (CIF). The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00630.

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Notes

The authors declare no competing financial interest.

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