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Total Synthesis of Murrayamine-E, Murrayamine-I, and Murrayamine-K

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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.5b00630 • Publication Date (Web): 27 Apr 2015

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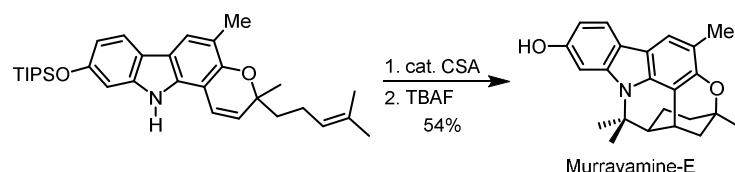
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ABSTRACT

We describe an efficient synthetic route to murrayamine-A (mukoenine-C), *O*-methylmurrayamine-A, mahanine, *O*-methylnahanine, and murrayamine-D and the first total synthesis of murrayamine-E, murrayamine-I, and murrayamine-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 Asian traditional 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 from *Murraya euchrestifolia* (Figure 1).² Two years later, Furukawa *et al.* obtained the same alkaloid from *M. koenigii* and named it mukoenine-C (**1**).³ In the course of the structural elucidation, Wu described the *O*-methylation of **1** to provide *O*-methylmurrayamine-A (**2**),² which was isolated as a natural product in 2003 by Nakatani *et al.* from the leaves of *M. koenigii*.⁴ The geranyl-derived pyranocarbazole mahanine (**3**) has been isolated from the same natural sources as compound **1**. In 1991, Wu isolated (+)-**3** from the leaves of *Murraya euchrestifolia* and assigned an (*S*)-configuration based on the Cotton effect.^{2,5} (–)-Mahanine [(–)-**3**] had been isolated already in 1970 by

Narasimhan and co-workers from the leaves of *M. koenigii*.⁶ More than 30 years later, Nakatani *et al.* obtained the enantiomer (+)-**3** from the same species.⁷ The corresponding *O*-methyl derivative (±)-**4** was first described as synthetic compound by Kapil and co-workers in 1972.⁸ In 2003, Nakatani *et al.* obtained (+)-*O*-methylnahanine [(+)-**4**] from the leaves of *M. koenigii*.⁴ 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.* from the leaves of *M. euchrestifolia*.⁹ 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.* from *M. euchrestifolia*.¹¹ 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).

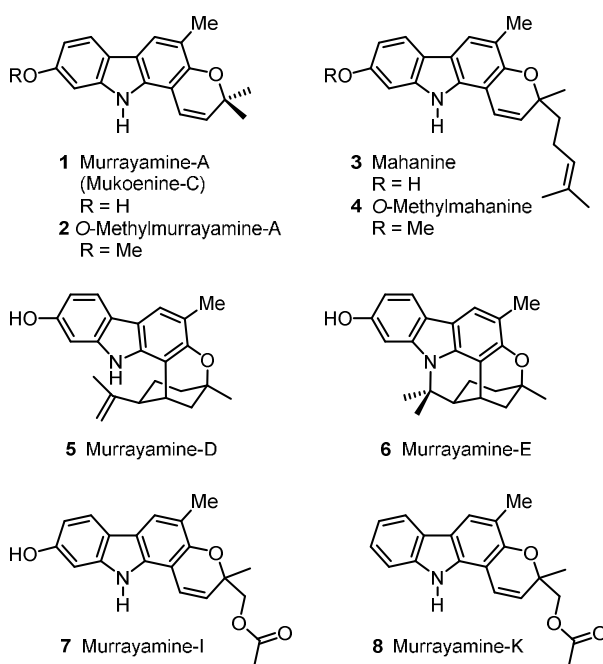
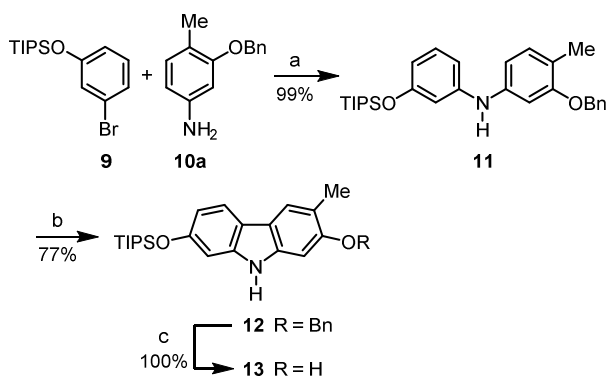


Figure 1. Naturally occurring 7-oxygenated pyrano[3,2-*a*]carbazole alkaloids **1–7** and murrayamine-K (**8**).

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 amination¹³ of the silyl-protected bromophenol **9** with the aniline **10a**¹⁰ using catalytic amounts of palladium(II) acetate and *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.

Scheme 1. Synthesis of the 2-hydroxycarbazole **13**^a

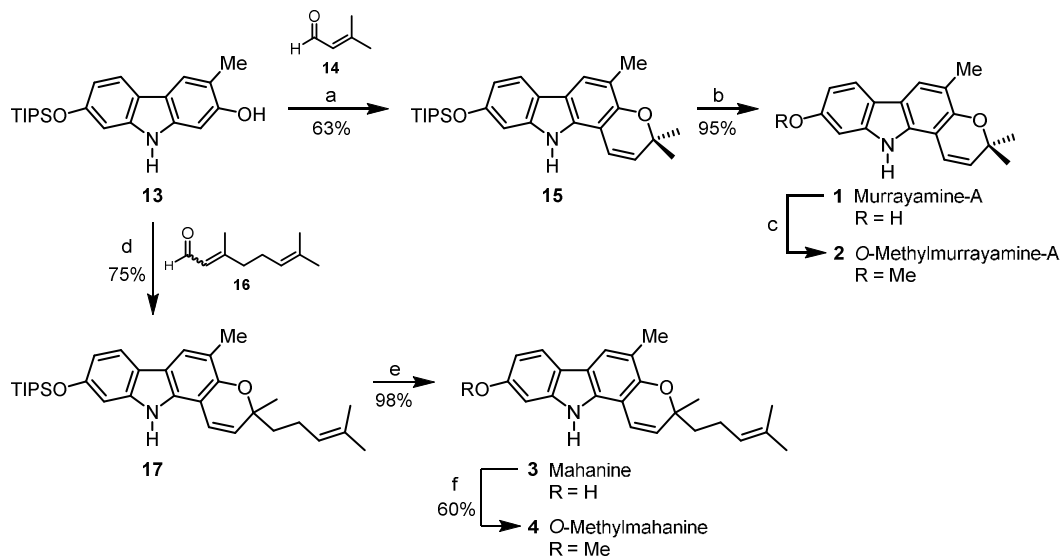


^a Reagents and conditions: (a) 1.0 equiv. **9**, 1.2 equiv. **10a**, 6 mol% Pd(OAc)₂, 6 mol% *rac*-BINAP, 1.5 equiv. Cs₂CO₃, PhMe, reflux, 23.5 h; (b) 10 mol% Pd(OAc)₂, 2.5 equiv. Cu(OAc)₂, AcOH, microwave, 300 W, 130 °C, 2 h; (c) 20 wt% Pd/C, H₂ (1 atm), MeOH–CH₂Cl₂, (5:2), rt, 24 h.

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 the 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**.¹⁵ Subsequent cleavage of the silyl ether using TBAF transformed **15** into murrayamine-A (**1**), which was obtained in 5 steps and 46% overall yield based on the protected 3-bromophenol **9**. *O*-Methylmurrayamine-A (**2**) is available from **1** following Wu's procedure.² The prenylated analogs 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**) 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 5 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*-methilmahanine (**4**). Thus, our present route provides the hydroxycarbazole alkaloids **1** and **3** and their corresponding methyl ethers **2** and **4**. A synthetic access to the latter compounds, *O*-methilmurrayamine-A (**2**) and *O*-methilmahanine (**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

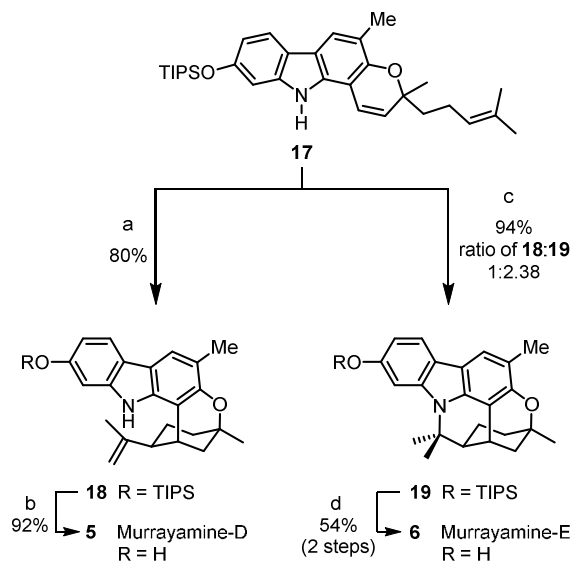
Scheme 2. Synthesis of the pyrano[3,2-*a*]carbazole alkaloids **1–4**^a



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

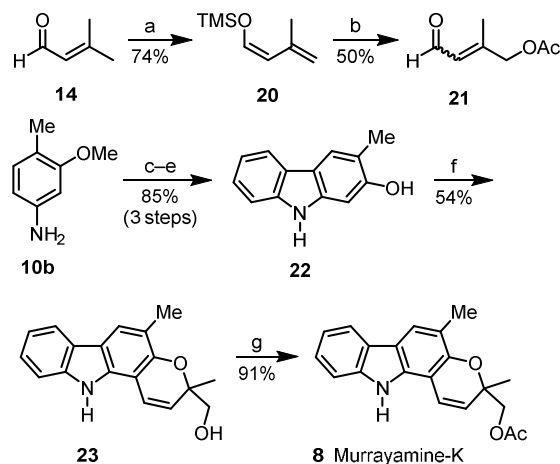
Based on our studies on the synthesis of cyclized monoterpenoid pyrano[3,2-*a*]carbazole alkaloids, like cyclomahanimbine (curryanin, murrayazolidine), mahanimbidine (curryangin, murrayazoline),¹⁰ murrayamine-G, and isomurrayazoline,¹⁹ we envisaged the total synthesis of murrayamine-D (**5**) and murrayamine-E (**6**) by proton-catalyzed cyclization of the protected mahanine **17** (Scheme 3). Treatment of **17** with 0.5 equivalents of trifluoroacetic acid (TFA) in toluene led to the 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% of 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 compound **19** from the solvent prevents further proton-catalyzed isomerization of **19** to **18** (*cf.*,¹⁰ the corresponding proton-catalyzed transformation of mahanimbidine to cyclomahanimbine). After cleavage of the silyl ether, the isomers **5** and **6** could be separated and pure murrayamine-E (**6**) was obtained in 54% yield based on compound **17**. The structure of murrayamine-E (**6**) has been unequivocally confirmed by a single-crystal X-ray analysis (see Supporting Information, Figure S1). Based on 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, compound **19** is then converted to **18**. Using *n*-hexane as solvent, the latter process is retarded due to precipitation of the cyclization products.

Scheme 3. Synthesis of murrayamine-D (**5**) and murrayamine-E (**6**)^a



^a Reagents and conditions: (a) 0.5 equiv. TFA, PhMe, rt, 16.5 h; (b) 1.4 equiv. 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. TBAF, THF, 0 °C, 5 min.

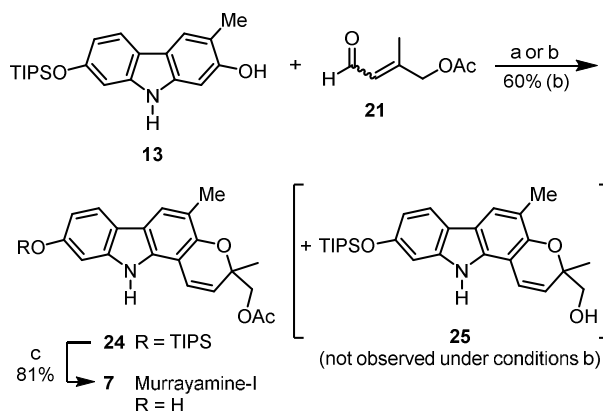
For the synthesis of murrayamine-K (**8**) and murrayamine-I (**7**), we required the known acetoxy substituted prenal derivative **21** (Scheme 4). Treatment of prenal (**14**) with chlorotrimethylsilane and triethylamine in the presence of zinc chloride provided the silyl dienolate **20**.²⁰ Oxidation of compound **20** using 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** using our well-established palladium-catalyzed route.¹⁰ Buchwald–Hartwig coupling¹³ of iodobenzene and compound **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 Based on our previous syntheses of non-oxygenated pyrano[3,2-*a*]carbazoles,¹⁰ the pyran ring was annulated at **22** using 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 compound **23**. Esterification of **23** with acetic anhydride afforded murrayamine-K (**8**) in 5 steps and 42% overall yield.

Scheme 4. Synthesis of murrayamine-K (**8**)^a

^a Reagents and conditions: (a) 1.1 equiv. TMSCl, 1.9 equiv. NEt₃, 0.9 mol% ZnCl₂, reflux, 25 h (ref. ²⁰); (b) 0.85 equiv. Pd(OAc)₂, 0.85 equiv. NaOAc, MeCN, 40 °C, 3 h (ref. ²¹); (c) 1.2 equiv. **10b**, 1.0 equiv. PhI, 5 mol% Pd(OAc)₂, 10 mol% SPhos, 1.4 equiv. Cs₂CO₃, PhMe, 100 °C, 26 h, 96%; (d) 5 mol% Pd(OAc)₂, 5 mol% K₂CO₃, PivOH, air, 100 °C, 24 h, 90%; (e) 1.6 equiv. BBr₃, CH₂Cl₂, -78 °C to rt, 15.5 h, 98%; (f) 1. 1.5 equiv. **21**, 2.7 equiv. Ti(OiPr)₄, PhMe, -78 °C to rt, 19.5 h; 2. 0.5 equiv. K₂CO₃, MeOH, rt, 19 h; (g) 1.2 equiv. Ac₂O, 1.5 equiv. NEt₃, 5 mol% DMAP, CH₂Cl₂, rt, 1 h.

Analogously, murrayamine-I (**7**) was obtained by pyran annulation at the monoprotected 2,7-dioxygenated carbazole **13** (Scheme 5). Reaction of 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 using TBAF afforded murrayamine-I (**7**) in 5 steps and 37% overall yield.

Scheme 5. Synthesis of murrayamine-I (**7**)^a



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

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 obtained in 5 steps and 46% overall yield, mahanine (**3**) in 5 steps and 56% overall yield, *O*-methylmahanine (**4**) in 6 steps and 34% overall yield, and murrayamine-D (**5**) in 6 steps and 42% overall yield. We have shown that the titanium(IV)-mediated and the 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**) (6 steps, 31% overall yield), murrayamine-I (**7**) (5 steps, 37% overall yield), and murrayamine-K (**8**) (5 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 using dry solvents under an argon atmosphere unless stated otherwise. Acetonitrile, dichloromethane, tetrahydrofuran, and toluene were dried using 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 using a CEM Discover

microwave apparatus with a maximum power of 300 W and a maximum pressure of 20 bar. Flash chromatography: silica gel (0.035–0.070 mm). UV spectra were recorded on a UV/VIS spectrometer. IR spectra were recorded on an FT-IR spectrometer using 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 non-deuterated solvent as internal standard. The following abbreviations have been used: s: singlet, d: doublet, t: triplet, m: multiplet and br: broad. Mass spectra and HRMS: double focusing sector field analyzer, electron impact, 70 eV. Elemental analyses were measured on an elemental analyzer. X-ray crystal structure analyses were performed with a 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 Windows²⁷ were used as software.

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 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), then with a sat. aqueous solution of NaCl (20 mL), and dried over MgSO₄. 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%): 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, CDCl₃, δ): 1.09 (d, J = 7.4 Hz, 18 H), 1.21–1.28 (m, 3 H), 6.79–6.81 (m, 1 H), 7.04–7.09 (m, 3 H). ¹³C NMR and DEPT (125 MHz, CDCl₃, δ): 12.6 (3 CH), 17.9 (6 CH₃), 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 C₁₅H₂₅BrOSi 328.0858; found: 328.0855. Anal. Calcd for C₁₅H₂₅BrOSi: 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 μ mol), and *rac*-BINAP (31.4 mg, 50.4 μ mol) 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%): 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, 18 H), 1.19–1.27 (m, 3 H), 2.23 (s, 3 H), 5.02 (s, 2 H), 5.57 (br s, 1 H), 6.42 (dd, $J = 8.0, 2.0$ Hz, 1 H), 6.54 (dd, $J = 8.0, 2.0$ Hz, 1 H), 6.57 (t, $J = 2.0$ Hz, 1 H), 6.60 (dd, $J = 8.0, 2.0$ Hz, 1 H), 6.67 (d, $J = 2.0$ Hz, 1 H), 7.04 (t, $J = 8.0$ Hz, 2 H), 7.32 (m, 1 H), 7.37–7.43 (m, 4 H). ^{13}C NMR and DEPT (125 MHz, CDCl_3 , δ): 12.7 (3 CH), 15.8 (CH_3), 17.9 (6 CH_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 (2 CH), 129.8 (CH), 131.0 (CH), 137.3 (C), 141.7 (C), 144.9 (C), 157.05 (C), 157.4 (C). EIMS (70 eV) m/z : 461 (100) $[\text{M}]^+$, 418 (16), 326 (22), 91 (50). HRMS m/z : $[\text{M}]^+$ Calcd for $\text{C}_{29}\text{H}_{39}\text{NO}_2\text{Si}$ 461.2750; found: 461.2761. Anal. Calcd for $\text{C}_{29}\text{H}_{39}\text{NO}_2\text{Si}$: C, 75.44; H, 8.51; N, 3.03. Found: C, 75.52; H, 8.58; N, 3.15.

2-Benzoyloxy-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 $^\circ\text{C}$ 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-benzoyloxy-3-methyl-7-(triisopropylsilyloxy)carbazole (**12**) (242 mg, 77%): Light brown solid; mp 123–125 $^\circ\text{C}$. UV (MeOH) λ_{max} 211 (sh), 237, 263, 308, 322 nm. Fluorescence (MeOH) λ_{ex} 287; 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, 18 H), 1.23–1.32 (m, 3 H), 2.41 (s, 3 H), 5.15 (s, 2 H), 6.76 (dd, $J = 8.4, 2.1$ Hz, 1 H), 6.85 (d, $J = 2.1$ Hz, 1 H), 6.86 (s, 1 H), 7.32 (m, 1 H), 7.36–7.40 (m, 2 H), 7.48 (m, 2 H), 7.69 (s, 1 H), 7.71 (br s, 1 H), 7.73 (d, $J = 8.4$ Hz, 1 H). ^{13}C NMR and DEPT (125 MHz, CDCl_3 , δ): 12.7 (CH_3), 16.9 (3 CH), 18.0 (6 CH_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 (2 CH), 127.7 (CH), 128.5 (2 CH), 137.6 (C), 138.9 (C), 140.5 (C), 153.9 (C), 155.4 (C). EIMS (70 eV) m/z : 459 (44) $[\text{M}]^+$, 369 (46), 368 (100), 91 (12). HRMS m/z : $[\text{M}]^+$ Calcd for $\text{C}_{29}\text{H}_{37}\text{NO}_2\text{Si}$ 459.2594; found: 459.2587. Anal. Calcd for $\text{C}_{29}\text{H}_{37}\text{NO}_2\text{Si}$: 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%): Colorless solid; mp 126 °C. UV (MeOH) λ_{max} 231, 237, 264, 315, 322 nm. Fluorescence (MeOH) λ_{ex} 286; 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, 18 H), 1.30–1.39 (m, 3 H), 2.36 (s, 3 H), 6.76 (dd, $J = 8.4, 2.2$ Hz, 1 H), 6.94 (s, 1 H), 6.97 (d, $J = 2.2$ Hz, 1 H), 7.71 (s, 1 H), 7.80 (d, $J = 8.4$ Hz, 1 H), 8.15 (s, 1 H), 9.81 (br s, 1 H). ^{13}C NMR and DEPT (125 MHz, acetone- d_6 , δ): 13.4 (3 CH), 16.7 (CH₃), 18.3 (6 CH₃), 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 C₂₂H₃₁NO₂Si: C, 71.50; H, 8.46; N, 3.79. Found: C, 71.76; H, 8.43; N, 3.82.

***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%): Light brown oil. UV (MeOH) λ_{max} 219, 241, 269, 294, 311, 361 nm. Fluorescence (MeOH) λ_{ex} 240; 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, CDCl₃, δ): 1.12 (d, $J = 7.4$ Hz, 18 H), 1.25–1.32 (m, 3 H), 1.46 (s, 6 H), 2.31 (s, 3 H), 5.68 (d, $J = 9.7$ Hz, 1 H), 6.58 (d, $J = 9.7$ Hz, 1 H), 6.75 (dd, $J = 8.3, 2.1$ Hz, 1 H), 6.88 (d, $J = 2.1$ Hz, 1 H), 7.55 (s, 1 H), 7.70 (d, $J = 8.3$ Hz, 1 H), 7.74 (br s, 1 H). ^{13}C NMR and DEPT (125 MHz, CDCl₃, δ): 12.7 (3 CH), 16.0 (CH₃), 18.0 (6 CH₃), 27.5 (2 CH₃), 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 C₂₇H₃₇NO₂Si 435.2594; found: 435.2588.

Murrayamine-A (Mukoenine-C, 7-Hydroxygirinimbine) (1**)**

Tetrabutylammonium fluoride (110 μL , 110 μmol ; 1 M in THF) 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 \times 50 mL). The combined organic layers were washed with water (50 mL), then with a sat. 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%); Yellow oil (ref.² mp 162–163 °C). UV (MeOH) λ_{max} 220, 240, 285 (sh), 294, 324, 362 nm. Fluorescence (MeOH) λ_{ex} 280; 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, 6 H), 2.30 (d, J = 0.4 Hz, 3 H), 5.67 (d, J = 9.7 Hz, 1 H), 6.56 (d, J = 9.7 Hz, 1 H), 6.66 (dd, J = 8.3, 2.0 Hz, 1 H), 6.77 (d, J = 2.0 Hz, 1 H), 7.54 (s, 1 H), 7.70 (d, J = 8.3 Hz, 1 H), 7.74 (br s, 1 H). ^{13}C NMR and DEPT (125 MHz, CDCl_3 , δ): 16.0 (CH_3), 27.5 (2 CH_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) $[\text{M}]^+$, 264 (100). HRMS m/z : $[\text{M}]^+$ Calcd for $\text{C}_{18}\text{H}_{17}\text{NO}_2$ 279.1259; found: 279.1258.

***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 d 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%): Light yellow oil. UV (MeOH) λ_{max} 242, 283 (sh), 294, 325, 359 (sh) nm. Fluorescence (MeOH) λ_{ex} 325; 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, 18 H), 1.24–1.34 (m, 3 H), 1.43 (s, 3 H), 1.57 (s, 3 H), 1.65 (s, 3 H), 1.72–1.78 (m, 2 H), 2.12–2.18 (m, 2 H), 2.31 (s, 3 H), 5.08–5.11 (m, 1 H), 5.64 (d, J = 9.8 Hz, 1 H), 6.60 (d, J = 9.8 Hz, 1 H), 6.75 (dd, J = 8.4, 2.1 Hz, 1 H), 6.88 (d, J = 2.1 Hz, 1 H), 7.54 (s, 1 H), 7.69 (d, J = 8.4 Hz, 1 H), 7.72 (br s, 1 H). ^1H NMR (500 MHz, acetone- d_6 , δ): 1.17 (d, J = 7.4 Hz, 18 H), 1.31–1.39 (m, 3 H), 1.47 (s, 3 H), 1.60 (s, 3 H), 1.67 (d, J = 0.7 Hz, 3 H), 1.78–1.81 (m, 2 H), 2.19–2.25 (m, 2 H), 2.33 (d, J = 0.7 Hz, 3 H), 5.15–5.18 (m, 1 H), 5.78 (d, J = 9.8 Hz, 1 H), 6.78 (dd, J = 8.4, 2.1 Hz, 1 H), 6.94 (d, J = 9.8 Hz, 1 H), 6.98 (d, J = 2.1 Hz, 1 H), 7.65 (s, 1 H), 7.82 (d, J = 8.4 Hz, 1 H), 10.13 (br s, 1 H). ^{13}C NMR and DEPT (125 MHz, CDCl_3 , δ): 12.7 (3 CH), 16.0 (CH_3), 17.6 (CH_3), 18.0 (6 CH_3), 22.7 (CH_2), 25.7 (2 CH_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 (3 CH), 16.2 (CH_3), 17.6 (CH_3), 18.3 (6 CH_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) $[\text{M}]^+$.

Mahanine (3)

Tetrabutylammonium fluoride (241 μ L, 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%): Light yellow solid; mp 110–115 °C (ref.^{6a} mp 100 °C for (–)-**3**; ref.² mp 95–96 °C for (+)-**3**). UV (MeOH) λ_{max} 219, 241, 296, 327, 362 (sh) nm. Fluorescence (MeOH) λ_{ex} 327; 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, 3 H), 1.60 (s, 3 H), 1.67 (s, 3 H), 1.77–1.81 (m, 2 H), 2.19–2.25 (m, 2 H), 2.33 (s, 3 H), 5.17 (m, 1 H), 5.76 (d, *J* = 9.8 Hz, 1 H), 6.72 (dd, *J* = 8.4, 2.1 Hz, 1 H), 6.90 (d, *J* = 2.1 Hz, 1 H), 6.95 (d, *J* = 9.8 Hz, 1 H), 7.60 (s, 1 H), 7.76 (d, *J* = 8.4 Hz, 1 H), 8.02 (br s, 1 H), 8.28 (br s, 1 H). ¹³C NMR and DEPT (125 MHz, acetone-*d*₆, δ): 16.2 (CH₃), 17.6 (CH₃), 23.4 (CH₂), 25.7 (CH₃), 26.1 (CH₃), 41.4 (CH₂), 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 C₂₃H₂₅NO₂: 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 μ L, 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%): Colorless solid; mp 179–183 °C (ref.⁸ mp 180 °C). UV (MeOH) λ_{max} 221, 242, 284 (sh), 294, 341, 361 (sh) nm. Fluorescence (MeOH) λ_{ex} 300; 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, CDCl₃, δ): 1.43 (s, 3 H), 1.57 (s, 3 H), 1.65 (s, 3 H), 1.75 (t, *J* = 8.4 Hz, 2 H), 2.12–2.19 (m, 2 H), 2.31 (s, 3 H), 3.87 (s, 3 H), 5.09–5.12 (m, 1 H), 5.64 (d, *J* = 9.8 Hz, 1 H), 6.61 (d, *J* = 9.8 Hz, 1 H), 6.79 (dd, *J* = 8.5, 2.2 Hz, 1 H), 6.87 (d, *J* = 2.2 Hz, 1 H), 7.55 (s, 1 H), 7.76 (d, *J* = 8.5 Hz, 1 H and br s, 1 H). ¹³C NMR and DEPT (125 MHz, CDCl₃, δ): 16.0 (CH₃), 17.6

(CH₃), 22.7 (CH₂), 25.7 (CH₃), 25.7 (CH₃), 40.7 (CH₂), 55.6 (CH₃), 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 C₂₄H₂₇NO₂: 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%): Colorless crystals; mp 105–110 °C. UV (MeOH) λ_{max} 214, 241, 266, 315 nm. Fluorescence (MeOH) λ_{ex} 315; 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, CDCl₃, δ): 1.12 (d, *J* = 7.3 Hz, 18 H), 1.21–1.36 (m, 3 H), 1.42 (s, 3 H), 1.47 (m, 1 H), 1.48 (s, 3 H), 1.59–1.63 (m, 2 H), 1.85–1.88 (m, 1 H), 2.00 (dd, *J* = 12.8, 2.7 Hz, 1 H), 2.07 (dt, *J* = 8.9, 2.3 Hz, 1 H), 2.30 (s, 3 H), 2.55–2.57 (m, 1 H), 3.36 (d, *J* = 2.7 Hz, 1 H), 4.73 (s, 1 H), 4.81 (s, 1 H), 6.71 (dd, *J* = 8.3, 2.1 Hz, 1 H), 6.81 (d, *J* = 2.1 Hz, 1 H), 7.51 (s, 1 H), 7.55 (br s, 1 H), 7.66 (d, *J* = 8.3 Hz, 1 H). ¹³C NMR and DEPT (125 MHz, CDCl₃, δ): 12.7 (3 CH), 16.7 (CH₃), 18.0 (6 CH₃), 21.6 (CH₃), 23.1 (CH₂), 29.0 (CH₃), 36.3 (CH), 37.4 (CH₂), 39.9 (CH₂), 48.7 (CH), 73.7 (C), 101.4 (CH), 105.3 (C), 112.0 (CH₂), 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 C₃₂H₄₅NO₂Si 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%): Light yellow solid; mp 105–109 °C (ref.⁹ oil). UV (MeOH) λ_{max} 246, 275 (sh), 318 nm. Fluorescence (MeOH) λ_{ex} 318; 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, CDCl₃, δ): 1.42 (s, 3 H), 1.44–1.47 (m, 1 H), 1.48 (s, 3 H), 1.53–1.61 (m, 2 H), 1.85–1.89 (m, 1 H), 2.00 (dd, *J* = 12.8, 2.0 Hz, 1 H), 2.05–

2.10 (m, 1 H), 2.30 (s, 3 H), 2.55–2.57 (m, 1 H), 3.36 (m, 1 H), 4.73 (s, 1 H), 4.80 (t, $J = 1.4$ Hz, 1 H), 6.64 (dd, $J = 8.3, 2.2$ Hz, 1 H), 6.77 (d, $J = 2.2$ Hz, 1 H), 7.52 (s, 1 H), 7.60 (br s, 1 H), 7.68 (d, $J = 8.3$ Hz, 1 H). ^1H NMR (500 MHz, acetone- d_6 , δ): 1.43 (s, 3 H), 1.64 (s, 3 H), 1.62–1.68 (m, 1 H), 1.74 (dt, $J = 4.7, 13.3$ Hz, 1 H), 1.85–1.89 (m, 2 H), 2.13–2.16 (m, 2 H), 2.31 (s, 3 H), 2.59 (dt, $J = 12.5, 2.9$ Hz, 1 H), 3.60 (m, 1 H), 4.49 (s, 1 H), 4.66 (t, $J = 1.5$ Hz, 1 H), 6.67 (dd, $J = 8.4, 2.2$ Hz, 1 H), 6.87 (d, $J = 2.2$ Hz, 1 H), 7.54 (s, 1 H), 7.70 (d, $J = 8.4$ Hz, 1 H), 8.14 (s, 1 H), 8.91 (br s, 1 H). ^{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), 153.1 (C), 153.1 (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) $[\text{M}]^+$, 332 (61), 264 (46). HRMS m/z : $[\text{M}]^+$ Calcd for $\text{C}_{23}\text{H}_{25}\text{NO}_2$ 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 hydrogencarbonate 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 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, p. 28).

TBAF (1 M in THF, 0.13 mL, 0.133 mmol) was added at 0 °C to a solution of a mixture of the 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 of **6**: Light yellow solid; mp > 260 °C (decomp.) (ref.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, 1 H), 1.27 (s, 3 H), 1.28–1.33 (m, 1 H), 1.45 (s, 3 H), 1.50–1.64 (m, 2 H), 1.86 (s, 3 H), 1.89 (d, $J = 13.2$ Hz, 1 H), 1.94–1.97 (m, 1 H), 2.31 (s, 3 H), 2.37 (ddd, $J = 13.2, 5.2, 3.3$ Hz, 1 H), 3.27 (d, $J = 5.2$ Hz, 1 H), 6.65 (dd, $J = 8.3, 2.0$ Hz, 1 H), 6.95 (d, $J = 2.0$ Hz, 1 H), 7.36 (s, 1 H), 7.69 (d, $J = 8.3$ Hz, 1 H). ^1H NMR (500 MHz, $\text{DMSO}-d_6$, δ): –0.08–0.00 (m, 1 H), 1.16 (s, 3 H), 1.22–1.27 (m, 1 H), 1.38 (s, 3 H), 1.42–1.47 (m, 1 H), 1.50–1.57 (m, 1 H), 1.80 (s, 3 H), 1.95 (d, $J = 13.0$ Hz, 1 H), 2.01 (ddd, $J = 10.9, 5.3, 2.0$ Hz, 1 H), 2.20 (s, 3 H), 2.20–2.24 (m, 1 H), 3.20 (d, $J = 4.3$ Hz, 1 H), 6.58 (dd, $J = 8.3, 2.0$ Hz, 1 H), 6.90 (d, $J = 2.0$ Hz, 1 H), 7.29 (s, 1 H), 7.61 (d, $J = 8.3$ Hz, 1 H), 9.17 (s, 1 H). ^{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, $\text{DMSO}-d_6$, 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 $[\text{M}]^+$ (100), 332 (68), 304 (17), 264 (59). Anal. Calcd for $\text{C}_{23}\text{H}_{25}\text{NO}_2$: 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**): $\text{C}_{23}\text{H}_{25}\text{NO}_2$, $M = 347.44 \text{ g mol}^{-1}$, crystal size: $0.39 \times 0.18 \times 0.09 \text{ mm}^3$, monoclinic, space group: $P2_1/c$, $a = 10.845(3)$, $b = 11.246(2)$, $c = 15.472(3) \text{ \AA}$, $\beta = 107.92(2)^\circ$, $V = 1795.5(7) \text{ \AA}^3$, $Z = 4$, $\rho_{\text{calcd}} = 1.285 \text{ g cm}^{-3}$, $\mu = 0.081 \text{ mm}^{-1}$, $\lambda = 0.71073 \text{ \AA}$, $T = 198(2) \text{ K}$, θ range = $3.28\text{--}25.40^\circ$, reflections collected: 44140, independent: 3298 ($R_{\text{int}} = 0.0551$), 240 parameters. The structure was solved by direct methods and refined by full-matrix least squares on F^2 ; final R indices [$I > 2\sigma(I)$]: $R_1 = 0.0490$; $wR_2 = 0.1010$; maximal residual electron density: 0.190 e \AA^{-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.

(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%): Slightly yellow solid; mp 140 °C. UV (MeOH) λ_{max} 222, 237, 277 (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, 3 H), 2.00 (t, $J = 6.2$ Hz, 1 H), 2.34 (d, $J = 0.7$ Hz, 3 H), 3.70 (dd, $J = 11.6, 5.4$ Hz, 1 H), 3.77 (dd, $J = 11.6, 6.2$ Hz, 1 H), 5.70 (d, $J = 9.8$ Hz, 1 H), 6.77 (d, $J = 9.8$ Hz, 1 H), 7.19 (ddd, $J = 8.0, 7.0, 1.0$ Hz, 1 H), 7.33 (ddd, $J = 8.1, 7.0, 1.1$ Hz, 1 H), 7.39 (d, $J = 8.1$ Hz, 1 H), 7.69 (s, 1 H), 7.92 (br s, 1 H), 7.93 (d, $J = 7.4$ Hz, 1 H). ^{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 (2 CH), 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, 3 H), 2.30 (s, 3 H), 3.68 (dd, $J = 11.3, 6.2$ Hz, 1 H), 3.73 (dd, $J = 11.3, 6.2$ Hz, 1 H), 4.02 (t, $J = 6.2$ Hz, 1 H), 5.79 (d, $J = 9.8$ Hz, 1 H), 7.00 (d, $J = 9.8$ Hz, 1 H), 7.11 (t, $J = 7.7$ Hz, 1 H), 7.26 (br t, $J = 7.7$ Hz, 1 H), 7.41 (d, $J = 8.0$ Hz, 1 H), 7.71 (s, 1 H), 7.94 (d, $J = 7.7$ Hz, 1 H), 10.28 (br s, 1 H). ^{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) $[\text{M}]^+$, 248 (100), 217 (4), 204 (4). HRMS m/z : $[\text{M}]^+$ Calcd for $\text{C}_{18}\text{H}_{17}\text{NO}_2$ 279.1259; found: 279.1258. Anal. Calcd for $\text{C}_{18}\text{H}_{17}\text{NO}_2$: 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 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, 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 20:5:1 to 16:5:1) provided murrayamine-K (**8**) (85.4 mg, 91%): Colorless solid; mp 137 °C (ref.¹¹ mp 127–128 °C). UV (MeOH) λ_{max} 222, 237, 278, 288, 326, 329, 344, 359 nm. Fluorescence (MeOH) λ_{ex} 237; 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, 3 H), 2.02 (s, 3 H), 2.32 (s, 3 H), 4.18 (d, J = 11.5 Hz, 1 H), 4.27 (d, J = 11.5 Hz, 1 H), 5.63 (d, J = 9.8 Hz, 1 H), 6.77 (d, J = 9.8 Hz, 1 H), 7.19 (ddd, J = 7.9, 7.0, 0.9 Hz, 1 H), 7.32 (ddd, J = 8.1, 7.0, 1.1 Hz, 1 H), 7.38 (d, J = 8.1 Hz, 1 H), 7.67 (s, 1 H), 7.91 (d, J = 7.9 Hz, 1 H), 7.94 (br s, 1 H). ^{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) $[\text{M}]^+$, 248 (100), 233 (3), 217 (5), 204 (6). Anal. Calcd for $\text{C}_{20}\text{H}_{19}\text{NO}_3$: C, 74.75; H, 5.96; N, 4.36. Found: C, 74.93; H, 5.98; N, 4.55.

***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). The pyranocarbazolylmethanol **25** was obtained from the more polar fraction (44.8 mg, 17%): Light yellow oil. UV (MeOH) λ_{max} 221, 241, 284 (sh), 293, 324, 359 nm. Fluorescence (MeOH) λ_{ex} 293; 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, 18 H), 1.26–1.33 (m, 3 H), 1.41 (s, 3 H), 2.32 (s, 3 H), 3.68 (dd, J = 11.5, 3.9 Hz, 1 H), 3.75 (dd, J = 11.5, 4.8 Hz, 1 H), 5.67 (d, J = 9.8 Hz, 1 H), 6.73 (d, J = 9.8 Hz, 1 H), 6.77 (dd, J = 8.4, 2.1 Hz, 1 H), 6.89 (d, J = 2.1 Hz, 1 H), 7.57 (s, 1 H), 7.71 (d, J = 8.4 Hz, 1 H), 7.82 (br s, 1 H). ^{13}C NMR and DEPT (125 MHz, CDCl_3 , δ): 12.8 (3 CH), 16.2 (CH_3), 18.1 (6 CH_3), 22.3 (CH_3), 68.6 (CH_2), 79.1 (C), 101.7 (CH), 104.3 (C), 113.3 (CH), 117.6 (C), 118.1 (C), 118.1 (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 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{27}\text{H}_{37}\text{NO}_3\text{Si}$: 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; spectroscopic data: see 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. After cooling 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%): Brownish solid; mp 62–65 °C. UV (MeOH) λ_{max} 220, 240, 284 (sh), 294, 324, 360 nm. Fluorescence (MeOH) λ_{ex} 294; 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, 18 H), 1.24–1.35 (m, 3 H), 1.50 (s, 3 H), 2.03 (s, 3 H), 2.30 (d, $J = 0.4$ Hz, 3 H), 4.17 (d, $J = 11.5$ Hz, 1 H), 4.26 (d, $J = 11.5$ Hz, 1 H), 5.63 (d, $J = 9.8$ Hz, 1 H), 6.73 (d, $J = 9.8$ Hz, 1 H), 6.76 (dd, $J = 8.4, 2.1$ Hz, 1 H), 6.88 (d, $J = 2.1$ Hz, 1 H), 7.56 (s, 1 H), 7.70 (d, $J = 8.4$ Hz, 1 H), 7.77 (br s, 1 H). ^{13}C NMR and DEPT (125 MHz, CDCl_3 , δ): 12.9 (3 CH), 16.1 (CH_3), 18.1 (6 CH_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): $m/z = 494$ $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{29}\text{H}_{39}\text{NO}_4\text{Si}$: 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%): Light yellow solid; mp 182–185 °C (ref.¹¹ oil). UV (MeOH) λ_{max} 218, 239, 285 (sh), 295, 327, 359 nm. Fluorescence (MeOH) λ_{ex} 295; 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, 3 H), 2.02 (s, 3 H), 2.30 (s, 3 H), 4.17 (d, $J = 11.5$ Hz, 1 H), 4.26 (d, $J = 11.5$ Hz, 1 H), 4.90 (br s, 1 H), 5.63 (d, $J = 9.8$ Hz, 1 H), 6.69 (dd, $J = 8.4, 2.2$ Hz, 1 H), 6.73 (d, $J = 9.8$ Hz, 1 H), 6.83 (d, $J = 2.2$ Hz, 1 H), 7.56 (s, 1 H), 7.72 (d, $J = 8.4$ Hz, 1 H),

7.79 (br s, 1 H). ^{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) $[\text{M}]^+$, 264 (100), 234 (6), 220 (5), 43 (11). Anal. Calcd for $\text{C}_{20}\text{H}_{19}\text{NO}_4$: C, 71.20; H, 5.68; N, 4.15. Found: C, 71.13; H, 6.02; N, 4.14.

ASSOCIATED CONTENT

Supporting Information: ^1H NMR and ^{13}C NMR spectra of the compounds **1**, **3–9**, **11–13**, **15**, **17**, **18**, **23–25**; ^1H NMR spectrum of the mixture of **18** and **19**; 2D NMR spectra of the compounds **6**, **7**, and **23**; X-ray crystal structure determination of compound **6**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

REFERENCES

- (1) (a) Knölker, H.-J.; Reddy, K. R. *Chem. Rev.* **2002**, *102*, 4303; (b) Chakraborty, D. P.; Roy, S. In *Progress in the Chemistry of Organic Natural Products*; Herz, W., Grisebach, H., Kirby, G. W., Steglich, W., Tamm, C., Eds.; Springer-Verlag: Wien, 2003; Vol 85, p 125; (c) Knölker, H.-J.; Reddy, K. R. In *The Alkaloids*; Cordell, G. A., Ed.; Academic Press: Amsterdam, 2008; Vol 65, p 1; (d) Kongkathip, N.; Kongkathip, B. *Heterocycles* **2009**, *79*, 121; (e) Nagappan, T.; Ramasamy, P.; Wahid, M. E. A.; Segaran, T. C.; Vairappan, C. S. *Molecules* **2011**, *16*, 9651; (f) Roy, J.; Jana, A. K.; Mal, D. *Tetrahedron* **2012**, *68*, 6099; (g) Schmidt, A. W.; Reddy, K. R.; Knölker, H.-J. *Chem. Rev.* **2012**, *112*, 3193; (h) Ishikura, M.; Abe, T.; Choshi, T.; Hibino, S.

- Nat. Prod. Rep.* **2013**, *30*, 694.
- (2) Wu, T.-S. *Phytochemistry* **1991**, *30*, 1048.
- (3) Ito, C.; Thoyama, Y.; Omura, M.; Kajiura, I.; Furukawa, H. *Chem. Pharm. Bull.* **1993**, *41*, 2096.
- (4) Tachibana, Y.; Kikuzaki, H.; Lajis, N. H.; Nakatani, N. *J. Agric. Food. Chem.* **2003**, *51*, 6461.
- (5) Crabbé, P.; Klyne, W. *Tetrahedron* **1967**, *23*, 3449.
- (6) (a) Narasimhan, N. S.; Paradkar, M. V.; Kelkar, S. L. *Indian J. Chem.* **1970**, *8*, 473; (b) Narasimhan, N. S.; Paradkar, M. V.; Chitguppi, V. P.; Kelkar, S. L. *Indian J. Chem.* **1975**, *13*, 993.
- (7) Tachibana, Y.; Kikuzaki, H.; Lajis, N. H.; Nakatani, N. *J. Agric. Food. Chem.* **2001**, *49*, 5589.
- (8) Anwer, F.; Kapil, R. S.; Popli, S. P. *Experientia* **1972**, *28*, 769.
- (9) Wu, T.-S.; Wang, M.-L.; Wu, P.-L.; Jong, T.-T. *Phytochemistry* **1995**, *40*, 1817.
- (10) Hesse, R.; Gruner, K. K.; Kataeva, O.; Schmidt, A. W.; Knölker, H.-J. *Chem. Eur. J.* **2013**, *19*, 14098.
- (11) Wu, T.-S.; Wang, M.-L.; Wu, P.-L.; Ito, C.; Furukawa, H. *Phytochemistry* **1996**, *41*, 1433.
- (12) (a) Knölker, H.-J.; O'Sullivan, N. *Tetrahedron* **1994**, *50*, 10893; (b) Åkermark, B.; Oslob, J. D.; Heuschert, U. *Tetrahedron Lett.* **1995**, *36*, 1325; (c) Knölker, H.-J. *Top. Curr. Chem.* **2005**, *244*, 115; (d) Knölker, H.-J. *Chem. Lett.* **2009**, *38*, 8; (e) Bauer, I.; Knölker, H.-J. *Top. Curr. Chem.* **2012**, *309*, 203; (f) Hesse, R.; Krah, M. P.; Jäger, A.; Kataeva, O.; Schmidt, A. W.; Knölker, H.-J. *Eur. J. Org. Chem.* **2014**, 4014; (g) Schuster, C.; Börger, C.; Jülich-Gruner, K. K.; Hesse, R.; Jäger, A.; Kaufmann, G.; Schmidt, A. W.; Knölker, H.-J. *Eur. J. Org. Chem.* **2014**, 4741; (h) Jülich-Gruner, K. K.; Schmidt, A. W.; Knölker, H.-J. *Synthesis* **2014**, *46*, 2651.
- (13) (a) Surry, D. S.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2008**, *47*, 6338; (b) Hartwig, J. F. *Angew. Chem. Int. Ed.* **1998**, *37*, 2046.
- (14) (a) Iwai, I.; Ide, J. *Chem. Pharm. Bull.* **1962**, *10*, 926; (b) Iwai, I.; Ide, J. *Chem. Pharm. Bull.* **1963**, *11*, 1042; (c) Zsindely, J.; Schmid, H. *Helv. Chim. Acta* **1968**, *51*, 1510; (d) Godfrey Jr, J. D.; Mueller, R. H.; Sedergran, T. C.; Soundararajan, N.; Colandrea, V. J. *Tetrahedron Lett.* **1994**, *35*, 6405; (e) Sartori, G.; Casiraghi, G.; Bolzoni, L.; Casnati, G. *J. Org. Chem.* **1979**, *44*, 803; (f) Bissada, S.; Lau, C. K.; Bernstein, M. A.; Dufresne, C. *Can. J. Chem.* **1994**, *72*, 1866;

- (g) Chauder, B. A.; Lopes, C. C.; Lopes, R. S. C.; da Silva, A. J. M.; Snieckus, V. *Synthesis* **1998**, 279.
- (15) Julich-Gruner, K. K.; Kataeva, O.; Schmidt, A. W.; Knölker, H.-J. *Chem. Eur. J.* **2014**, *20*, 8536.
- (16) (a) Kureel, S. P.; Popli, S. P. *Chem. Commun.* **1969**, 1120; (b) Chakraborty, D. P.; Chatterji, D.; Ganguly, S. N. *Chem. Ind. (London)* **1969**, 1662; (c) Narasimhan, N. S.; Paradkar, M. V.; Gokhale, A. M. *Tetrahedron Lett.* **1970**, 1665; (d) Bandaranayake, W. M.; Begley, M. J.; Brown, B. O.; Clarke, D. G.; Crombie, L.; Whiting, D. A. *J. Chem. Soc., Perkin Trans. I* **1974**, 998; (e) Zeng, H.; Duan, D.; Tang, B. *Synlett* **2015**, *26*, 927.
- (17) Hesse, R.; Jäger, A.; Schmidt, A. W.; Knölker, H.-J. *Org. Biomol. Chem.* **2014**, *12*, 3866.
- (18) Gruner, K. K.; Hopfmann, T.; Matsumoto, K.; Jäger, A.; Katsuki, T.; Knölker, H.-J. *Org. Biomol. Chem.* **2011**, *9*, 2057.
- (19) Gassner, C.; Hesse, R.; Schmidt, A. W.; Knölker, H.-J. *Org. Biomol. Chem.* **2014**, *12*, 6490.
- (20) (a) Bazouin, A. R. M.; Dunogues, J. P.; Lefort, M. J. C. French Patent 1436568, 1964; (b) Gaonac'h, O.; Maddaluno, J.; Chauvin, J.; Duhamel, L. *J. Org. Chem.* **1991**, *56*, 4045.
- (21) Söderberg, B. C.; Berry, A. K.; Jones, P. C. *Organometallics* **1998**, *17*, 1069.
- (22) Bhattacharyya, P.; Chowdhury, B. K. *Indian J. Chem.* **1985**, *24B*, 452.
- (23) Bhattacharyya, P.; Jash, S. S.; Chowdhury, B. K. *Chem. Ind.* **1986**, 246.
- (24) Sheldrick, G. M. *SHELXS-97, Programs for Crystal Structure Solution*: University of Göttingen, Germany, 1997.
- (25) Sheldrick, G. M. *SADABS, v. 2.10, Bruker/Siemens Area Detector Absorption Correction Program*: Bruker AXS Inc., Madison, WI, USA, 2002.
- (26) Sheldrick, G. M. *SHELXL-97, Programs for Crystal Structure Refinement*: University of Göttingen, Germany, 1997.
- (27) Farrugia, L. *J. Appl. Crystallogr.* **1997**, *30*, 565.