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Total synthesis of the cyclic monoterpenoid pyrano[3,2-*a*]carbazole alkaloids derived from 2-hydroxy-6-methylcarbazole†‡

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The synthesis of seven pyrano[3,2-*a*]carbazole alkaloids has been achieved using their putative biogenetic precursor 2-hydroxy-6-methylcarbazole as key intermediate.

Introduction

The research groups of Chakraborty, Furukawa, Ito and Wu have isolated a wide range of biologically active carbazole alkaloids from plants of the family Rutaceae (genera *Murraya*, *Clausena* and *Glycosmis*).[1,2] The pyrano[3,2-*a*]carbazoles, *e.g.* **1–9**, are an important subgroup of carbazole alkaloids which exhibit diverse structural features (Fig. 1).[2] In 1964, girinimbine (**1**) was among the first carbazole alkaloids which have been isolated by Chakraborty *et al.* from terrestrial plants.[3] Only two years later, the same group described the isolation of the corresponding prenyl-substituted homologue mahanimbine (**2**).[4] Biogenetically, both compounds derive from 2-hydroxy-3-methylcarbazole by fusion with either prenyl or geranyl diphosphate.[2] Originally, girinimbine was erroneously assigned as structure **3**,[3a] but subsequently it had to be reassigned as **1**.[3b,c,d] Isogirinimbine (**3**) biogenetically could have been formed from 2-hydroxy-6-methylcarbazole (**10**) and prenyl diphosphate as C_5 building block (Scheme 1). Interestingly, although isogirinimbine (**3**) has not been found in nature so far, the corresponding carbazole alkaloids **4–9** resulting from fusion of 2-hydroxy-6-methylcarbazole (**10**) and geranyl diphosphate were isolated from natural sources.[2] In 1970, Kapil *et al.* isolated mahanimbicine [(+)-**4**] and bicyclomahanimbicine (**6**) from *Murraya koenigii*.[5] Subsequently, Crombie and Whiting *et al.* proposed the correct structure for bicyclomahanimbicine (**6**).[6] It is interesting to note that also in 1970, Joshi *et al.* obtained (−)-**4** from the leaves of the same plant and named it isomahanimbine,[7] however, the absolute configuration was not determined. The structures of **4** and **6** were supported by synthesis.[4c,d,5]

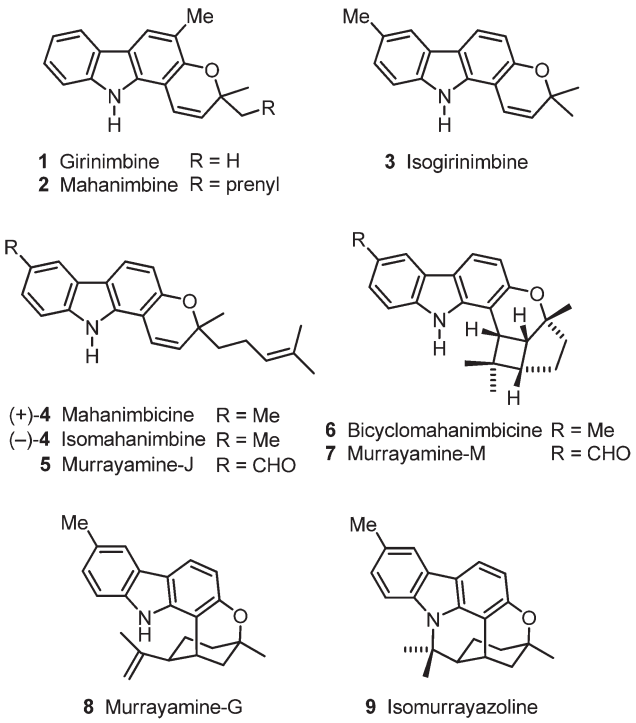

Fig. 1 Naturally occurring pyrano[3,2-*a*]carbazole alkaloids **1–9**.

Wu *et al.* isolated murrayamine-J (**5**),[8] murrayamine-M (**7**)[8] and murrayamine-G (**8**),[9] from the leaves of *Murraya euchrestifolia*. The hexacyclic pyrano[3,2-*a*]carbazole alkaloid isomurrayazoline (**9**) was obtained in 1982 by Chakraborty *et al.* from the stem bark of *Murraya koenigii*.[10]

We have developed diverse synthetic approaches to pyrano[3,2-*a*]carbazoles including girinimbine (**1**), mahanimbine (**2**), pyrayafoline A–E and monoterpenoid pyrano[3,2-*a*]carbazole alkaloids.[11–14] Herein, we describe the synthesis of isogirinimbine (**3**), (±)-mahanimbicine [(±)-isomahanimbine] [(±)-**4**], murrayamine-J (**5**) and the cyclic monoterpenoid pyrano[3,2-*a*]-carbazole alkaloids **6–9**, which biogenetically derive from

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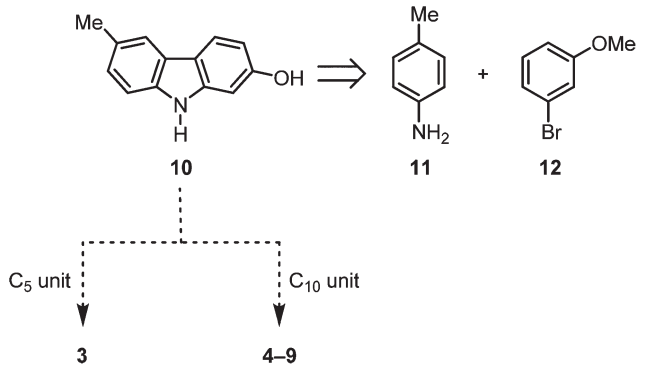
‡ Electronic supplementary information (ESI) available: ^{1}H and ^{13}C NMR spectra for all compounds. CCDC 1000251. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c4ob01151a



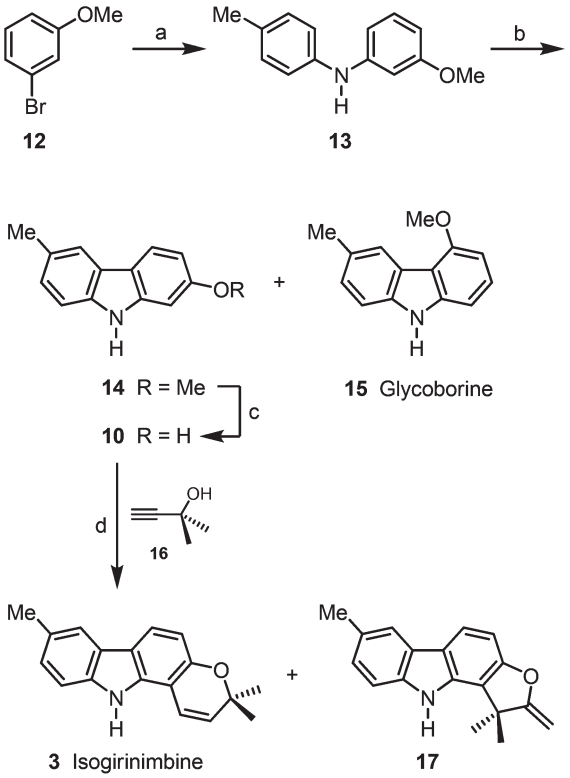
Scheme 1 Synthetic route to the pyrano[3,2-*a*]carbazoles **3–9**.

2-hydroxy-6-methylcarbazole (**10**). Key steps of our approach are an efficient construction of the carbazole **10** based on our palladium-catalyzed route[15] and a subsequent annulation of either a C_5 or a C_{10} building block (Scheme 1). The substitution pattern present in compound **10** has been generated previously in our synthesis of 7-oxygenated carbazole alkaloids.[16]

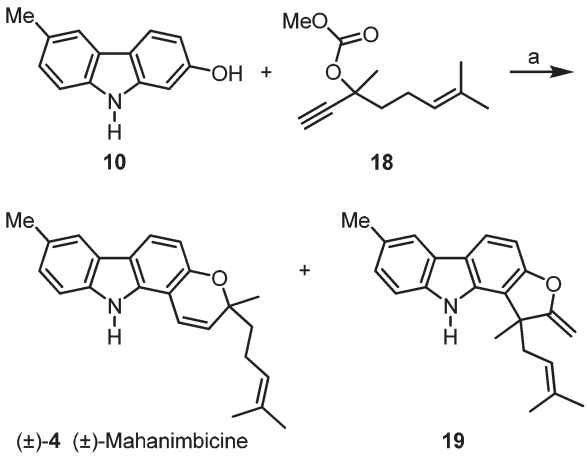
Results and discussion

Buchwald–Hartwig coupling of *p*-toluidine (**11**) and *m*-bromoanisole (**12**) in the presence of SPhos (2-dicyclohexylphosphino-2′,6′-dimethoxybiphenyl)[17] afforded the diarylamine **13** (Scheme 2). Alternatively, compound **13** has been prepared quantitatively on a 25 g scale by Buchwald–Hartwig coupling of *m*-anisidine and *p*-bromotoluene (see Experimental section).[16] Palladium(II)-catalyzed oxidative cyclization of **13** provided the desired 2-methoxy-6-methylcarbazole (**14**)[16] as major product (89% yield) and up to 5% of glycoborine (**15**)[18] as by-product. Cleavage of the methyl ether led to 2-hydroxy-6-methylcarbazole (**10**). Formation of the dimethylpropargyl ether *via* Godfrey's method,[19] followed by a thermally induced sequence of Claisen rearrangement, 1,5-hydrogen shift and electrocyclic ring closure[20] provided isogirinimbine (**3**) in 63% yield and as a by-product the furo[3,2-*a*]carbazole **17** in up to 3% yield. The structure of isogirinimbine (**3**) has been fully supported by its spectroscopic data which confirm it as an isomer of the natural product girinimbine (**1**). The 3-methyl-regioisomer of **17** was obtained previously as by-product in our synthesis of girinimbine (**1**).[12]

We envisaged (±)-mahanimbicine [(±)-isomahanimbine] [(±)-**4**] as crucial intermediate for the synthesis of the formyl derivative murrayamine-J (**5**) and the cyclic monoterpenoid pyrano[3,2-*a*]carbazole alkaloids **6–9.** Thus, we have developed two alternative synthetic routes for the synthesis of (±)-**4.** The first approach requires no protecting group (Scheme 3). Reaction of 2-hydroxy-6-methylcarbazole (**10**) with the carbonate **18**[21] in the presence of catalytic amounts of copper(I) iodide and subsequent thermally induced rearrangement provided



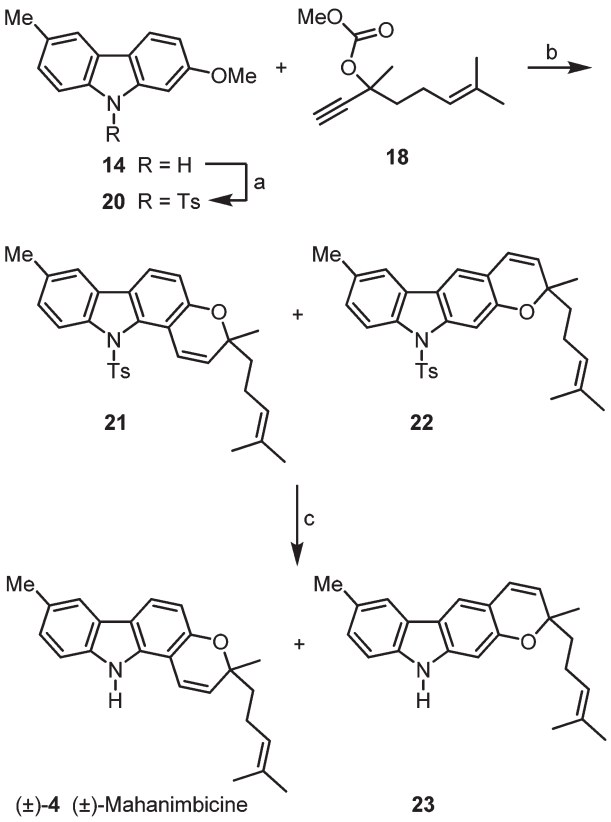
Scheme 2 Synthesis of isogirinimbine (**3**). *Reagents and conditions*: (a) 1.3 equiv. **11**, 5 mol% $Pd(OAc)_2$, 10 mol% SPhos, 1.4 equiv. Cs_2CO_3, toluene, reflux, 17.5 h, 98%; (b) 3 mol% $Pd(OAc)_2$, 10 mol% K_2CO_3, PivOH, 100 °C, 20.5 h, 89% **14** and ≤5% **15**; (c) 1.9 equiv. BBr_3, −78 °C to rt, 2 h, 91%; (d) 1. 1.1 equiv. **16**, 1.1 equiv. TFAA, 2.8 equiv. DBU, 0.2 mol% CuI, MeCN, −15 °C to rt, 6.5 h; 2. toluene, reflux, 23 h, 63% **3** and ≤3% **17**.



Scheme 3 Synthesis of (±)-mahanimbicine [(±)-**4**]. *Reagents and conditions*: (a) 1. 1.5 equiv. **18**, 2.0 equiv. DBU, 0.5 mol% CuI, MeCN, rt, 22 h; 2. toluene, reflux, 22.5 h, 49% (±)-**4** and ≤5% **19**.

(±)-mahanimbicine [(±)-**4**] in 49% yield along with the furo-[3,2-*a*]carbazole **19** in up to 5% yield as by-product.

Alternatively, 2-methoxy-6-methylcarbazole (**14**) was initially protected by transformation to the *N*-tosylcarbazole **20**

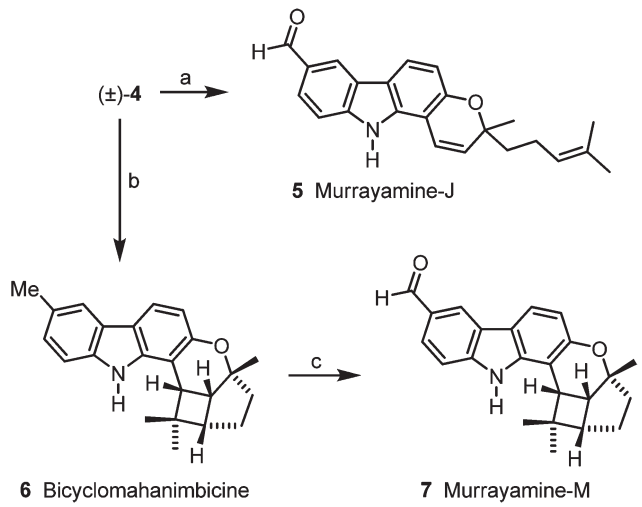


Scheme 4 Alternative route to (±)-mahanimbicine [(±)-**4**]. *Reagents and conditions*: (a) 4.1 equiv. NaH, 1.5 equiv. TsCl, THF, 0 °C to rt, 16.25 h, 80%; (b) 1. 3.0 equiv. BBr_3, CH_2Cl_2, −78 °C to rt, 2.5 h; 2. 2.0 equiv. **18**, 3.0 equiv. DBU, 0.5 mol% CuI, MeCN, rt, 22 h; 3. xylene, reflux, 27.5 h, 82% (3 steps, ratio **21**/**22** = 7.7 : 1); (c) 4.0 equiv. TBAF, THF, 75 °C, 6 h, 79% (±)-**4** and 9% **23**.

(Scheme 4). Cleavage of the methyl ether, copper-catalyzed reaction with the carbonate **18** and thermal rearrangement led in 82% yield to a mixture of the pyrano[3,2-*a*]carbazole **21** and the pyrano[2,3-*b*]carbazole **22** in a ratio of 7.7 : 1. Finally, removal of the tosyl group by treatment with tetrabutylammonium fluoride[22] at elevated temperature provided (±)-mahanimbicine [(±)-**4**].

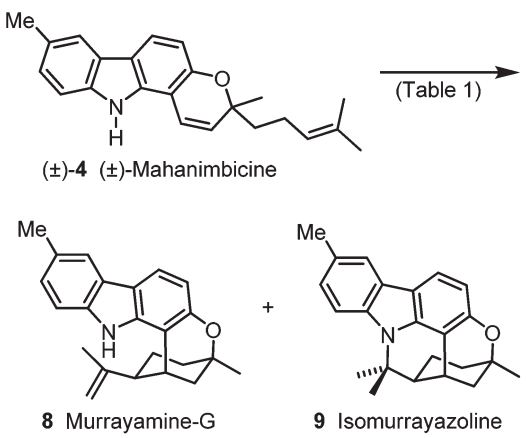
Using the first approach (Scheme 3), (±)-mahanimbicine [(±)-**4**] is available in 5 steps and 40% overall yield based on *p*-bromotoluene. Our second route (Scheme 4) leads to (±)-**4** in 7 steps and 46% overall yield based on the same starting material. It is interesting to note, that annulation of the pyran ring with the carbonate **18** at 2-hydroxy-6-methylcarbazole (**10**) provides the furo[3,2-*a*]carbazole **19** as by-product, whereas annulation at the corresponding *N*-tosylcarbazole gives the pyrano[2,3-*b*]carbazole **22** as by-product. This outcome is explained by the steric demand of the tosyl group which suppresses the formation of *N*-tosyl-**19** with the quaternary carbon center in close proximity to the protecting group; instead linear pyran annulation and thus formation of compound **22** is observed.

Using (±)-mahanimbicine [(±)-**4**] as relay compound the carbazole alkaloids **5**–**9** are accessible, following putative biogenetic routes. Oxidation of (±)-mahanimbicine [(±)-**4**] with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) afforded murrayamine-J (**5**) (Scheme 5). Intramolecular [2 + 2] cycloaddition of [(±)-**4**] led to bicyclomahanimbicine (**6**). Oxidation of **6** with DDQ gave murrayamine-M (**7**).



Scheme 5 Synthesis of murrayamine-J (**5**), bicyclomahanimbicine (**6**) and murrayamine-M (**7**). *Reagents and conditions*: (a) 8.0 equiv. DDQ, MeOH–THF–water (10 : 1 : 1), rt, 6.25 h, 67%; (b) $h\nu$, toluene, rt, 14 d, 39%; (c) 6.6 equiv. DDQ, MeOH–THF–water (10 : 1 : 2), rt, 5 h, 51%.

For the Brønsted acid promoted cycloisomerization of (±)-mahanimbicine [(±)-**4**], we took advantage of our previous study on the conversion of mahanimbine (**2**) into cyclomahanimbine and mahanimbidine.[12] On treatment of (±)-**4** with one equivalent camphor-10-sulfonic acid (CSA) at room temperature to 70 °C for 16 d, (±)-**4** and rapidly formed **9** were both completely converted into **8**. Thus, murrayamine-G (**8**) was obtained in 65% yield (Scheme 6, Table 1). Cycloisomerization of (±)-mahanimbicine [(±)-**4**] in the presence of catalytic amounts of CSA in hexane at room temperature afforded in 70% yield a 1 : 1 mixture of **8** and **9** which after separation by preparative HPLC led to pure isomurrayazoline (**9**). Our syn-



Scheme 6 Synthesis of murrayamine-G (**8**) and isomurrayazoline (**9**). *Reagents and conditions*: see Table 1.

Table 1 Cycloisomerization of (±)-mahanimbicine [(±)-**4**]

Reaction conditions	Yield	Ratio, **8** : **9**
1.0 equiv. CSA, PhMe, rt to 70 °C, 16 d	65% **8**	—
8 mol% CSA, hexane, rt, 11.5 d	70% **8**, **9**	1 : 1

thetic route leads to isomurrayazoline (**9**) in 8 steps and 16% overall yield based on *p*-bromotoluene.

Conclusions

We have developed a highly efficient palladium-catalyzed route to 2-hydroxy-6-methylcarbazole (**10**) (3 steps, 81% overall yield). Using appropriate C_5 or C_{10} building blocks, compound **10** has been transformed into isogirinimbine (**3**) and (±)-mahanimbicine [(±)-**4**], respectively. (±)-Mahanimbicine [(±)-**4**] served as central intermediate for the synthesis of cyclic monoterpenoid pyrano[3,2-*a*]carbazole alkaloids and could be converted into murrayamine-J (**5**), bicyclomahanimbicine (**6**), murrayamine-M (**7**), murrayamine-G (**8**) and isomurrayazoline (**9**). The spectroscopic data of the alkaloids were in full agreement with those reported for the corresponding natural products. For the compounds **3**, **5** and **7–9** we have achieved the first total synthesis. The present results emphasize the utility of our synthetic methodology and demonstrate that for the first time also the whole series of carbazole alkaloids which is isomeric to girinimbine (**1**) and mahanimbine (**2**) is available by synthesis on large scale. The biological properties of **3–9**, *e.g.* their potential anti-TB activity,[23] are under further investigation.

Experimental

General methods

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 (MBraun-SPS). Palladium(II) acetate was recrystallized from glacial acetic acid. All other chemicals were used as received from commercial sources. Flash chromatography was performed on a Büchi Sepacore system equipped with an UV monitor using silica gel from Acros Organics (0.035–0.070 mm). Thin layer chromatography was performed with TLC plates from Merck (60 F_{254}) using UV-light for visualization. Melting points were measured on a Gallenkamp MPD 350 melting point apparatus. Ultraviolet spectra were recorded on a Perkin Elmer 25 UV/VIS spectrometer. Infrared spectra were recorded on a Thermo Nicolet Avatar 360 FT-IR spectrometer using the ATR method (Attenuated Total Reflectance). NMR spectra were recorded on Bruker Avance II 300, DRX 500 and Avance III 600 spectrometers. Chemical shifts δ are reported in parts per million with the non-deuterated solvent as internal standard.[24] The following abbreviations have been used: s: singlet, d: doublet, t: triplet, m: multiplet and br: broad. Mass spectra were recorded on a Finnigan MAT-95 spectrometer (electron impact, 70 eV) or by GC/MS-coupling using an Agilent Technologies 6890 N GC System equipped with a 5973 Mass Selective Detector (electron impact, 70 eV). ESI-MS spectra were recorded on an Esquire LC with an ion trap detector from Bruker. Positive and negative ions were detected. Elemental analyses were measured on an EuroVector EuroEA3000 elemental analyzer.

3-Methoxy-*N*-(4-methylphenyl)aniline (13). *Method A*: A solution of *m*-bromoanisole (**12**) (2.00 g, 10.7 mmol) in toluene (5 mL) was added dropwise over a period of 5 h to a suspension of *p*-toluidine (**11**) (1.51 g, 14.1 mmol), palladium(II) acetate (123 mg, 548 μmol), SPhos (440 mg, 1.07 mmol) and caesium carbonate (4.90 g, 15.0 mmol) in toluene (18 mL) at reflux and the mixture was heated at reflux for 12.5 h (total reaction time: 17.5 h). After cooling to room temperature, the mixture was filtered through a short pad of Celite (diethyl ether) and the solvent was evaporated. Purification of the residue by column chromatography on silica gel (pentane–dichloromethane–ethyl acetate, 12 : 5 : 1) provided 3-methoxy-*N*-(4-methylphenyl)aniline (**13**) as colourless solid, yield: 2.24 g (98%), m.p. 68–70 °C. UV (MeOH): λ = 283 nm. IR (ATR): ν = 3365, 3000, 1596, 1512, 1492, 1463, 1438, 1389, 1324, 1302, 1283, 1256, 1237, 1198, 1158, 1107, 1032, 992, 951, 832, 774, 753, 686, 649, 632 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.31 (s, 3 H), 3.77 (s, 3 H), 5.62 (br s, 1 H), 6.43–6.45 (m, 1 H), 6.58–6.60 (m, 2 H), 7.01–7.04 (m, 2 H), 7.09–7.11 (m, 2 H), 7.13–7.16 (m, 1 H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 20.68 (CH_3), 55.16 (CH_3), 102.33 (CH), 105.43 (CH), 109.32 (CH), 119.36 (2 CH), 129.83 (2 CH), 130.03 (CH), 131.18 (C), 139.91 (C), 145.39 (C), 160.67 (C). EI-MS: *m*/*z* (%) = 213 (100) [M^+], 197 (4), 182 (4), 168 (4), 154 (5). HRMS: *m*/*z* calcd for $C_{14}H_{15}NO$ [M^+]: 213.1154; found: 213.1158. Elemental analysis calcd for $C_{14}H_{15}NO$: C 78.84, H 7.09, N 6.57; found: C 78.97, H 7.08, N 6.40%.

Crystal data for **13**: $C_{14}H_{15}NO$, M = 213.27 g mol^{-1}, crystal size: 0.50 × 0.40 × 0.10 mm^3, monoclinic, space group $P2_1/c$, a = 8.856(1) Å, b = 13.861(1) Å, c = 10.868(1) Å, β = 92.41(1)°, V = 1332.9(2) $Å^3$, Z = 4, ρ_{calcd} = 1.063 g cm^{-3}, μ = 0.067 mm^{-1}, T = 293(2) K, λ = 0.71073 Å, θ range 3.26–25.37°, 18 034 reflections collected, 2165 independent reflections (R_{int} = 0.0280), 151 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 = 0.0436, wR_2 = 0.1205; maximal residual electron density: 0.179 e $Å^{-3}$ (Fig. S1‡) CCDC 1000251.

Method B: *m*-Anisidine (18.9 g, 153 mmol) was added portionwise over a period of 3 h to a solution of *p*-bromotoluene (20.0 g, 117 mol), caesium carbonate (45.7 g, 140 mmol), *rac*-BINAP (3.61 g, 5.80 mmol) and palladium(II) acetate (1.53 g, 6.82 mmol) in toluene (80 mL) at reflux. The mixture was heated at reflux for 13 h (total reaction time 16 h), then cooled to room temperature, filtered over a short pad of silica gel and Celite (diethyl ether), and the solvent was removed. Purification of the residue by column chromatography on silica gel (petroleum ether–acetone, 15 : 1) provided the diarylamine **13**

as light yellow solid, yield: 25.4 g (100%). Spectroscopic data, see above.

2-Methoxy-6-methylcarbazole (14) and glycoborine (5-methoxy-3-methylcarbazole) (15). Palladium(II) acetate (126 mg, 561 μmol) was added at 100 °C to a mixture of the diarylamine **13** (4.02 g, 18.8 mmol), potassium carbonate (261 mg, 1.89 mmol) and pivalic acid (10.2 g) in a 50 mL test tube. The mixture was heated and vigorously stirred at 100 °C for 20.5 h, then cooled to room temperature, diluted with ethyl acetate and washed with a saturated solution of potassium carbonate, brine and water. The aqueous layers were extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate and the solvent was evaporated. Purification of the residue by column chromatography on silica gel (pentane–dichloromethane–ethyl acetate, gradient elution, 119 : 1 : 0.2 to 29 : 1 : 0.2) provided 2-methoxy-6-methylcarbazole (**14**) as colourless solid, yield: 3.52 g (89%), m.p. 230–233 °C (ref. 16: 227–228 °C). For spectroscopic data, see ref. 16. Glycoborine (5-methoxy-3-methylcarbazole) (**15**) was obtained from the less polar fraction as by-product in up to 5% yield, m.p. 138–140 °C (ref. 18*a*: 155–156 °C). UV (MeOH): λ = 226, 238, 244, 254 (sh), 277 (sh), 287, 323, 337 mm. Fluorescence (MeOH): λ_{ex} = 287 nm, λ_{em} = 345, 359 nm. IR (ATR): ν = 3398, 3048, 3012, 2913, 2846, 1624, 1604, 1585, 1554, 1506, 1473, 1453, 1438, 1388, 1345, 1314, 1294, 1258, 1225, 1178, 1101, 1058, 973, 915, 879, 802, 781, 745, 716, 698, 620, 590, 535 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.54 (s, 3 H), 4.09 (s, 3 H), 6.67 (d, J = 8.0 Hz, 1 H), 7.02 (d, J = 8.0 Hz, 1 H), 7.21 (dd, J = 8.2, 1.3 Hz, 1 H), 7.29 (d, J = 8.2 Hz, 1 H), 7.32 (t, J = 8.0 Hz, 1 H), 7.94 (br s, 1 H), 8.12 (d, J = 0.8 Hz, 1 H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 21.43 (CH_3), 55.37 (CH_3), 100.10 (CH), 103.48 (CH), 109.52 (CH), 112.40 (C), 122.77 (C), 122.89 (CH), 126.16 (CH), 126.42 (CH), 128.86 (C), 136.82 (C), 141.16 (C), 156.19 (C). EI-MS (70 eV): m/z (%) = 211 (100) [M^+], 196 (27), 168 (68), 167 (19). Elemental analysis calcd for $C_{14}H_{13}NO$: C 79.59, H 6.20, N 6.63; found: C 79.86, H 6.36, N 6.69%.

2-Hydroxy-6-methylcarbazole (10). A 1 M solution of boron tribromide in dichloromethane (1.00 mL, 1.00 mmol) was added at −78 °C to a solution of 2-methoxy-6-methylcarbazole (**14**) (109 mg, 516 μmol) in dichloromethane (25 mL) and the solution was stirred at −78 °C for 30 min. The cooling was removed and the mixture was stirred for 90 min. Methanol (1 mL) was added at 0 °C and the mixture was washed with a small amount of water. The aqueous layer was extracted once with diethyl ether, the combined organic layers were dried over sodium sulfate and the solvent was evaporated. Purification of the residue by column chromatography on silica gel (petroleum ether–acetone, 2 : 1) provided 2-hydroxy-6-methylcarbazole (**10**) as colourless solid, yield: 93 mg (91%), m.p. 262–264 °C (ref. 5: 245 °C, decomp.). UV (MeOH): λ = 260, 305, 322 (sh), 335 (sh) nm. IR (ATR): ν = 3399, 3286, 2913, 2855, 1617, 1508, 1488, 1461, 1416, 1343, 1308, 1295, 1275, 1218, 1158, 1134, 1106, 1036, 955, 937, 885, 836, 824, 805, 766, 730, 690, 652, 627 cm^{-1}. ^1H NMR (500 MHz, acetone-d_6): δ = 2.45 (s, 3 H), 6.71 (dd, J = 8.4, 2.1 Hz, 1 H), 6.90 (d, J = 2.1 Hz, 1 H), 7.08 (dd, J = 8.2, 1.0 Hz, 1 H), 7.28 (d, J = 8.2 Hz, 1 H), 7.74 (s, 1 H), 7.85 (d, J = 8.4 Hz, 1 H), 8.32 (s, 1 H), 9.94 (br s, 1 H). ^{13}C NMR and DEPT (125 MHz, acetone-d_6): δ = 21.48 (CH_3), 97.34 (CH), 109.06 (CH), 110.92 (CH), 117.03 (C), 119.78 (CH), 121.46 (CH), 124.65 (C), 125.99 (CH), 128.42 (C), 139.17 (C), 142.93 (C), 157.38 (C). EI-MS (70 eV): m/z (%) = 197 (100) [M^+], 196 (55), 167 (7). HRMS: m/z calcd for $C_{13}H_{11}NO$ [M^+]: 197.0841; found: 197.0855.

Isogirinimbine (3,3,8-trimethyl-3,11-dihydropyrano[3,2-*a*]-carbazole) (3) and 1,1,7-trimethyl-2-methylene-1,10-dihydro-2*H*-furo[3,2-*a*]carbazole (17). A solution of 2-methylbut-3-yn-2-ol (**16**) (54 μL, 47 mg, 0.56 mmol), DBU (114 μL, 116 mg, 762 μmol) and trifluoroacetic anhydride (78 μL, 0.12 g, 0.56 mmol) in acetonitrile (2 mL) was stirred at −15 °C for 90 min. The mixture was then added to a solution of 2-hydroxy-6-methylcarbazole (**10**) (100 mg, 507 μmol) and copper(I) iodide (0.2 mg, 1 μmol) in acetonitrile (4 mL) and the mixture was stirred at −15 °C for 40 min. DBU (98 μL, 0.10 g, 0.66 mmol) was added and the mixture was stirred at −15 °C for 3 h and at room temperature for 90 min. The mixture was washed twice with water and brine and the solvent was evaporated. Toluene (10 mL) was added to the residue, the solution was heated at reflux for 23 h and the solvent was evaporated. Purification of the residue by column chromatography on silica gel (petroleum ether–dichloromethane, gradient elution, 99 : 1 to 3 : 1) provided isogirinimbine (**3**) as colourless solid, yield: 84.4 mg (63%), m.p. 186–187 °C. UV (MeOH): λ = 221 (sh), 237, 278 (sh), 289, 332, 337, 353 nm. Fluorescence (MeOH): λ_{ex} = 289 nm, λ_{em} = 362, 378 nm. IR (ATR): ν = 3415, 2969, 2919, 2853, 1640, 1606, 1519, 1474, 1460, 1418, 1400, 1373, 1359, 1339, 1295, 1207, 1157, 1114, 1071, 1036, 898, 882, 859, 800, 746, 721, 704, 652, 585, 578, 562, 540 cm^{-1}. ^1H NMR (500 MHz, acetone-d_6): δ = 1.44 (s, 6 H), 2.45 (s, 3 H), 5.76 (d, J = 9.8 Hz, 1 H), 6.63 (d, J = 8.4 Hz, 1 H), 6.90 (d, J = 9.8 Hz, 1 H), 7.11 (dd, J = 8.2, 1.1 Hz, 1 H), 7.30 (d, J = 8.2 Hz, 1 H), 7.76 (d, J = 0.6 Hz, 1 H), 7.79 (d, J = 8.4 Hz, 1 H), 10.25 (br s, 1 H). ^{13}C NMR and DEPT (125 MHz, acetone-d_6): δ = 21.48 (CH_3), 27.84 (2 CH_3), 76.48 (C), 105.66 (C), 109.71 (CH), 111.18 (CH), 118.18 (C), 118.34 (CH), 119.98 (CH), 121.01 (CH), 124.70 (C), 126.42 (CH), 128.88 (C), 129.99 (CH), 137.99 (C), 139.34 (C), 152.32 (C). EI-MS: m/z (%) = 263 (28) [M^+], 248 (100), 233 (5), 217 (4), 204 (9), 124 (14). HRMS: m/z calcd for $C_{18}H_{17}NO$ [M^+]: 263.1310; found: 263.1302.

1,1,7-Trimethyl-2-methylene-1,10-dihydro-2*H*-furo[3,2-*a*]carbazole (**17**) was obtained as a by-product in up to 3% yield as colourless oil. ^1H NMR (300 MHz, acetone-d_6): δ = 1.68 (s, 6 H), 2.46 (s, 3 H), 4.35 (d, J = 2.6 Hz, 1 H), 4.61 (d, J = 2.6 Hz, 1 H), 6.80 (d, J = 8.3 Hz, 1 H), 7.14 (dd, J = 8.1, 1.0 Hz, 1 H), 7.32 (d, J = 8.1 Hz, 1 H), 7.82 (d, J = 1.0 Hz, 1 H), 7.92, (d, J = 8.3 Hz, 1 H), 10.21 (br s, 1 H). ^{13}C NMR and DEPT (75 MHz, acetone-d_6): δ = 21.46 (CH_3), 28.69 (2 CH_3), 44.78 (C), 82.07 (CH_2), 105.52 (CH), 111.39 (CH), 116.22 (C), 120.02 (CH), 120.25 (C), 120.48 (CH), 124.56 (C), 126.83 (CH), 129.07 (C), 136.56 (C), 139.62 (C), 155.55 (C), 173.56 (C). ESI-MS (−25 V): m/z = 262 [$(M - H)^-$].

Methyl 3,7-dimethyloct-6-en-1-yn-3-yl carbonate (18). A 0.5 M solution of ethynylmagnesium bromide in THF (51.0 mL,

25.5 mmol) was added dropwise over a period of 15 min to a solution of 6-methylhept-5-en-2-one (2.94 mL, 2.52 g, 20.0 mmol) in THF (20 mL) at −78 °C. The cooling was removed and the mixture was stirred for 2.5 h. The mixture was cooled to −78 °C, methyl chloroformate (3.06 mL, 3.74 g, 39.6 mmol) was added dropwise over a period of 5 min, the cooling was removed and the mixture was stirred for 2 h. A saturated aqueous solution of sodium hydrogencarbonate and diethyl ether were added, and the layers were separated. The organic layer was washed with water 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 of the residue by column chromatography on silica gel (pentane–diethyl ether, gradient elution, 100 : 1 to 20 : 1) provided carbonate **18** as colourless liquid, yield: 3.68 g (88%). IR (ATR): ν = 3287, 2959, 2923, 2853, 1754, 1699, 1684, 1651, 1635, 1441, 1376, 1338, 1257, 1165, 1114, 1074, 1022, 940, 884, 834, 790, 666, 631 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.60 (s, 3 H), 1.66 (d, J = 0.8 Hz, 3 H), 1.70 (s, 3 H), 1.82 (ddd, J = 13.6, 11.0, 5.9 Hz, 1 H), 1.96 (ddd, J = 13.6, 10.6, 6.0 Hz, 1 H), 2.11–2.23 (m, 2 H), 2.58 (s, 1 H), 3.75 (s, 3 H), 5.09 (m, 1 H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ (ppm) = 17.57 (CH_3), 22.79 (CH_2), 25.59 (CH_3), 26.17 (CH_3), 41.17 (CH_2), 54.29 (CH_3), 73.85 (CH), 76.78 (C), 83.03 (C), 122.85 (CH), 132.43 (C), 153.49 (C═O). EI-MS (70 eV): m/z (%) = 210 (0.4) [M$^+$], 151 (7), 119 (100), 105 (13), 91 (50), 69 (44). Elemental analysis calcd for $C_{12}H_{18}O_3$: C 68.54, H 8.63; found: C 68.38, H 8.93%.

(±)-Mahanimbicine [(±)-isomahanimbine] [(±)-4] and 1,7-dimethyl-2-methylene-1-(4-methylpent-3-en-1-yl)-1,10-dihydro-2*H*-furo[3,2-*a*]carbazole (19). *Method A*: A solution of 3,7-dimethyloct-6-en-1-yn-3-yl methyl carbonate (**18**) (724 mg, 3.44 mmol) in acetonitrile (11.5 mL) was added at room temperature over a period of 8 h to a solution of 2-hydroxy-6-methylcarbazole (**10**) (453 mg, 2.30 mmol), DBU (0.69 mL, 0.70 g, 4.6 mmol), and copper(I) iodide (2.3 mg, 12 μmol) in acetonitrile (59 mL). The mixture was stirred at room temperature for 14 h (total reaction time: 22 h). Diethyl ether was added and the mixture was washed with 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, the solvent was evaporated and the residue was dried in vacuum. The crude product was dissolved in toluene (40 mL), the solution was heated at reflux for 22.5 h and the solvent was evaporated. Purification of the residue by column chromatography on silica gel (pentane–dichloromethane–ethyl acetate, gradient elution, 294 : 5 : 1 to 69 : 5 : 1) provided **10** (154 mg, 34%) and (±)-mahanimbicine [(±)-**4**] as colourless solid, yield: 372 mg (49%), m.p. 137–139 °C (ref. 5 and 7: 142 °C). UV (MeOH): λ = 238, 289, 335, 353 nm. Fluorescence (MeOH): λ_{ex} = 289 nm, λ_{em} = 361 nm. IR (ATR): ν = 3428, 3409, 3012, 2968, 2916, 2856, 2727, 1639, 1608, 1517, 1473, 1454, 1419, 1402, 1374, 1338, 1297, 1223, 1208, 1190, 1164, 1126, 1090, 1036, 945, 909, 882, 816, 798, 748, 719, 673, 584 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.45 (s, 3 H), 1.58 (s, 3 H), 1.66 (d, J = 0.8 Hz, 3 H), 1.70–1.82 (m, 2 H), 2.11–2.21 (m, 2 H), 2.50 (s, 3 H), 5.11 (m, 1 H), 5.66 (d, J = 9.8 Hz, 1 H), 6.64 (d, J = 9.8 Hz, 1 H), 6.72 (dd, J = 8.3, 0.5 Hz, 1 H), 7.14 (dd, J = 8.2, 1.1 Hz, 1 H), 7.28 (d, J = 8.2 Hz, 1 H), 7.73 (s, 1 H), 7.74 (d, J = 8.3 Hz, 1 H), 7.84 (br s, 1 H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 17.63 (CH_3), 21.44 (CH_3), 22.73 (CH_2), 25.66 (CH_3), 25.95 (CH_3), 40.80 (CH_2), 78.30 (C), 104.51 (C), 109.44 (CH), 110.06 (CH), 117.30 (CH), 117.39 (C), 119.45 (CH), 120.39 (CH), 124.11 (CH), 124.14 (C), 125.73 (CH), 128.65 (CH), 129.01 (C), 131.71 (C), 136.56 (C), 137.70 (C), 151.70 (C). EI-MS (70 eV): m/z (%) = 331 (45) [M$^+$], 288 (11), 248 (100), (10), 210 (51), 209 (36), 180 (17). Elemental analysis calcd for $C_{23}H_{25}NO$: C 83.34, H 7.60, N 4.23; found: C 83.59, H 7.88, N 4.23%.

The furo[3,2-*a*]carbazole **19** was obtained as by-product in up to 5% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.35 (s, 3 H), 1.47–1.53 (m, 1 H), 1.53 (s, 3 H), 1.64 (s, 3 H), 1.78 (ddd, J = 13.4, 11.9, 4.6 Hz, 1 H), 1.90–1.98 (m, 1 H), 2.12 (ddd, J = 13.4, 11.9, 4.8 Hz, 1 H), 2.51 (s, 3 H), 4.24 (d, J = 2.8 Hz, 1 H), 4.77 (d, J = 2.8 Hz, 1 H), 4.97 (m, 1 H), 6.84 (d, J = 8.3 Hz, 1 H), 7.17 (dd, J = 8.2, 1.0 Hz, 1 H), 7.30 (d, J = 8.2 Hz, 1 H), 7.74 (m, 1 H), 7.77 (d, J = 1.0 Hz, 1 H), 7.83 (d, J = 8.3 Hz, 1 H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ (ppm) = 17.61 (CH_3), 21.58 (CH_3), 24.21 (CH_2), 25.70 (CH_3), 28.65 (CH_3), 41.95 (CH_2), 48.39 (C), 82.67 (CH_2), 102.61 (CH), 110.29 (CH), 113.24 (C), 119.47 (C), 119.67 (CH), 119.99 (CH), 123.52 (CH), 124.10 (C), 126.29 (CH), 129.40 (C), 132.30 (C), 135.74 (C), 137.95 (C), 155.63 (C), 170.22 (C).

2-Methoxy-6-methyl-9-tosylcarbazole (20). Sodium hydride (539 mg of a 60% dispersion in mineral oil, 13.5 mmol) was added at 0 °C to a solution of 2-methoxy-6-methylcarbazole (**14**) (701 mg, 3.32 mmol) in THF (35 mL) and the mixture was stirred at 0 °C for 1.25 h. *p*-Toluenesulfonyl chloride (949 mg, 4.98 mmol) was added at 0 °C, the cooling was removed and the mixture was stirred for 16.25 h. The mixture was diluted with diethyl ether and washed with water 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 of the residue by flash chromatography on silica gel (pentane–dichloromethane–ethyl, 70 : 5 : 1) provided 2-methoxy-6-methyl-9-tosylcarbazole (**20**) as colourless solid, yield: 969 mg (80%), m.p. 145–148 °C. UV (MeOH): λ = 224, 268, 296, 309, 326 nm. Fluorescence (MeOH): λ_{ex} = 268 nm, λ_{em} = 396 nm. IR (ATR): ν = 3091, 2992, 2949, 2917, 2831, 1622, 1580, 1493, 1477, 1453, 1361, 1299, 1280, 1253, 1190, 1167, 1147, 1130, 1090, 1044, 985, 938, 869, 842, 801, 777, 736, 705, 675 cm^{-1}. ^{1}H NMR (500 MHz, acetone-d_6): δ = 2.27 (s, 3 H), 2.43 (s, 3 H), 3.95 (s, 3 H), 7.01 (dd, J = 8.6, 2.3 Hz, 1 H), 7.25–7.29 (m, 3 H), 7.73–7.77 (m, 3 H), 7.86 (d, J = 2.3 Hz, 1 H), 7.90 (d, J = 8.6 Hz, 1 H), 8.14 (d, J = 8.5 Hz, 1 H). ^{13}C NMR and DEPT (125 MHz, acetone-d_6): δ = 21.21 (CH_3), 21.35 (CH_3), 56.07 (CH_3), 100.72 (CH), 112.87 (CH), 115.55 (CH), 120.43 (CH), 120.60 (C), 121.76 (CH), 127.38 (2 CH), 127.63 (C), 128.10 (CH), 130.73 (2 CH), 134.78 (C), 135.54 (C), 137.25 (C), 140.76 (C), 146.38 (C), 160.86 (C). EI-MS (70 eV): m/z (%) = 365 (65) [M$^+$], 210 (100), 167 (26). HRMS: m/z calcd for $C_{21}H_{19}NO_3S$ [M$^+$]: 365.1086; found: 365.1099. Elemental analysis calcd for $C_{21}H_{19}NO_3S$: C 69.02, H 5.24, N 3.83, S 8.77; found: C 69.14, H 5.20, N 3.82, S 9.31%.

***N*-Tosylmahanimbicine (21).** A 1 M solution of boron tribromide in dichloromethane (4.1 mL, 4.1 mmol) was added dropwise at −78 °C to a solution of 2-methoxy-6-methyl-9-tosylcarbazole (**20**) (502 mg, 1.37 mmol). The cooling was removed and the mixture was stirred for 2.5 h. Methanol (4 mL) was added, the mixture was diluted with diethyl ether, and washed with water and brine. The aqueous layer was extracted with diethyl ether, the combined organic layers were dried over sodium sulfate and the solvent was evaporated. Drying in vacuum provided crude 2-hydroxy-6-methyl-9-tosylcarbazole (539 mg) as light yellow solid, m.p. 166–168 °C.

2-Hydroxy-6-methyl-9-tosylcarbazole: UV (MeOH): λ = 222, 244 (sh), 260, 267, 275, 297, 308 nm. Fluorescence (MeOH): λ_{ex} = 260 nm, λ_{em} = 381 nm. IR (ATR): ν = 3482, 3035, 2919, 1612, 1558, 1499, 1442, 1398, 1346, 1296, 1268, 1215, 1186, 1161, 1114, 1088, 1027, 991, 952, 854, 811, 790, 739, 718, 701, 679, 660, 604 cm^{-1}. ^1H NMR (500 MHz, acetone-d_6): δ = 2.28 (s, 3 H), 2.42 (s, 3 H), 6.92 (dd, J = 8.5, 2.1 Hz, 1 H), 7.23–7.27 (m, 3 H), 7.69–7.74 (m, 3 H), 7.81 (d, J = 2.4 Hz, 1 H), 7.82 (d, J = 8.2 Hz, 1 H), 8.11 (d, J = 8.5 Hz, 1 H), 8.80 (s, 1 H). ^{13}C NMR and DEPT (125 MHz, acetone-d_6): δ = 21.17 (CH_3), 21.32 (CH_3), 102.55 (CH), 113.72 (CH), 115.44 (CH), 119.70 (C), 120.16 (CH), 121.77 (CH), 127.28 (2 CH), 127.72 (CH), 127.87 (C), 130.66 (2 CH), 134.62 (C), 135.64 (C), 137.09 (C), 140.90 (C), 146.26 (C), 158.55 (C). EI-MS (70 eV): m/z (%) = 351 (79) [M^+], 196 (100), 167 (12), 91 (5). HRMS: m/z calcd for $C_{20}H_{17}NO_3S$ [M^+]: 351.0929; found: 351.0926. Elemental analysis calcd for $C_{20}H_{17}NO_3S$: C 68.36, H 4.88, N 3.99, S 9.12; found: C 68.55, H 4.86, N 3.94, S 9.78%.

A solution of 3,7-dimethyloct-6-en-1-yn-3-yl methyl carbonate (**18**) (577 mg, 2.74 mmol) in acetonitrile (12 mL) was added over a period of 12 h at room temperature to a solution of the crude 2-hydroxy-6-methyl-9-tosylcarbazole (539 mg), DBU (0.62 mL, 0.63 g, 4.1 mmol) and copper(I) iodide (1.3 mg, 7 μmol) in acetonitrile (35 mL) and the mixture was stirred at room temperature for 10 h (total reaction time 22 h). The mixture was diluted with diethyl ether and washed with water, 10% aqueous HCl and brine. The aqueous layers were extracted with diethyl ether, the combined organic layers were dried over sodium sulfate, the solvent was evaporated and the residue was dried in vacuum. The crude product was dissolved in xylenes (25 mL), the solution was heated at reflux for 27.5 h and the solvent was evaporated. Purification of the residue by column chromatography on silica gel (pentane–dichloromethane–ethyl acetate, gradient elution, 99 : 1 to 15 : 1) provided a mixture of *N*-tosylmahanimbicine (**21**) and compound **22**, combined yield: 546 mg (82%), ratio of **21** : **22** = 7.7 : 1 (determined by ^1H NMR integration). UV (MeOH): λ = 230, 266, 313 nm. Fluorescence (MeOH): λ_{ex} = 266 nm, λ_{em} = 359, 419 nm. IR (ATR): ν = 2967, 2921, 2853, 1725, 1631, 1596, 1476, 1451, 1398, 1368, 1272, 1172, 1086, 1035, 960, 918, 890, 810, 782, 749, 726, 703, 672, 662, 629, 575, 542 cm^{-1}. ^1H NMR (500 MHz, acetone-d_6): δ (major isomer) = 1.52 (s, 3 H), 1.58 (s, 3 H), 1.67 (s, 3 H), 1.80–1.90 (m, 2 H), 2.18–2.24 (m, 2 H), 2.21 (s, 3 H), 2.39 (s, 3 H), 5.18 (m, 1 H), 5.80 (d, J = 10.0 Hz, 1 H), 6.88 (dd, J = 8.5, 0.7 Hz, 1 H), 7.00 (d, J = 8.2 Hz, 2 H), 7.08 (m, 2 H), 7.24 (d, J = 10.0 Hz, 1 H), 7.24 (m, 1 H), 7.52 (d, J = 0.7 Hz, 1 H), 7.61 (d, J = 8.3 Hz, 1 H), 8.04 (d, J = 8.3 Hz, 1 H). ^{13}C NMR and DEPT (125 MHz, acetone-d_6): δ (major isomer) = 17.66 (CH_3), 21.23 (CH_3), 21.27 (CH_3), 23.37 (CH_2), 25.83 (2 CH_3), 40.99 (CH_2), 78.40 (C), 115.19 (C), 115.89 (CH), 119.61 (CH), 120.02 (CH), 121.02 (CH), 122.80 (CH), 124.49 (C), 124.97 (CH), 127.53 (CH), 127.82 (2 CH), 127.83 (CH), 129.73 (2 CH), 130.55 (C), 132.08 (C), 133.15 (C), 136.34 (C), 138.19 (C), 139.75 (C), 145.67 (C), 154.82 (C). ESI-MS (+25 V): m/z (%) = 486.3 [$(M + H)^+$], 988.7 [$(2M + NH_4)^+$]. Elemental analysis calcd for $C_{30}H_{31}NO_3S$: C 74.20, H 6.43, N 2.88, S 6.60; found: C 74.46, H 6.68, N 2.97, S 6.49%.

(±)-Mahanimbicine [(±)-isomahanimbine] [(±)-4] and 2,10-dihydro-2,7-dimethyl-2-(4-methylpent-3-enyl)pyrano[2,3-*b*]carbazole (23). *Method B*: A 1 M solution of TBAF in THF (0.28 mL, 0.28 mmol) was added at room temperature to a mixture of the carbazoles **21** and **22** (68.7 mg, 141 μmol, ratio **21** : **22** = 7.7 : 1, see above). The mixture was irradiated in the microwave reactor at 300 W and 70 °C for 3 h and then at 75 °C for 2 h. A 1 M solution of TBAF in THF (0.28 mL, 0.28 mmol) was added and the mixture was irradiated in the microwave reactor at 300 W and 75 °C for 1 h. The mixture was diluted with diethyl ether, and washed first with an aqueous solution of ammonium chloride and then with brine. The aqueous layers were extracted with diethyl ether, the combined organic layers were dried over sodium sulfate and the solvent was evaporated. Purification of the residue by column chromatography on silica gel (pentane–dichloromethane–diethyl ether, gradient elution, 119 : 1 : 0.2 to 14 : 1 : 0.2) provided (±)-mahanimbicine [(±)-**4**] as colourless solid (yield: 37.1 mg, 79%; spectroscopic data, see above) and **23** as light yellow solid, yield: 4.0 mg (9%). ^1H-NMR (500 MHz, $CDCl_3$): δ = 1.43 (s, 3 H), 1.57 (s, 3 H), 1.65 (s, 3 H), 1.67–1.80 (m, 2 H), 2.14–2.17 (m, 2 H), 2.49 (s, 3 H), 5.10 (br t, J = 7.1 Hz, 1 H), 5.55 (d, J = 9.8 Hz, 1 H), 6.53 (d, J = 9.8 Hz, 1 H), 6.78 (s, 1 H), 7.12 (dd, J = 8.1, 1.1 Hz, 1 H), 7.23 (d, J = 8.1 Hz, 1 H), 7.57 (s, 1 H), 7.71 (br s, 1 H), 7.82 (br s, 1 H).

Murrayamine-J (5). DDQ (109 mg, 480 μmol) was added at room temperature to a solution of (±)-mahanimbicine [(±)-**4**] (39.7 mg, 120 μmol) in methanol (20 mL), THF (2 mL) and water (2 mL). The mixture was stirred at room temperature for 2 h. DDQ (54.4 mg, 240 μmol) was added, the mixture was stirred for 1.5 h, an additional portion of DDQ (54.4 mg, 240 μmol) was added and the mixture was stirred at room temperature for 2.75 h (total reaction time: 6.25 h). The mixture was diluted with diethyl ether and washed with 2 N aqueous NaOH, water 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 of the residue by column chromatography on silica gel (pentane–dichloromethane–ethyl acetate, gradient elution, 1 : 0 : 0 to 13 : 5 : 1) provided murrayamine-J (**5**) as colourless solid, yield: 27.9 mg (67%), m.p. 93–97 °C (ref. 8: oil). UV (MeOH): λ = 246, 267, 311, 347 (sh) nm. Fluorescence (MeOH): λ_{ex} = 311 nm, λ_{em} = 350 nm. IR (ATR): ν = 3322, 3045, 2966, 2918, 2848, 2757, 1771, 1735, 1717, 1698, 1662, 1604, 1580,

1508, 1474, 1462, 1415, 1393, 1343, 1320, 1278, 1224, 1176, 1121, 1085, 1031, 962, 895, 813, 784, 754, 721, 662, 629 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 1.46 (s, 3 H), 1.58 (s, 3 H), 1.66 (s, 3 H), 1.71–1.83 (m, 2 H), 2.11–2.21 (m, 2 H), 5.10 (m, 1 H), 5.71 (d, J = 9.8 Hz, 1 H), 6.67 (d, J = 9.8 Hz, 1 H), 6.81 (d, J = 8.4 Hz, 1 H), 7.47 (d, J = 8.4 Hz, 1 H), 7.83 (d, J = 8.4 Hz, 1 H), 7.89 (dd, J = 8.4, 1.4 Hz, 1 H), 8.35 (br s, 1 H), 8.46 (s, 1 H), 10.07 (s, 1 H). ^{13}C NMR and DEPT (150 MHz, $CDCl_3$): δ = 17.62 (CH_3), 22.70 (CH_2), 25.65 (CH_3), 26.05 (CH_3), 40.88 (CH_2), 78.69 (C), 104.98 (C), 110.69 (CH), 110.91 (CH), 116.75 (CH), 117.07 (C), 120.85 (CH), 122.77 (CH), 123.93 (CH), 124.23 (C), 126.33 (CH), 129.35 (C), 129.43 (CH), 131.85 (C), 136.75 (C), 143.42 (C), 152.65 (C), 192.01 (CHO). EI-MS (70 eV): m/z (%) = 345 (33) [M^+], 330 (4), 262 (100), 234 (4). HRMS: m/z calcd for $C_{23}H_{23}NO_2$ [M^+]: 345.1729; found: 345.1731. Elemental analysis calcd for $C_{23}H_{23}NO_2$: C 79.97, H 6.71, N 4.05; found: C 79.22, H 6.94, N 4.14%.

Bicyclomahanimbicine (6). A solution of (±)-mahanimbicine [(±)-**4**] (40.1 mg, 121 μmol) in toluene (40 mL) was placed in a water bath and irradiated using a daylight lamp (600 lm, 6500 K) for 14 d under continuous stirring at room temperature. Evaporation of the solvent and purification of the residue by column chromatography on silica gel (pentane–dichloromethane–ethyl acetate, gradient elution, 120 : 1 : 0.2 to 23 : 1 : 0.2) provided bicyclomahanimbicine (**6**) as colourless solid, yield: 15.7 mg (39%), m.p. 224–225 °C (ref. 5: 218 °C, decomp.). UV (MeOH): λ = 223, 242, 256, 261, 288 (sh), 304, 322 (sh), 335 (sh) nm. Fluorescence (MeOH): λ_{ex} = 242 nm, λ_{em} = 344, 359 nm. IR (ATR): ν = 3452, 3021, 2964, 2944, 2913, 2856, 1711, 1609, 1508, 1483, 1454, 1415, 1381, 1365, 1339, 1293, 1217, 1194, 1177, 1142, 1085, 1022, 976, 918, 873, 802, 766, 740, 672, 645, 589 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.77 (s, 3 H), 1.45 (s, 3 H), 1.57 (s, 3 H), 1.63–1.76 (m, 3 H), 2.07–2.14 (m, 1 H), 2.49–2.54 (m, 1 H), 2.50 (s, 3 H), 2.72 (dd, J = 9.4, 7.7 Hz, 1 H), 3.28 (d, J = 9.4 Hz, 1 H), 6.77 (d, J = 8.4 Hz, 1 H), 7.14 (dd, J = 8.2, 1.2 Hz, 1 H), 7.28 (d, J = 8.2 Hz, 1 H), 7.40 (br s, 1 H), 7.75 (s, 1 H), 7.76 (d, J = 8.4 Hz, 1 H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 18.53 (CH_3), 21.42 (CH_3), 25.61 (CH_2), 27.57 (CH_3), 35.08 (CH_3), 37.12 (CH), 37.65 (CH), 38.00 (CH_2), 39.22 (C), 46.39 (CH), 83.54 (C), 106.48 (C), 109.99 (CH), 111.14 (CH), 116.62 (C), 118.94 (CH), 119.46 (CH), 124.35 (C), 125.41 (CH), 128.88 (C), 137.46 (C), 139.64 (C), 151.85 (C). EI-MS (70 eV): m/z (%) = 331 (30) [M^+], 248 (100), 234 (3), 218 (2). HRMS: m/z calcd for $C_{23}H_{25}NO$ [M^+]: 331.1936; found: 331.1937.

Murrayamine-M (7). DDQ (59 mg, 260 μmol) was added at 0 °C to a solution of bicyclomahanimbicine (**6**) (28.3 mg, 85.4 μmol) in methanol (10 mL), THF (1 mL) and water (2 mL). The cooling was removed and the mixture was stirred for 2 h at room temperature. DDQ (38.6 mg, 0.17 mmol) was added, the mixture was stirred for 1.5 h, an additional portion of DDQ (29 mg, 130 μmol) was added and the mixture was stirred for 1.5 h (total reaction time: 5 h). The mixture was diluted with diethyl ether and washed with 2 N aqueous NaOH, water 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 of the residue by column chromatography on silica gel (pentane–dichloromethane–ethyl acetate, gradient elution, 1 : 0 : 0 to 14 : 5 : 1) provided murrayamine-M (**7**) as light yellow solid, yield: 15 mg (51%), m.p. 216–218 °C (ref. 8: oil). UV (MeOH): λ = 243, 255 (sh), 293, 329 (sh) nm. Fluorescence (MeOH): λ_{ex} = 293 nm, λ_{em} = 368 nm. IR (ATR): ν = 3416, 3385, 2947, 2863, 1735, 1698, 1673, 1654, 1605, 1572, 1508, 1474, 1458, 1414, 1318, 1220, 1182, 1151, 1114, 1088, 1021, 926, 891, 818, 787, 729, 686, 632, 610 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.78 (s, 3 H), 1.45 (s, 3 H), 1.59 (s, 3 H), 1.66–1.78 (m, 3 H), 2.04–2.12 (m, 1 H), 2.54 (m, 1 H), 2.74 (dd, J = 9.5, 7.7 Hz, 1 H), 3.30 (d, J = 9.5 Hz, 1 H), 6.88 (d, J = 8.5 Hz, 1 H), 7.48 (d, J = 8.4 Hz, 1 H), 7.82 (br s, 1 H), 7.85 (d, J = 8.5 Hz, 1 H), 7.88 (dd, J = 8.4, 1.6 Hz, 1 H), 8.48 (m, 1 H), 10.07 (s, 1 H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 18.72 (CH_3), 25.59 (CH_2), 27.42 (CH_3), 35.10 (CH_3), 36.96 (CH), 37.66 (CH), 38.19 (CH_2), 39.30 (C), 46.40 (CH), 83.88 (C), 107.17 (C), 110.68 (CH), 112.77 (CH), 116.48 (C), 119.44 (CH), 122.88 (CH), 124.46 (C), 126.01 (CH), 129.32 (C), 139.84 (C), 143.10 (C), 152.92 (C), 192.03 (CHO). EI-MS (70 eV): m/z (%) = 345 (24) [M^+], 262 (100), 233 (3), 204 (4). HRMS: m/z calcd for $C_{23}H_{23}NO_2$ [M^+]: 345.1729; found: 345.1746.

Murrayamine G (8). A solution of (±)-mahanimbicine [(±)-**4**] (63.8 mg, 193 μmol) and CSA (22.8 mg, 98.2 μmol) in toluene (9 mL) was stirred at room temperature for 6 d. An additional portion of CSA (22.4 mg, 96.4 μmol) was added and the mixture was stirred at room temperature for 7 d and at 70 °C for 3 d (total reaction time: 16 d). The mixture was diluted with diethyl ether and washed with an aqueous solution of sodium hydrogencarbonate and brine. The aqueous layers were extracted with diethyl ether. Subsequently, the combined organic layers were dried over sodium sulfate and the solvent was evaporated. Purification of the residue by column chromatography on silica gel (pentane–dichloromethane–ethyl acetate, gradient elution, 60 : 1 : 0.2 to 17 : 1 : 0.2) provided murrayamine-G (**8**) as colourless crystals, yield: 41.4 mg (65%), m.p. 166–169 °C (ref. 9: 173–176 °C). (MeOH): λ = 219 (sh), 241, 257 (sh), 262, 307, 323 (sh) nm. Fluorescence (MeOH): λ_{ex} = 307 nm, λ_{em} = 358 nm. IR (ATR): ν = 3463, 3074, 2963, 2920, 2862, 1613, 1519, 1481, 1445, 1420, 1378, 1312, 1297, 1217, 1172, 1159, 1100, 1027, 989, 963, 915, 888, 816, 798, 744, 658, 621, 584, 559 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.43 (s, 3 H), 1.48–1.50 (m, 1 H), 1.50 (s, 3 H), 1.61–1.67 (m, 2 H), 1.94 (dt, J = 12.9, 3.1 Hz, 1 H), 2.03 (dd, J = 12.9, 2.7 Hz, 1 H), 2.11 (dt, J = 9.3, 2.3 Hz, 1 H), 2.49 (s, 3 H), 2.58 (m, 1 H), 3.41 (m, 1 H), 4.73 (s, 1 H), 4.81 (t, J = 1.5 Hz, 1 H), 6.72 (d, J = 8.5 Hz, 1 H), 7.11 (dd, J = 8.1, 1.2 Hz, 1 H), 7.22 (d, J = 8.1 Hz, 1 H), 7.70 (br s, 1 H), 7.71 (s, 1 H), 7.73 (d, J = 8.5 Hz, 1 H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 21.41 (CH_3), 21.57 (CH_3), 23.00 (CH_2), 28.89 (CH_3), 35.95 (CH), 37.40 (CH_2), 39.67 (CH_2), 48.54 (CH), 74.08 (C), 105.67 (C), 108.70 (CH), 109.89 (CH), 112.09 (CH_2), 115.36 (C), 119.08 (CH), 119.22 (CH), 124.40 (C), 125.05 (CH), 128.65 (C), 137.60 (C), 140.08 (C), 149.89 (C), 155.17 (C). EI-MS (70 eV): m/z (%) = 331 (80) [M^+], 316 (11), 248 (100), 210 (9). HRMS: m/z calcd for $C_{23}H_{25}NO$ [M^+]: 331.1936; found: 331.1936. Elemental analysis calcd for $C_{23}H_{25}NO$: C 83.34, H 7.60, N 4.23; found: C 83.03, H 7.79, N 4.18%.

Isomurrayazoline (9). A solution of (±)-mahanimbicine [(±)-**4**] (40.5 mg, 122 μmol) and CSA (2.3 mg, 10 μmol) in hexane (12 mL) was stirred at room temperature for 11.5 d. The mixture was diluted with diethyl ether and washed with an aqueous solution of sodium hydrogencarbonate 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 of the residue by column chromatography on silica gel (pentane–dichloromethane–ethyl acetate, gradient elution, 59 : 1 : 0.2 to 16 : 1 : 0.2) provided a mixture of murrayamine G (**8**) and isomurrayazoline (**9**) as colourless solid, yield: 28.4 mg (70%), ratio of **8** : **9** = 1 : 1 (determined by the ^{1}H NMR spectrum). The two isomers were separated by preparative HPLC on a Grace Vydac C8 column (208TP1050, 50 × 250 mm), gradient elution with 55 mL min^{-1} (THF–H_2O, 20–70% THF in 25 min) to afford murrayamine-G (**8**) as colourless crystals (spectroscopic data: see above) and isomurrayazoline (**9**) as colourless solid, m.p. 224–227 °C (ref. 10: 269–270 °C). UV (MeOH): λ = 239 (sh), 246, 262 (sh), 307, 327 (sh), 340 (sh) nm. Fluorescence (MeOH): λ_{ex} = 246 nm, λ_{em} = 366 nm. IR (ATR): ν = 3047, 2965, 2922, 2900, 1631, 1592, 1446, 1416, 1347, 1307, 1288, 1221, 1204, 1180, 1152, 1134, 1087, 1068, 1037, 985, 941, 914, 882, 855, 801, 787, 771, 744, 680, 625, 602, 593, 556 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.13–0.21 (m, 1 H), 1.26–1.33 (m, 1 H), 1.28 (s, 3 H), 1.44 (s, 3 H), 1.47–1.54 (m, 1 H), 1.68 (ddd, J = 15.3, 6.8, 3.2 Hz, 1 H), 1.90 (s, 3 H), 1.90–1.93 (m, 1 H), 1.98 (ddd, J = 11.1, 5.5, 2.4 Hz, 1 H), 2.41 (ddd, J = 13.3, 5.3, 3.4 Hz, 1 H), 2.49 (s, 3 H), 3.29 (d, J = 4.6 Hz, 1 H), 6.64 (d, J = 8.2 Hz, 1 H), 7.09 (dd, J = 8.3, 1.3 Hz, 1 H), 7.38 (d, J = 8.3 Hz, 1 H), 7.58 (d, J = 8.2 Hz, 1 H), 7.72 (m, 1 H). ^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 21.31 (CH_3), 21.70 (CH_2), 22.91 (CH_3), 28.12 (CH), 29.15 (CH_3), 30.14 (CH_3), 36.06 (CH_2), 36.56 (CH_2), 48.35 (CH), 60.47 (C), 76.26 (C), 107.73 (C), 108.87 (CH), 113.16 (CH), 114.51 (C), 119.00 (CH), 120.16 (CH), 124.10 (CH), 127.50 (C), 128.82 (C), 138.92 (C), 144.32 (C), 156.37 (C). EI-MS (70 eV): m/z (%) = 331 (99) [M^+], 316 (100), 288 (15), 248 (63). Elemental analysis calcd for $C_{23}H_{25}NO$: C 83.34, H 7.60, N 4.23; found: C 83.00, H 7.89, N 4.26%.

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