Synthesis C. Schuster et al. Paper

Synthesis of the Pyrano[3,2-*a*]carbazole Alkaloids Koenine, Koenimbine, Koenigine, Koenigicine, and Structural Reassignment of Mukonicine

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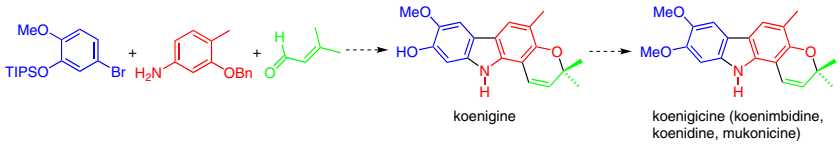


Received: 30.09.2015
Accepted: 01.10.2015
Published online: 08.10.2015
DOI: 10.1055/s-0035-1560359; Art ID: ss-2015-z0560-op

Abstract Using the palladium(II)-catalyzed oxidative cyclization of a diarylamine and the annulation of a dimethylpyran ring by Lewis acid promoted reaction with prenal as key steps, the total syntheses of the 6-oxygenated pyrano[3,2-*a*]carbazole alkaloids koenine and koenimbine, and of the 6,7-dioxygenated pyrano[3,2-*a*]carbazole alkaloids koenigine and koenigicine (koenimbidine, koenidine) were achieved. Moreover, these studies led to an improved synthetic route to the 2,6-dioxygenated carbazole alkaloid glycozolidol. Mukonicine, originally published as 6,8-dimethoxypyrano[3,2-*a*]carbazole, was found to be identical with koenigicine.

Key words alkaloids, catalysis, cyclization, natural products, palladium

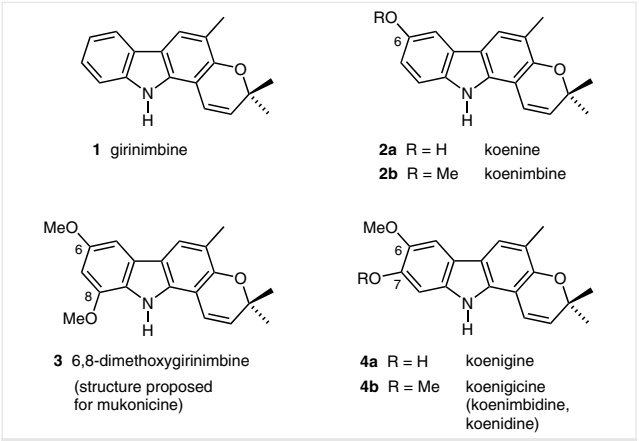


Figure 1 Oxygenated pyrano[3,2-*a*]carbazole alkaloids

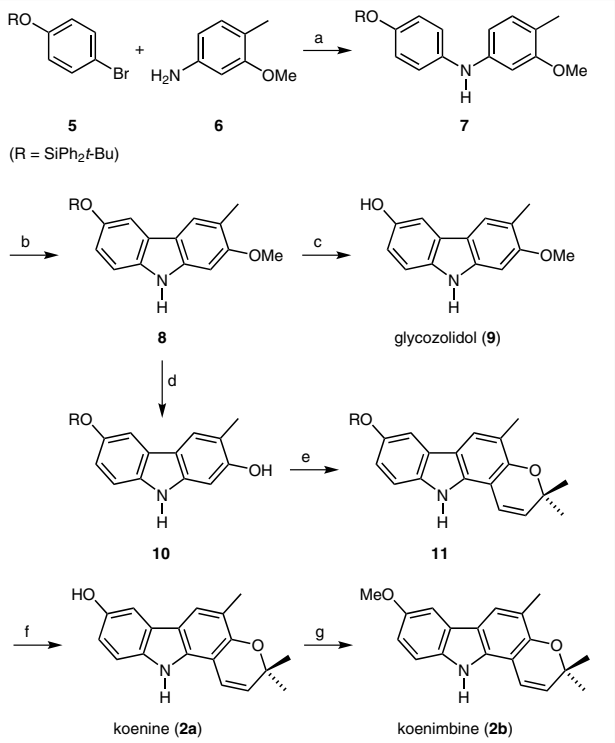
Carbazole alkaloids are intriguing because of their structural variety and their broad range of useful biological activities.[1–3] One important structural family are the pyrano[3,2-*a*]carbazoles featuring girinimbine (**1**) as the parent compound (Figure 1).[4] Several oxygenated pyrano[3,2-*a*]-carbazole alkaloids have been isolated from various plant sources. Koenine (**2a**), a 6-hydroxygirinimbine, was isolated by Narasimhan et al. from the leaves of *Murraya koenigii*.[5,6] Koenimbine (**2b**) was obtained by Narasimhan et al.[6,7] from the fruits of *M. koenigii* and by Kapil et al. from the leaves of the same plant.[8] Koenimbine (**2b**) was found to have a significant antidiarrhoeal activity.[9]

Mukonicine, which has been assigned as 6,8-dimethoxygirinimbine (**3**), was isolated from the leaves of *M. koenigii*.[10] The 6,7-dioxygenated pyrano[3,2-*a*]carbazole alkaloid koenigine (**4a**) was isolated by Narasimhan et al. from the same natural source.[5,6] The corresponding 6,7-dimethoxygirinimbine (**4b**) was obtained from the leaves of *M. koenigii* first in 1969 by Kapil et al. (named koenigicine),[8] and one year later by Joshi et al. (named koenimbidine),[11] and by Narasimhan et al. (named koenidine).[5,6]

Over the past two decades, we have developed four different synthetic routes to girinimbine (**1**).[12–15] The palladium-catalyzed synthesis of 2-hydroxy-3-methylcarbazole followed by annulation of the pyran ring in a Lewis acid promoted reaction with prenal provided the best access to **1** (4 steps, 69% overall yield).[15] Our palladium-catalyzed route provides an efficient access to a broad range of carbazoles[16] and has been applied to the total syntheses of 2,6-dioxygenated carbazole alkaloids,[17] and 7- and 8-oxygenated pyrano[3,2-*a*]carbazole alkaloids.[18–22] In the present work,[22] we describe the application of our methodology to the synthesis of the pyrano[3,2-*a*]carbazoles **2**–**4**.

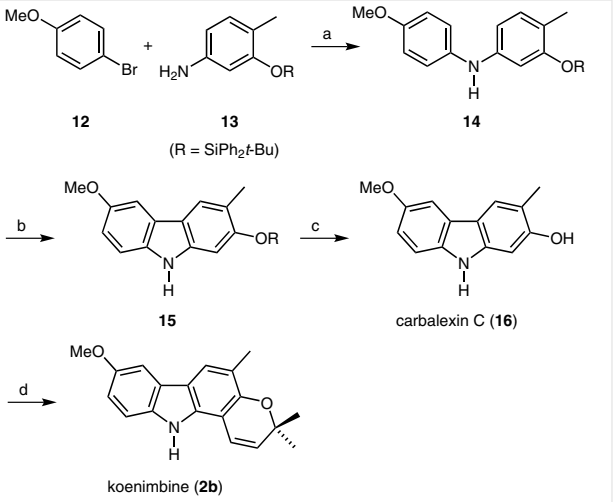
Buchwald–Hartwig coupling of the bromoarene **5** and the arylamine **6** in the presence of DavePhos[23] as ligand afforded the *N*,*N*-diarylamine **7** (Scheme 1). The palladium(II)-catalyzed oxidative cyclization[24] of **7** led to the or-

thogonally diprotected 2,6-dioxygenated carbazole **8** in 67% yield over both steps. Removal of the silyl protecting group with tetrabutylammonium fluoride (TBAF) afforded glycozolidol (**9**) via an improved route (3 steps, 54% overall yield).[25] Cleavage of the methyl ether of compound **8** by treatment with boron tribromide provided the 2-hydroxycarbazole **10**. Annulation of the pyran ring following Casiraghi's method (reaction with prenal in the presence of titanium tetraisopropoxide in toluene at r.t.)[15,26] afforded the pyrano[3,2-*a*]carbazole **11**. Desilylation using TBAF provided koenine (**2a**), which was obtained in five steps and 35% overall yield. Finally O-methylation of koenine (**2a**) led to koenimbine (**2b**). The spectroscopic data of our products **2a** and **2b** are in full agreement with those reported in the literature for the corresponding compounds isolated from natural sources.[5–8] The approach depicted in Scheme 1 provided koenimbine (**2b**) in six steps and only 20% overall yield. Therefore, we sought a shorter route that would provide this natural product in a better overall yield.



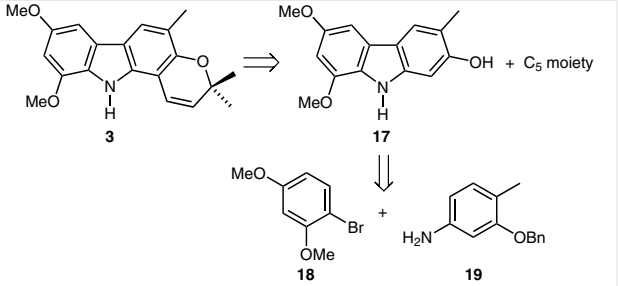
Scheme 1 Synthesis of glycozolidol (**9**), koenine (**2a**), and koenimbine (**2b**). *Reagents and conditions*: a) **6** (1.1 equiv), $Pd_2(dba)_3$ (6 mol%), DavePhos (12 mol%), NaO*t*-Bu (1.4 equiv), toluene, reflux, 24 h (quant.); b) $Pd(OAc)_2$ (10 mol%), $Cu(OAc)_2$ (2.5 equiv), DMF (3 drops), 130 °C (MW, 300 W), 45 min (67%); c) TBAF (1.5 equiv, 1 M in THF), DMF, 0 °C, 20 min (81%); d) BBr_3 (2.1 equiv), CH_2Cl_2, –78 °C (30 min), –10 to 0 °C (2 h), r.t. (16 h) (85%); e) Ti(O*i*-Pr)$_4$ (4 equiv), prenal (2 equiv), toluene, r.t., 16 h (70%); f) TBAF (1.2 equiv, 1 M in THF), DMF, 0 °C, 10 min (87%); g) MeI (1.1 equiv), NaH (1.8 equiv), THF, 0 °C to r.t., 24 h (57%).

For the alternative approach to koenimbine (**2b**), the *N*,*N*-diarylamine **14** was prepared by Buchwald–Hartwig coupling of *p*-bromoanisole (**12**) and the arylamine **13** (Scheme 2). Palladium(II)-catalyzed oxidative cyclization of **14** afforded the 2,6-dioxygenated carbazole **15** in 65% yield over both steps. Cleavage of the silyl ether with TBAF led to carbalexin C (**16**).[17,27] Annulation of the pyran ring afforded koenimbine (**2b**) in four steps and 39% overall yield based on compound **12**. Our approach to koenine (**2a**) and koenimbine (**2b**) is much superior to the previous syntheses reported by Kapil et al.[28]



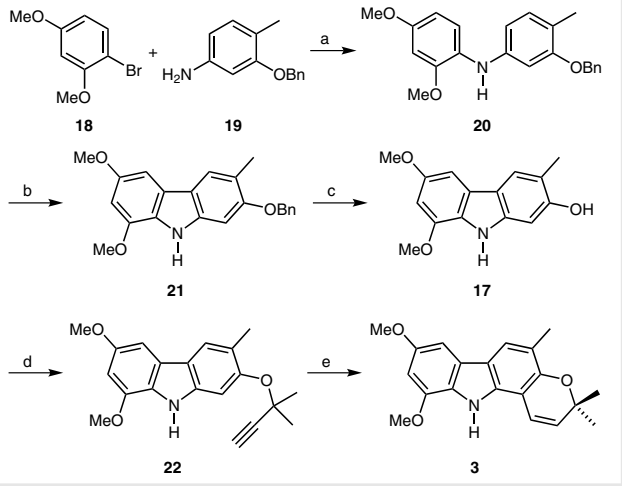
Scheme 2 Synthesis of carbalexin C (**16**) and koenimbine (**2b**). *Reagents and conditions*: a) **13** (1.2 equiv), $Pd(OAc)_2$ (6 mol%), BINAP (6 mol%), Cs_2CO_3 (1.2 equiv), toluene, reflux, 1 d (86%); b) $Pd(OAc)_2$ (10 mol%), $Cu(OAc)_2$ (2.5 equiv), AcOH, air, 130 °C (MW, 300 W), 2 h (76%); c) TBAF (1.6 equiv, 1 M in THF), DMF, 0 °C to r.t., 1 h (90%); d) Ti(O*i*-Pr)$_4$ (4 equiv), prenal (2 equiv), toluene, r.t., 16 h (67%).

Mukonicine has been described as 6,8-dimethoxygirinimbine (**3**).[10] Based on this structural assignment, our retrosynthetic analysis led to 2-hydroxy-6,8-dimethoxy-3-methylcarbazole (**17**) (Scheme 3). Using carbazole **17** as precursor, annulation of the pyran ring by reaction with an appropriate C_5-building block would lead directly to 6,8-dimethoxygirinimbine (**3**). Carbazole **17** should be accessible from the bromoarene **18** and the arylamine **19** following our palladium-catalyzed route.



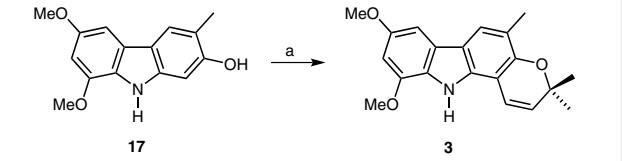
Scheme 3 Retrosynthetic analysis of 6,8-dimethoxygirinimbine (**3**)

We have demonstrated previously that our approach to carbazoles can be efficiently applied to the synthesis of trioxygenated derivatives.[29] Thus, palladium(0)-catalyzed coupling of 2,4-dimethoxybromobenzene (**18**) with the arylamine **19** to the *N*,*N*-diarylamine **20** and subsequent palladium(II)-catalyzed oxidative cyclization provided the carbazole **21** (Scheme 4). Removal of the benzyl protecting group by hydrogenolysis afforded 2-hydroxy-6,8-dimethoxy-3-methylcarbazole (**17**). Preparation of the dimethylpropargyl ether **22** using Godfrey's procedure[30] followed by thermally induced rearrangement[31] provided 6,8-dimethoxygirinimbine (**3**). Since the yield for the annulation of the pyran ring at carbazole **17** was only 40% over both steps, we also tested an alternative procedure (Scheme 5).



Scheme 4 Synthesis of 6,8-dimethoxygirinimbine (**3**) via Godfrey's method. *Reagents and conditions*: a) **19** (1.2 equiv), $Pd(OAc)_2$ (20 mol%), XPhos (40 mol%), Cs_2CO_3 (1.4 equiv), toluene, reflux, 16 h (92%); b) $Pd(OAc)_2$ (10 mol%), K_2CO_3 (10 mol%), PivOH, 85 °C, 24 h (67%); c) 20% $Pd(OH)_2/C$, H_2, MeOH–CH_2Cl_2 (4:1), r.t., 2 d (88%); d) 1. 2-methylbut-3-yn-2-ol (1.15 equiv), $(CF_3CO)_2O$ (1.15 equiv), DBU (1.5 equiv), MeCN, –5 °C, 20 min, 2. **17** (1.0 equiv), DBU (1.3 equiv), $CuCl_2·H_2O$ (1 mol%), MeCN, 0 °C, 18 h; e) toluene, reflux, 24 h (40% over 2 steps).

The boronic acid catalyzed pyran ring annulation was recently applied by us to the synthesis of pyranocarbazole alkaloids.[19,32] Thus, we treated compound **17** with prenal in the presence of 20 mol% phenylboronic acid in propanoic acid–toluene and obtained 6,8-dimethoxygirinimbine (**3**) in 69% yield (Scheme 5).



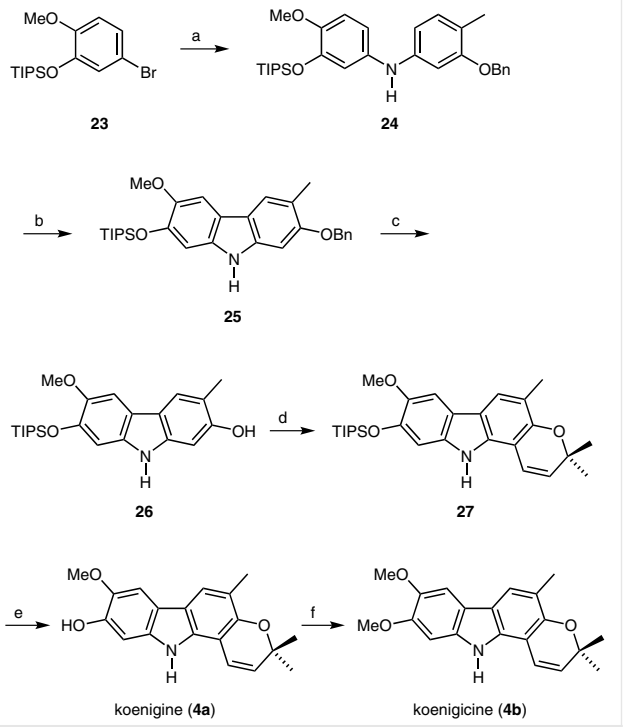
Scheme 5 Synthesis of 6,8-dimethoxygirinimbine (**3**) via the boronic acid catalyzed pyran annulation. *Reagents and conditions*: a) prenal (1.5 equiv), $PhB(OH)_2$ (20 mol%), $EtCO_2H$ (110 equiv), toluene, reflux, 46 h (69%).

However, a careful comparison of the ^1H NMR spectroscopic data of compound **3** with those which have been reported for the natural product mukonicine showed that the data are not in agreement (Table 1). There are significant differences especially in the chemical shifts observed for the protons at C5 and C7. Also the melting points for both compounds differ by more than 60 °C. Thus, we concluded that the structure of mukonicine may be isomeric to 6,8-dimethoxygirinimbine (**3**) and focused on our next synthetic target, koenigicine (**4b**), which in fact represents a regioisomer of compound **3**.

Table 1 Comparison of the ^1H NMR Data (Solvent: $CDCl_3$) and Melting Point of Mukonicine with Those of Compound **3**

	Mukonicine[10]	Compound **3**
C3-CH_3	2.30 (s)	2.31 (s)
C4-H	7.56 (s)	7.59 (s)
C5-H	7.40 (s)	6.99 (br s)
C6-OCH_3	3.90 (s)	3.90 (s)
C7-H	6.88 (s)	6.49 (d, *J* = 2.1 Hz)
C8-OCH_3	3.90 (s)	3.96 (s)
NH	7.81 (br s)	7.88 (br s)
C2′-CH_3 (2 ×)	1.44 (s)	1.47 (s)
C3′-H	5.65 (d, *J* = 9 Hz)	5.67 (d, *J* = 9.7 Hz)
C4′-H	6.55 (d, *J* = 9 Hz)	6.63 (d, *J* = 9.7 Hz)
mp	233–234 °C	165–170 °C

Buchwald–Hartwig coupling of the bromoarene **23** and the arylamine **19** in the presence of XPhos as ligand to the *N*,*N*-diarylamine **24** followed by palladium(II)-catalyzed oxidative cyclization gave the orthogonally protected 2,6,7-trioxygenated carbazole **25** in 66% yield over both steps (Scheme 6). Debenzylation of **25** to the 2-hydroxycarbazole **26** and subsequent Lewis acid promoted annulation of the pyran ring led to the pyrano[3,2-*a*]carbazole **27**. Removal of the silyl protecting group using TBAF afforded koenigine (**4a**). The O-methylation of koenigine (**4a**) provided koenigicine (**4b**) in six steps and 33% overall yield based on the bromoarene **23**. Thus, we have achieved the first total synthesis of koenigine (**4a**) and a novel considerably improved total synthesis of koenigicine (koenimbidine, koenidine) (**4b**).[33]



Scheme 6 Synthesis of koenigine (**4a**) and koenigicine (**4b**). *Reagents and conditions*: a) 3-benzyloxy-4-methylaniline (**19**) (1.2 equiv), $Pd(OAc)_2$ (6 mol%), XPhos (12 mol%), Cs_2CO_3 (1.2 equiv), toluene, reflux, 19.5 h (93%); b) $Pd(OAc)_2$ (15 mol%), $Cu(OAc)_2$ (2.5 equiv), AcOH, 130 °C (MW, 300 W), 1 h (71%); c) 10% Pd/C, H_2, EtOAc, r.t., 19 h (89%); d) Ti(O*i*-Pr)$_4$ (4 equiv), prenal (2 equiv), toluene, r.t., 15.5 h (65%); e) TBAF (1.5 equiv, 1 M in THF), THF, 0 °C, 10 min (94%); f) Me_2SO_4 (5 equiv), K_2CO_3 (2 equiv), acetone, 56 °C, 18.5 h (93%).

An unequivocal confirmation of our structural assignment of compound **4b** was achieved by the X-ray analysis of a single crystal (Figure 2).

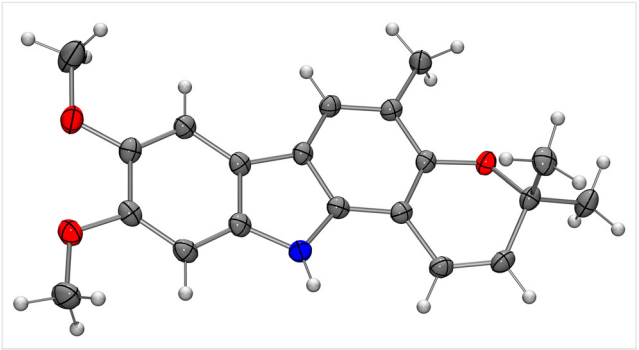


Figure 2 Molecular structure of koenigicine (koenimbidine, koenidine) (**4b**) in the crystal (orthorhombic, $P2_12_12_1$); ORTEP plot showing thermal ellipsoids at the 50% probability level.

A comparison of the ^{1}H NMR data and the melting point of our synthetic compound **4b** with those reported for koenigicine (**4b**), as well as with the corresponding data reported on the other isolations of this alkaloid, koenimbidine (**4b**), and koenidine (**4b**) confirmed a very good agreement (Table 2). Moreover, we found that the data of our compound **4b** also matched those reported for mukonicine. Therefore, we concluded that the structure for mukonicine must be reassigned as **4b** and that mukonicine is in fact identical with koenigicine (koenimbidine, koenidine).

In conclusion, we have developed an efficient route to the oxygenated pyrano[3,2-*a*]carbazole alkaloids **2**–**4**. Key steps of our approach are the palladium(0)-catalyzed C–N bond formation followed by a palladium(II)-catalyzed oxidative cyclization of the corresponding *N*,*N*-diarylamine to generate the carbazole framework. Thus, koenine (**2a**) was obtained in five steps and 35% overall yield and koenimbine (**2b**) in four steps and 39% overall yield. In the course of this work, we also developed an improved synthesis of the 2,6-dioxygenated carbazole alkaloid glycozolidol (**9**), which be-

Table 2 Comparison of the ^{1}H NMR Data (Solvent: $CDCl_3$) and the Melting Points of Koenigicine, Koenimbidine, Koenidine, and Mukonicine with Those of Synthetic **4b**

	Koenigicine (**4b**)[8]	Koenimbidine (**4b**)[11]	Koenidine (**4b**)[5,6]	Mukonicine	Synthetic **4b**
C3-CH_3	2.33 (s)	2.30 (s)		2.30 (s)	2.33 (s)
C4-H	7.50 (s)	7.53 (s)	7.52 (s)	7.56 (s)	7.55 (br s)
C5-H	7.40 (s)	7.40 (s)	7.36 (s)	7.40 (s)	7.38 (s)
C6-OCH_3	3.86 (s)	3.90 (s)		3.90 (s)	3.93 (s)
C7-OCH_3	3.96 (s)	3.90 (s)		3.90 (s)	3.98 (s)
C8-H	6.83 (s)	6.90 (s)	6.87 (s)	6.88 (s)	6.90 (s)
NH	7.81 (br s)			7.81 (br s)	7.74 (br s)
C2′-CH_3 (2 ×)	1.50 (s)	1.49		1.44 (s)	1.48 (s)
C3′-H	5.63 (d, *J* = 10 Hz)	5.63 (d, *J* = 10 Hz)	5.65	5.65 (d, *J* = 9 Hz)	5.68 (d, *J* = 9.7 Hz)
C4′-H	6.58 (d, *J* = 10 Hz)	6.78 (d, *J* = 10 Hz)	6.58	6.55 (d, *J* = 9 Hz)	6.60 (d, *J* = 9.7 Hz)
mp	224–225 °C	225 °C	224–225 °C	233–234 °C	223–224 °C

came available in three steps and 54% overall yield. 6,8-Dimethoxygirinimbine (**3**) was synthesized in four steps and 37% overall yield and was found not to be identical with mukonicine. Finally, we have completed the first total synthesis of koenigine (**4a**) in five steps and 36% overall yield and an improved synthesis of koenigicine (koenimbidine, koenidine) (**4b**) in six steps and 33% overall yield. Moreover, by comparison of the ^{1}H NMR data and the melting points, we concluded that mukonicine has to be reassigned and is identical with koenigicine (koenimbidine, koenidine) (**4b**).

All reactions were carried out in oven-dried glassware using anhydrous solvents under an argon atmosphere, unless stated otherwise. CH_2Cl_2, THF, and toluene were dried using a solvent purification system (MBraun-SPS). Petroleum ether (PE) used refers to the hydrocarbon mixture with a boiling range of 40–65 °C. $Pd(OAc)_2$ was recrystallized from glacial AcOH. 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). TLC 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 PerkinElmer 25 UV/Vis spectrometer. IR 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 DRX 500 and Avance III 600 spectrometers. Chemical shifts δ are reported in parts per million with the solvent signal as internal standard. Standard abbreviations were used to denote the multiplicities of the signals. 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.

4-Bromphenyl *tert*-Butyldiphenylsilyl Ether (5)

Imidazole (3.94 g, 57.8 mmol) was added to a solution of 4-bromophenol (5.00 g, 28.9 mmol) in DMF (60 mL). The mixture was stirred for 15 min at r.t., *t*-$BuPh_2SiCl$ (11.2 mL, 43.3 mmol) was added, and stirring was continued for 3 h at r.t. H_2O (30 mL) and aq 1 M HCl (50 mL) were added and the reaction mixture was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were washed with brine and sat. aq NH_4Cl, and dried ($MgSO_4$). Removal of the solvent and flash chromatography (silica gel, PE–EtOAc, 15:1) of the crude product provided **5** as a colorless solid; yield: 11.5 g (97%); mp 50 °C (Lit.[34] 43.5–45 °C).

IR (ATR): 3055, 2959, 2929, 2890, 2856, 1517, 1481, 1459, 1427, 1390, 1362, 1272, 1254, 1191, 1166, 1112, 1067, 1004, 918, 823, 736, 694, 630, 613 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.10 (s, 9 H), 6.63–6.65 (m, 2 H), 7.17–7.20 (m, 2 H), 7.37–7.40 (m, 4 H), 7.43–46 (m, 2 H), 7.69–7.71 (m, 4 H).

^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 19.40 (C), 26.41 (3 CH_3), 113.31 (C), 121.45 (2 CH), 127.84 (4 CH), 130.03 (2 CH), 132.05 (2 CH), 132.38 (2 C), 135.43 (4 CH), 154.71 (C).

MS (EI): *m*/*z* (%) = 412 (4), 410 (4, [M$^+$]), 355 (100), 353 (96), 273 (18).

HRMS: *m*/*z* [M$^+$] calcd for $C_{22}H_{23}BrOSi$: 410.0702; found: 410.0715.

N-[4-(*tert*-Butyldiphenylsilyloxy)phenyl]-3-methoxy-4-methylaniline (7)

A solution of the bromoarene **5** (1.00 g, 2.43 mmol) in toluene (15 mL) was added dropwise over a period of 2 h to a solution of 3-methoxy-4-methylaniline (**6**) (366 mg, 2.67 mmol), $Pd_2(dba)_3$ (134 mg, 0.146 mmol), DavePhos (115 mg, 0.292 mmol), and NaO*t*-Bu (321 mg, 3.34 mmol) in toluene (35 mL) at reflux. The reaction mixture was heated at reflux for 24 h, cooled to r.t., and the solvent was removed under vacuum. Flash chromatography (silica gel, PE–EtOAc, 30:1) of the crude product provided **7** as a red-brown viscous oil; yield: 1.13 g (quant.).

IR (ATR): 3395, 3068, 2952, 2931, 2857, 1609, 1591, 1570, 1558, 1542, 1501, 1458, 1426, 1392, 1250, 1230, 1161, 1128, 1110, 1038, 995, 915, 823, 742, 700, 637, 610 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.13 (s, 9 H), 2.14 (s, 3 H), 3.73 (s, 3 H), 5.55 (br s, 1 H), 6.42–6.43 (m, 2 H), 6.70–6.72 (m, 2 H), 6.85 (d, *J* = 8.7 Hz, 2 H), 6.94 (d, *J* = 8.5 Hz, 1 H), 7.37–7.45 (m, 6 H), 7.74–7.76 (m, 4 H).

^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 15.44 (CH_3), 19.42 (C), 26.52 (3 CH_3), 55.13 (CH_3), 99.75 (CH), 108.27 (CH), 118.15 (C), 120.23 (2 CH), 120.63 (2 CH), 127.69 (4 CH), 129.80 (2 CH), 130.82 (CH), 133.06 (2 C), 135.53 (4 CH), 136.58 (C), 143.66 (C), 150.49 (C), 158.28 (C).

MS (EI): *m*/*z* (%) = 467 (100, [M$^+$]), 410 (48).

HRMS: *m*/*z* [M$^+$] calcd for $C_{30}H_{33}NO_2Si$: 467.2281; found: 467.2275.

6-(*tert*-Butyldiphenylsilyloxy)-2-methoxy-3-methyl-9*H*-carbazole (8)

DMF (3 drops) was added to a mixture of the diarylamine **7** (60.0 mg, 0.128 mmol), $Pd(OAc)_2$ (2.9 mg, 13 μmol), and $Cu(OAc)_2$ (58.0 mg, 0.319 mmol), and the mixture was heated at 130 °C by microwave irradiation (300 W) for 45 min. Removal of the solvent under vacuum and flash chromatography (silica gel, PE–EtOAc, 20:1) of the crude product provided **8** as a light brown solid; yield: 40.0 mg (67%); mp 110–112 °C.

IR (ATR): 3406, 3048, 2995, 2932, 2857, 1631, 1583, 1485, 1458, 1427, 1392, 1319, 1271, 1194, 1130, 1110, 1037, 1003, 917, 871, 821, 810, 737, 699, 626, 606 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.14 (s, 9 H), 2.30 (s, 3 H), 3.88 (s, 3 H), 6.76 (dd, *J* = 8.6, 2.4 Hz, 1 H), 6.77 (s, 1 H), 7.04 (d, *J* = 8.6 Hz, 1 H), 7.33–7.42 (m, 7 H), 7.54 (s, 1 H), 7.64 (br s, 1 H), 7.77–7.79 (m, 4 H).

^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 16.61 (CH_3), 19.56 (C), 26.64 (3 CH_3), 55.49 (CH_3), 92.32 (CH), 109.35 (CH), 110.19 (CH), 116.18 (C), 116.85 (CH), 118.79 (C), 121.46 (CH), 124.08 (C), 127.66 (4 CH), 129.70 (2 CH), 133.51 (2 C), 134.27 (C), 135.63 (4 CH), 139.96 (C), 149.21 (C), 157.34 (C).

MS (EI): *m*/*z* (%) = 465 (63, [M$^+$]), 408 (100), 204 (11).

HRMS: *m*/*z* [M$^+$] calcd for $C_{30}H_{31}NO_2Si$: 465.2124; found: 465.2126.

UV (MeOH): λ = 219 (sh), 238, 259, 297 (sh), 310, 332 (sh), 346 (sh) nm.

Fluorescence (MeOH): λ_{ex} = 310 nm, λ_{em} = 375 nm.

Glycozolidol (6-Hydroxy-2-methoxy-3-methyl-9*H*-carbazole; 9)

A 1 M solution of TBAF in THF (1.15 mL, 1.15 mmol) was added to a solution of the carbazole **8** (355 mg, 0.762 mmol) in DMF (15 mL) at 0 °C. After stirring for 20 min at 0 °C, H_2O (10 mL) was added, and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with sat. aq NH_4Cl and dried ($MgSO_4$). Removal of

the solvent under vacuum and flash chromatography (silica gel, PE–EtOAc, 5:1) of the crude product provided **9** as a light yellow solid; yield: 140 mg (81%); mp 245–250 °C (Lit.[25a] 240 °C).

IR (ATR): 3520, 3387, 2959, 2940, 2917, 2848, 1629, 1585, 1485, 1457, 1434, 1373, 1347, 1310, 1281, 1220, 1195, 1158, 1135, 1113, 1032, 998, 908, 881, 853, 818, 789, 754, 614 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 2.25 (s, 3 H), 3.85 (s, 3 H), 6.75 (dd, *J* = 8.6, 2.4 Hz, 1 H), 6.87 (s, 1 H), 7.19 (d, *J* = 8.6 Hz, 1 H), 7.25 (d, *J* = 2.4 Hz, 1 H), 7.68 (s, 1 H), 8.78 (br s, 1 H), 10.62 (br s, 1 H).

^{13}C NMR and DEPT (125 MHz, DMSO-d_6): δ = 16.63 (CH_3), 55.25 (CH_3), 92.53 (CH), 104.13 (CH), 110.85 (CH), 112.94 (CH), 115.20 (C), 116.57 (C), 121.10 (CH), 123.30 (C), 133.54 (C), 140.27 (C), 150.32 (C), 156.61 (C).

MS (EI): *m*/*z* (%) = 227 (100, [M^+]), 212 (70), 184 (19), 183 (19), 154 (10).

UV (MeOH): λ = 216, 232, 262, 311 nm.

Fluorescence (MeOH): λ_{ex} = 311 nm, λ_{em} = 384 nm.

Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 73.74; H, 5.89; N, 6.17.

6-(*tert*-Butyldiphenylsilyloxy)-2-hydroxy-3-methyl-9*H*-carbazole (10)

A 1 M solution of BBr_3 in CH_2Cl_2 (0.16 mL, 0.16 mmol) was added slowly to a stirred solution of carbazole **8** (35 mg, 0.075 mmol) in CH_2Cl_2 (5 mL) at –78 °C. The mixture was stirred for 30 min at –78 °C, for 2 h at –10 to 0 °C, warmed to r.t., and stirred overnight at r.t. MeOH–H_2O (1:15, 16 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 × 8 mL), and the combined organic layers were dried ($MgSO_4$). Removal of the solvent under vacuum and flash chromatography (silica gel, PE–EtOAc, 4:1) of the crude product provided **10** as a yellow viscous oil, which solidified on standing; yield: 28 mg (85%); mp 93 °C.

IR (ATR): 3410, 3068, 2929, 2857, 1634, 1578, 1484, 1458, 1427, 1391, 1274, 1203, 1108, 1037, 1012, 933, 874, 821, 738, 699, 605 cm^{-1}.

^1H NMR (600 MHz, acetone-d_6): δ = 1.16 (s, 9 H), 2.31 (s, 3 H), 6.77 (dd, *J* = 8.6, 2.3 Hz, 1 H), 6.91 (s, 1 H), 7.13 (d, *J* = 8.6 Hz, 1 H), 7.41 (d, *J* = 2.3 Hz, 1 H), 7.44–7.49 (m, 7 H), 7.55 (s, 1 H), 7.84–7.86 (m, 4 H), 9.72 (s, 1 H).

^{13}C NMR and DEPT (150 MHz, acetone-d_6): δ = 16.63 (CH_3), 20.05 (C), 27.06 (3 CH_3), 96.87 (CH), 109.66 (CH), 111.17 (CH), 116.86 (C), 117.10 (CH), 117.28 (C), 122.08 (CH), 124.97 (C), 128.66 (4 CH), 130.77 (2 CH), 134.36 (2 C), 135.97 (C), 136.43 (4 CH), 141.81 (C), 149.54 (C), 155.58 (C).

MS (EI): *m*/*z* (%) = 451 (53, [M^+]), 394 (100), 197 (14).

HRMS: *m*/*z* [M^+] calcd for $C_{29}H_{29}NO_2Si$: 451.1968; found: 451.1961.

UV (MeOH): λ = 216, 240, 264, 311, 333 (sh), 349 (sh) nm.

Fluorescence (MeOH): λ_{ex} = 311 nm, λ_{em} = 375 nm.

8-(*tert*-Butyldiphenylsilyloxy)-3,3,5-trimethyl-3,11-dihydropyrano[3,2-*a*]carbazole (11)

3-Methylbut-2-enal (prenal) (23 µL, 0.240 mmol) and Ti(O*i*-Pr)$_4$ (0.14 mL, 0.473 mmol) were added to a solution of the 2-hydroxycarbazole **10** (54.0 mg, 0.120 mmol) in toluene (5 mL). The solution was stirred at r.t. for 16 h, H_2O (5 mL) and aq 1 M HCl (5 mL) were added, the mixture was extracted with EtOAc (3 × 15 mL), and the combined organic layers were dried ($MgSO_4$). Removal of the solvent under vacuum and flash chromatography (silica gel, PE–EtOAc, 20:1) of the crude product provided **11** as an orange viscous oil; yield: 43.5 mg (70%).

IR (ATR): 3428, 3068, 3045, 2955, 2925, 2855, 1643, 1458, 1427, 1392, 1360, 1334, 1280, 1205, 1138, 1110, 1057, 1026, 972, 892, 857, 821, 802, 742, 699, 664, 608 cm^{-1}.

^1H NMR (500 MHz, acetone-d_6): δ = 1.16 (s, 9 H), 1.47 (s, 6 H), 2.26 (s, 3 H), 5.76 (d, *J* = 9.8 Hz, 1 H), 6.80 (dd, *J* = 8.6, 2.4 Hz, 1 H), 6.88 (d, *J* = 9.8 Hz, 1 H), 7.16 (d, *J* = 8.6 Hz, 1 H), 7.42–7.51 (m, 8 H), 7.84–7.86 (m, 4 H), 10.07 (br s, 1 H).

^{13}C NMR and DEPT (125 MHz, acetone-d_6): δ = 16.16 (CH_3), 20.03 (C), 27.03 (3 CH_3), 27.83 (2 CH_3), 76.48 (C), 105.36 (C), 109.83 (CH), 111.40 (CH), 117.37 (C), 117.56 (CH), 118.01 (C), 118.60 (CH), 121.68 (CH), 124.98 (C), 128.66 (4 CH), 129.66 (CH), 130.78 (2 CH), 134.25 (2 C), 135.99 (C), 136.35 (4 CH), 137.17 (C), 149.75 (C), 150.52 (C).

MS (EI): *m*/*z* (%) = 517 (100, [M^+]), 502 (48), 460 (65), 223 (29).

HRMS: *m*/*z* [M^+] calcd for $C_{34}H_{35}NO_2Si$: 517.2437; found: 517.2425.

UV (MeOH): λ = 224, 238, 252 (sh), 272 (sh), 287 (sh), 296, 336, 352, 367 nm.

Fluorescence (MeOH): λ_{ex} = 296 nm, λ_{em} = 391 nm.

Koenine (2a)

A 1 M solution of TBAF in THF (0.20 mL, 0.20 mmol) was added slowly to a solution of the pyrano[3,2-*a*]carbazole **11** (85 mg, 0.164 mmol) in DMF (5 mL) at 0 °C and the mixture was stirred for 10 min at 0 °C. H_2O (5 mL) was added and the mixture was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with sat. aq NH_4Cl and dried ($MgSO_4$). Removal of the solvent under vacuum and flash chromatography (silica gel, PE–EtOAc, 2:1) of the crude product provided koenine (**2a**) as a light yellow solid; yield: 40 mg (87%); mp 244–247 °C (Lit.[5,6] 250–252 °C).

IR (ATR): 3457, 3327, 2970, 2922, 1703, 1643, 1492, 1466, 1402, 1362, 1324, 1210, 1177, 1130, 1110, 1052, 978, 887, 849, 802, 779, 745, 722, 688, 655, 603 cm^{-1}.

^1H NMR (500 MHz, acetone-d_6): δ = 1.49 (s, 6 H), 2.31 (s, 3 H), 5.78 (d, *J* = 9.8 Hz, 1 H), 6.88 (dd, *J* = 8.5, 2.0 Hz, 1 H), 6.91 (d, *J* = 9.8 Hz, 1 H), 7.26 (d, *J* = 8.5 Hz, 1 H), 7.41 (d, *J* = 1.5 Hz, 1 H), 7.65 (s, 1 H), 7.87 (br s, 1 H), 9.99 (br s, 1 H).

^{13}C NMR and DEPT (125 MHz, acetone-d_6): δ = 16.16 (CH_3), 27.83 (2 CH_3), 76.40 (C), 105.06 (CH), 105.28 (C), 111.66 (CH), 113.86 (CH), 117.49 (C), 117.67 (C), 118.66 (CH), 121.72 (CH), 125.16 (C), 129.50 (CH), 135.13 (C), 137.04 (C), 150.35 (C), 151.62 (C).

MS (EI): *m*/*z* (%) = 279 (29, [M^+]), 264 (100), 132 (11).

HRMS: *m*/*z* [M^+] calcd for $C_{18}H_{17}NO_2$: 279.1259; found: 279.1255.

UV (MeOH): λ = 227, 233, 252 (sh), 272 (sh), 297, 336, 356, 368 (sh) nm.

Fluorescence (MeOH): λ_{ex} = 297 nm, λ_{em} = 392 nm.

Koenimbine (2b)

NaH (3.9 mg, 0.163 mmol) (60% suspension in oil) was added to a solution of koenine (**2a**) (25 mg, 90 µmol) in THF (4 mL) at 0 °C. MeI (6 µL, 96 µmol) was added and the reaction mixture was stirred at r.t. for 24 h. H_2O (5 mL) was added and the mixture was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine

and dried ($MgSO_4$). Removal of the solvent under vacuum and flash chromatography (silica gel, PE–EtOAc, 20:1) of the crude product provided koenimbine (**2b**) as a colorless solid; yield: 15 mg (57%).

For spectroscopic data, see below.

2-(*tert*-Butyldiphenylsilyloxy)-4-nitrotoluene

Imidazole (4.44 g, 65.2 mmol) was added to a solution of 2-methyl-5-nitrophenol (5.00 g, 32.7 mmol) in DMF (60 mL). The mixture was stirred for 10 min at r.t., *t*-$BuPh_2SiCl$ (12.8 mL, 49.2 mmol) was added, and stirring at r.t. was continued for additional 4 h. H_2O (50 mL) and aq 1 M HCl (50 mL) were added and the mixture was extracted with EtOAc (3 × 100 mL). The combined organic layers were washed with brine and sat. aq NH_4Cl, and then dried ($MgSO_4$). Removal of the solvent under vacuum and flash chromatography (silica gel, hexane–Et_2O, 20:1) of the crude product provided the title compound as colorless crystals; yield: 12.8 g (quant.); mp 119–123 °C.

IR (ATR): 3074, 3030, 2953, 2932, 2855, 1588, 1516, 1492, 1427, 1409, 1341, 1320, 1278, 1256, 1191, 1115, 1087, 998, 963, 870, 854, 737, 699, 687, 637, 615 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.14 (s, 9 H), 2.45 (s, 3 H), 7.22 (d, *J* = 2.1 Hz, 1 H), 7.24 (d, *J* = 8.3 Hz, 1 H), 7.37–7.47 (m, 6 H), 7.64 (dd, *J* = 8.3, 2.1 Hz, 1 H), 7.68–7.70 (m, 4 H).

^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 17.48 (CH_3), 19.61 (C), 26.58 (3 CH_3), 113.12 (CH), 116.02 (CH), 128.08 (4 CH), 130.40 (2 CH), 130.73 (CH), 131.57 (2 C), 135.38 (4 CH), 136.77 (C), 146.58 (C), 153.95 (C).

MS (EI): *m*/*z* (%) = 391 (6, [M^+]), 335 (74), 334 (100), 287 (30), 257 (8), 227 (15), 210 (10), 197 (11).

HRMS: *m*/*z* [M^+] calcd for $C_{23}H_{25}NO_3Si$: 391.1604; found: 391.1620.

UV (MeOH): λ = 223 (sh), 241 (sh), 273, 279, 327 nm.

Anal. Calcd for $C_{23}H_{25}NO_3Si$: C, 70.56; H, 6.44; N, 3.58. Found: C, 70.62; H, 6.59; N, 3.55.

3-(*tert*-Butyldiphenylsilyloxy)-4-methylaniline (13)

A mixture of 2-(*tert*-butyldiphenylsilyloxy)-4-nitrotoluene (12.8 g, 32.7 mmol) and 10% Pd/C (1.28 g) in CH_2Cl_2 (200 mL) was stirred at r.t. for 24 h under a H_2 atmosphere at 5 bar. The mixture was filtered over Celite which was subsequently washed with EtOAc. Removal of the solvent from the combined filtrates and flash chromatography (silica gel, PE–EtOAc, 15:1) of the crude product provided **13** as an orange solid; yield: 11.8 g (quant.); mp 90–92 °C.

IR (ATR): 3419, 3337, 3030, 2931, 2857, 1609, 1588, 1508, 1463, 1428, 1389, 1360, 1314, 1277, 1208, 1176, 1116, 1000, 970, 861, 838, 823, 811, 794, 742, 711, 699, 683, 613 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.08 (s, 9 H), 2.27 (s, 3 H), 3.15 (br s, 2 H), 5.80 (d, *J* = 2.1 Hz, 1 H), 6.15 (dd, *J* = 7.9, 2.1 Hz, 1 H), 6.90 (d, *J* = 7.9 Hz, 1 H), 7.35–7.43 (m, 6 H), 7.72 (dd, *J* = 7.9, 1.2 Hz, 4 H).

^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 16.32 (CH_3), 19.60 (C), 26.54 (3 CH_3), 106.4 (CH), 107.95 (CH), 118.40 (C), 127.77 (4 CH), 129.80 (2 CH), 131.02 (CH), 133.09 (2 C), 135.43 (4 CH), 144.84 (C), 154.33 (C).

MS (EI): *m*/*z* (%) = 361 (89, [M^+]), 305 (60), 304 (100), 302 (27), 226 (82).

HRMS: *m*/*z* calcd [M^+] for $C_{23}H_{27}NOSi$: 361.1862; found: 361.1867.

UV (MeOH): λ = 213, 243 (sh), 265, 272, 291 nm.

Anal. Calcd for $C_{23}H_{27}NOSi$: C, 76.41; H, 7.53; N, 3.87. Found: C, 76.74; H, 7.62; N, 3.80.

3-(*tert*-Butyldiphenylsilyloxy)-*N*-(4-methoxyphenyl)-4-methylaniline (14)

A solution of 4-bromoanisole (**12**) (1.32 mL, 10.5 mmol) in toluene (15 mL) was added over a period of 2 h to a solution of $Pd(OAc)_2$ (144 mg, 0.641 mmol), *rac*-BINAP (400 mg, 0.642 mmol), Cs_2CO_3 (4.00 g, 12.3 mmol), and aniline **13** (4.50 g, 12.4 mmol) in toluene (70 mL) at reflux temperature. The reaction mixture was heated at reflux for 24 h and then cooled to r.t. The solvent was removed under vacuum. Flash chromatography (silica gel, PE–EtOAc, 40:1) of the crude product provided **14** as a brown solid; yield: 4.25 g (86%); mp 89–91 °C.

IR (ATR): 3396, 3070, 2959, 2929, 2853, 1606, 1580, 1510, 1466, 1425, 1391, 1339, 1283, 1240, 1183, 1169, 1128, 1112, 1039, 1001, 983, 880, 816, 769, 744, 697, 683, 631, 611 cm^{-1}.

^1H NMR (500 MHz, acetone-d_6): δ = 1.12 (s, 9 H), 2.34 (s, 3 H), 3.72 (s, 3 H), 6.31 (d, *J* = 1.9 Hz, 1 H), 6.43 (dd, *J* = 8.1, 1.9 Hz, 1 H), 6.57 (m, 4 H), 6.81 (br s, 1 H), 7.01 (d, *J* = 8.1 Hz, 1 H), 7.45–7.48 (m, 4 H), 7.51–7.54 (m, 2 H), 7.77–7.78 (m, 4 H).

^{13}C NMR and DEPT (125 MHz, acetone-d_6): δ = 16.48 (CH_3), 19.93 (C), 26.84 (3 CH_3), 55.53 (CH_3), 106.96 (CH), 110.39 (CH), 114.99 (2 CH), 118.88 (C), 120.02 (CH), 120.09 (CH), 128.71 (4 CH), 130.81 (2 CH), 131.88 (CH), 133.47 (2 C), 136.18 (4 CH), 137.32 (C), 144.52 (C), 154.66 (C), 154.81 (C).

MS (EI): *m*/*z* (%) = 467 (100, [M^+]), 410 (48), 332 (30), 205 (16), 181 (8), 166 (10), 158 (15).

Anal. Calcd for $C_{30}H_{33}NO_2Si$: C, 77.05; H, 7.11; N, 2.99. Found: C, 77.04; H, 7.09; N, 3.01.

2-(*tert*-Butyldiphenylsilyloxy)-6-methoxy-3-methyl-9*H*-carbazole (15)

AcOH (1.5 mL) was added to a mixture of the diarylamine **14** (132 mg, 0.282 mmol), $Pd(OAc)_2$ (6.3 mg, 28 μmol), and $Cu(OAc)_2$ (128 mg, 0.705 mmol), and the mixture was heated at 130 °C under air by microwave irradiation (300 W) for 2 h. Removal of the solvent under vacuum and flash chromatography (silica gel, PE–EtOAc, 20:1) of the crude product provided **15** as a yellow solid; yield: 100 mg (76%); mp 66 °C.

IR (ATR): 3420, 3070, 2930, 2856, 1635, 1587, 1485, 1468, 1428, 1389, 1361, 1329, 1294, 1275, 1216, 1173, 1135, 1109, 1032, 1017, 914, 860, 821, 801, 778, 743, 700, 686, 613 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.13 (s, 9 H), 2.55 (s, 3 H), 3.88 (s, 3 H), 6.40 (s, 1 H), 6.87 (dd, *J* = 8.7, 2.4 Hz, 1 H), 7.08 (d, *J* = 8.7 Hz, 1 H), 7.28 (br s, 1 H), 7.34–7.43 (m, 7 H), 7.76–7.78 (m, 5 H).

^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 17.70 (CH_3), 19.60 (C), 26.50 (3 CH_3), 56.02 (CH_3), 100.55 (CH), 102.54 (CH), 110.71 (CH), 113.02 (CH), 117.06 (C), 120.70 (C), 121.29 (CH), 123.73 (C), 127.83 (4 CH), 129.86 (2 CH), 132.90 (2 C), 134.22 (C), 135.45 (4 CH), 139.38 (C), 152.96 (C), 153.69 (C).

MS (EI): *m*/*z* (%) = 465 (100, [M^+]), 408 (36), 330 (43), 204 (13).

MS (ESI, +10 V): *m*/*z* = 466.2 [(M + H)$^+$].

HRMS: *m*/*z* [M^+] calcd for $C_{30}H_{31}NO_2Si$: 465.2124; found: 465.2114.

UV (MeOH): λ = 218, 240 (sh), 270 (sh), 311 nm.

Fluorescence (MeOH): λ_{ex} = 311 nm, λ_{em} = 379 nm.

Carbalexin C (2-Hydroxy-6-methoxy-3-methyl-9*H*-carbazole; 16)

A 1 M solution of TBAF in THF (0.31 mL, 0.31 mmol) was added to a solution of the carbazole **15** (89.9 mg, 0.193 mmol) in DMF (6 mL) at 0 °C. The reaction mixture was stirred and warmed to r.t. over a period of 1 h. After the addition of H_2O (4 mL), the mixture was extracted

with Et_2O (3 × 10 mL). The combined organic layers were washed with brine and dried ($MgSO_4$). Removal of the solvent under vacuum and flash chromatography (silica gel, PE–EtOAc, 2:1) of the crude product provided **16** as a light yellow solid; yield: 39.4 mg (90%); mp 187–191 °C (Lit.[27] colorless oil).

IR (ATR): 3392, 3293, 2922, 2840, 1632, 1580, 1460, 1437, 1326, 1293, 1262, 1209, 1135, 1110, 1027, 1010, 981, 885, 864, 838, 822, 793, 768, 721, 641, 609 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.39 (s, 3 H), 3.90 (s, 3 H), 4.83 (br s, 1 H), 6.81 (s, 1 H), 6.94 (dd, *J* = 8.7, 2.5 Hz, 1 H), 7.24 (d, *J* = 8.7 Hz, 1 H), 7.43 (d, *J* = 2.5 Hz, 1 H), 7.70 (br s, 1 H), 7.73 (s, 1 H).

^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 16.14 (CH_3), 56.07 (CH_3), 96.52 (CH), 102.71 (CH), 110.88 (CH), 113.20 (CH), 116.03 (C), 117.40 (C), 121.70 (CH), 123.97 (C), 134.36 (C), 140.15 (C), 153.16 (C), 153.89 (C).

MS (EI): *m*/*z* (%) = 227 (100, [M^+]), 212 (78), 184 (45), 154 (10).

UV (MeOH): λ = 215, 232, 262, 312 nm.

Fluorescence (MeOH): λ_{ex} = 312 nm, λ_{em} = 374 nm.

Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 73.32; H, 5.97; N, 6.26.

Koenimbine (2b)

3-Methylbut-2-enal (prenal) (0.050 mL, 0.521 mmol) and Ti(O*i*-Pr)$_4$ (0.31 mL, 1.02 mmol) were added to a solution of carbalexin C (**16**) (58.0 mg, 0.255 mmol) in toluene (5 mL). After stirring the solution at r.t. for 16 h, H_2O (5 mL) and aq 1 M HCl (5 mL) were added. The mixture was extracted with EtOAc (3 × 15 mL) and the combined organic layers were dried ($MgSO_4$). Removal of the solvent under vacuum and flash chromatography (silica gel, PE–EtOAc, 20:1) of the crude product provided koenimbine (**2b**) as a colorless solid; yield: 50.0 mg (67%); mp 194–195 °C (Lit.[6–8] 194–195 °C).

IR (ATR): 3403, 2955, 2920, 2851, 1724, 1643, 1457, 1436, 1401, 1380, 1335, 1294, 1246, 1209, 1139, 1124, 1110, 1057, 1025, 979, 894, 877, 845, 807, 768, 745, 717, 684, 664, 606 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.48 (s, 6 H), 2.32 (s, 3 H), 3.90 (s, 3 H), 5.67 (d, *J* = 9.7 Hz, 1 H), 6.59 (d, *J* = 9.7 Hz, 1 H), 6.93 (dd, *J* = 8.7, 2.4 Hz, 1 H), 7.25 (d, *J* = 8.4 Hz, 1 H), 7.40 (d, *J* = 2.4 Hz, 1 H), 7.62 (s, 1 H), 7.72 (br s, 1 H).

^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 16.07 (CH_3), 27.57 (2 CH_3), 56.01 (CH_3), 75.84 (C), 102.58 (CH), 104.48 (C), 111.00 (CH), 113.01 (CH), 116.83 (C), 117.22 (CH), 118.33 (C), 121.03 (CH), 124.43 (C), 129.26 (CH), 134.32 (C), 135.69 (C), 149.82 (C), 153.94 (C).

MS (EI): *m*/*z* (%) = 293 (16, [M^+]), 278 (100), 263 (10), 235 (11).

MS (ESI, +10 V): *m*/*z* = 294.1 [$(M + H)^+$].

UV (MeOH): λ = 230, 238, 251 (sh), 271 (sh), 282 (sh), 295, 336, 363 (sh) nm.

Fluorescence (MeOH): λ_{ex} = 295 nm, λ_{em} = 407 nm.

Anal. Calcd for $C_{19}H_{19}NO_2$: C, 77.79; H, 6.53; N, 4.77. Found: C, 77.68; H, 6.74; N, 4.57.

3-Benzyloxy-*N*-(2,4-dimethoxyphenyl)-4-methylaniline (20)

A solution of 2,4-dimethoxybromobenzene (**18**; 107 mg, 0.495 mmol) in toluene (5 mL) was added over a period of 3 h to a mixture of 3-benzyloxy-4-methylaniline (**19**)[15] (127 mg, 0.595 mmol), Cs_2CO_3 (245 mg, 0.693 mmol), $Pd(OAc)_2$ (22.2 mg, 99 µmol), and XPhos (94.4 mg, 0.198 mmol) in toluene (10 mL) at reflux. After a total reaction time of 16 h at reflux, the mixture was allowed to cool to r.t. Removal of the solvent under vacuum and flash chromatography (silica gel, PE–EtOAc, 7:1) of the crude product provided **20** as a brownish oil; yield: 159 mg (92%).

IR (ATR): 3403, 3058, 3026, 2998, 2934, 2832, 1611, 1588, 1558, 1512, 1452, 1437, 1400, 1281, 1253, 1205, 1157, 1123, 1028, 918, 824, 795, 736, 696 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.22 (s, 3 H), 3.80 (s, 3 H), 3.83 (s, 3 H), 5.03 (s, 2 H), 5.69 (br s, 1 H), 6.39 (dd, *J* = 8.7, 2.7 Hz, 1 H), 6.52 (d, *J* = 2.7 Hz, 1 H), 6.54 (dd, *J* = 8.0, 2.1 Hz, 1 H), 6.61 (d, *J* = 2.1 Hz, 1 H), 7.01 (d, *J* = 8.0 Hz, 1 H), 7.05 (d, *J* = 8.7 Hz, 1 H), 7.32 (m, 1 H), 7.37–7.43 (m, 4 H).

^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 15.67 (CH_3), 55.58 (CH_3), 55.63 (CH_3), 69.65 (CH_2), 99.33 (CH), 101.80 (CH), 103.73 (CH), 109.28 (CH), 117.64 (CH), 118.74 (C), 126.40 (C), 127.03 (2 CH), 127.62 (CH), 128.45 (2 CH), 130.92 (CH), 137.48 (C), 143.21 (C), 150.38 (C), 154.44 (C), 157.32 (C).

MS (EI): *m*/*z* (%) = 349 (100, [M^+]), 230 (51), 91 (34).

HRMS: *m*/*z* [M^+] calcd for $C_{22}H_{23}NO_3$: 349.1678; found: 349.1687.

2-Benzyloxy-6,8-dimethoxy-3-methyl-9*H*-carbazole (21)

A mixture of the diarylamine **20** (114 mg, 0.325 mmol), $Pd(OAc)_2$ (7.3 mg, 32.5 µmol), K_2CO_3 (4.5 mg, 32.5 µmol), and pivalic acid (418 mg) was heated at 85 °C under air by microwave irradiation (300 W) for 24 h. Subsequently, EtOAc was added and the mixture was washed several times with sat. aq K_2CO_3. The organic layer was dried ($MgSO_4$). Removal of the solvent under vacuum and flash chromatography (silica gel, PE–EtOAc, 15:1) of the crude product provided **21** as a yellow solid; yield: 75.7 mg (67%); mp 59–63 °C.

IR (ATR): 3430, 3068, 3028, 2924, 2850, 1735, 1634, 1591, 1506, 1452, 1424, 1388, 1326, 1304, 1277, 1234, 1204, 1165, 1142, 1102, 1043, 1016, 998, 929, 904, 874, 812, 733, 694, 621 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.41 (s, 3 H), 3.90 (s, 3 H), 3.95 (s, 3 H), 5.15 (s, 2 H), 6.50 (d, *J* = 2.0 Hz, 1 H), 6.89 (s, 1 H), 7.02 (d, *J* = 2.0 Hz, 1 H), 7.32 (m, 1 H), 7.40 (m, 2 H), 7.48 (m, 2 H), 7.74 (s, 1 H), 7.90 (br s, 1 H).

^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 16.93 (CH_3), 55.51 (CH_3), 56.01 (CH_3), 70.05 (CH_2), 93.60 (CH), 94.18 (CH), 96.02 (CH), 116.97 (C), 119.40 (C), 121.48 (CH), 123.78 (C), 124.38 (C), 127.08 (2 CH), 127.72 (CH), 128.52 (2 CH), 137.46 (C), 139.12 (C), 145.86 (C), 154.64 (C), 156.31 (C).

MS (EI): *m*/*z* (%) = 347 (48, [M^+]), 256 (100), 228 (13), 198 (19), 91 (96).

HRMS: *m*/*z* [M^+] calcd for $C_{22}H_{21}NO_3$: 347.1521; found: 347.1515.

UV (MeOH): λ = 236, 256 (sh), 268 (sh), 305 nm.

Fluorescence (MeOH): λ_{ex} = 305 nm, λ_{em} = 394 nm.

2-Hydroxy-6,8-dimethoxy-3-methyl-9*H*-carbazole (17)

A mixture of carbazole **21** (156 mg, 0.450 mmol) and $Pd(OH)_2$/C (20% Pd; 31 mg) in MeOH–CH_2Cl_2 (15 mL, 4:1) was stirred at r.t. for 2 d under a H_2 atmosphere at normal pressure. The mixture was filtered over Celite (Et_2O) and the solvent was removed under vacuum to afford **17** as a colorless solid; yield: 102 mg (88%); mp 145–150 °C.

IR (ATR): 3511, 3412, 3339, 2992, 2921, 2832, 2138, 2055, 2030, 2009, 1975, 1771, 1734, 1716, 1699, 1684, 1638, 1588, 1555, 1541, 1508, 1472, 1455, 1428, 1403, 1360, 1304, 1273, 1239, 1206, 1137, 1093, 1044, 991, 930, 868, 808, 751, 696, 619 cm^{-1}.

^{1}H NMR (500 MHz, acetone-d_6): δ = 2.36 (s, 3 H), 3.88 (s, 3 H), 3.96 (s, 3 H), 6.53 (d, *J* = 2.1 Hz, 1 H), 7.01 (s, 1 H), 7.12 (d, *J* = 2.1 Hz, 1 H), 7.73 (s, 1 H), 8.24 (s, 1 H), 9.74 (br s, 1 H).

^{13}C NMR and DEPT (125 MHz, acetone-d_6): δ = 16.72 (CH_3), 55.72 (CH_3), 55.98 (CH_3), 94.38 (CH), 96.40 (CH), 97.28 (CH), 117.38 (C), 117.48 (C), 122.06 (CH), 124.84 (C), 125.34 (C), 141.10 (C), 146.83 (C), 155.37 (C), 155.41 (C).

MS (EI): *m*/*z* (%) = 257 (100, [M$^+$]), 242 (37), 214 (11), 199 (22).

HRMS: *m*/*z* [M$^+$] calcd for $C_{15}H_{15}NO_3$: 257.1052; found: 257.1040.

UV (MeOH): λ = 235, 255 (sh), 267 (sh), 306, 329 (sh) 343 (sh) nm.

Fluorescence (MeOH): λ_{ex} = 306 nm, λ_{em} = 389 nm.

6,8-Dimethoxygirinimbine (3)

Propanoic acid (1.30 mL, 17.6 mmol) and prenal (24.6 µL, 0.240 mmol) were added to a solution of carbazole **17** (41.2 mg, 0.160 mmol) and phenylboronic acid (3.9 mg, 30 µmol) in toluene (6 mL). The mixture was heated at reflux for 46 h and then cooled to r.t. Removal of the solvent under vacuum and flash chromatography (silica gel, PE–EtOAc, 9:1) of the crude product provided **3** as a colorless solid; yield: 35.5 mg (69%); mp 165–170 °C.

IR (ATR): 3388, 3006, 2920, 2851, 2056, 2030, 1733, 1715, 1670, 1642, 1592, 1502, 1448, 1438, 1420, 1403, 1357, 1299, 1281, 1214, 1202, 1183, 1141, 1121, 1102, 1042, 977, 934, 879, 809, 779, 724, 688, 624, 604 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.47 (s, 6 H), 2.31 (s, 3 H), 3.90 (s, 3 H), 3.96 (s, 3 H), 5.67 (d, *J* = 9.7 Hz, 1 H), 6.49 (d, *J* = 2.1 Hz, 1 H), 6.63 (d, *J* = 9.7 Hz, 1 H), 6.99 (br s, 1 H), 7.59 (s, 1 H), 7.88 (br s, 1 H).

^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 16.10 (CH_3), 27.58 (2 CH_3), 55.53 (CH_3), 55.99 (CH_3), 75.82 (C), 93.65 (CH), 96.07 (CH), 104.74 (C), 117.26 (C), 117.33 (CH), 118.39 (C), 121.04 (CH), 124.27 (C), 124.44 (C), 129.18 (CH), 135.07 (C), 145.90 (C), 149.69 (C), 154.73 (C).

MS (EI): *m*/*z* (%) = 323 (74, [M$^+$]), 308 (100), 293 (16).

HRMS: *m*/*z* [M$^+$] calcd for $C_{20}H_{21}NO_3$: 323.1521; found: 323.1532.

UV (EtOH): λ = 239, 242, 255 (sh), 280 (sh), 291, 348 nm.

Fluorescence (EtOH): λ_{ex} = 348 nm, λ_{em} = 424 nm.

4-Bromo-2-(triisopropylsilyloxy)anisole (23)

Imidazole (671 mg, 9.85 mmol) and chlorotriisopropylsilane (1.60 mL, 7.39 mmol) were added to a solution of 5-bromo-2-methoxyphenol (1 g, 4.93 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred for 2 h at r.t. and then washed with H_2O. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layers were dried ($MgSO_4$). Removal of the solvent under vacuum and flash chromatography (silica gel, isohexane–EtOAc, 25:1) of the crude product provided **23** as a colorless oil; yield: 1.78 g (quant.).

IR (ATR): 2943, 2866, 1557, 1495, 1464, 1443, 1400, 1268, 1224, 1180, 1132, 1071, 1032, 1015, 996, 931, 881, 861, 793, 706, 679, 623 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.09 (d, *J* = 7.4 Hz, 18 H), 1.20–1.29 (m, 3 H), 3.77 (s, 3 H) 6.69–6.70 (m, 1 H) 6.99–7.01 (m, 2 H).

^{13}C NMR and DEPT (150 MHz, $CDCl_3$): δ = 12.82 (3 CH), 17.84 (6 CH_3), 55.55 (CH_3), 112.18 (C), 113.15 (CH), 123.53 (CH), 124.01 (CH), 146.43 (C), 150.32 (C).

MS (EI): *m*/*z* (%) = 317 (83), 315 (81, [M$^+$ – $CHMe_2$]), 302 (100), 300 (94), 260 (16), 258 (16), 231 (39), 229 (36), 216 (28), 214 (26).

Anal. Calcd for $C_{16}H_{27}BrO_2Si$: C, 53.47; H, 7.57. Found: C, 53.73; H, 7.55.

3-Benzyloxy-*N*-[4-methoxy-3-(triisopropylsilyloxy)phenyl]-4-methylaniline (24)

A solution of bromoanisole **23** (818 mg, 2.28 mmol) in toluene (8 mL) was added over a period of 2 h to a mixture of 3-benzyloxy-4-methylaniline (**19**)[15] (583 mg, 2.73 mmol), Cs_2CO_3 (890 mg, 2.73 mmol), $Pd(OAc)_2$ (30.7 mg, 0.137 mmol), and XPhos (130 mg, 0.273 mmol) in toluene (15 mL) at reflux. After a total reaction time of 19.5 h at reflux temperature, the mixture was filtered over a small path of Celite. Subsequent purification of the crude product by flash chromatography (silica gel, isohexane–EtOAc, 20:1) provided **24** as a brownish oil; yield: 1.04 g (93%).

IR (ATR): 3391, 3061, 3028, 2943, 2865, 1604, 1557, 1542, 1502, 1461, 1386, 1269, 1222, 1193, 1160, 1126, 1029, 998, 919, 882, 844, 800, 776, 735, 681 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.10 (d, *J* = 7.4 Hz, 18 H), 1.22–1.30 (m, 3 H), 2.21 (s, 3 H), 3.79 (s, 3 H), 4.99 (s, 2 H), 5.38 (br s, 1 H), 6.47 (br d, *J* = 7.5 Hz, 1 H), 6.54 (s, 1 H), 6.58 (br d, *J* = 7.9 Hz, 1 H), 6.68 (d, *J* = 1.9 Hz, 1 H), 6.76 (d, *J* = 8.6 Hz, 1 H), 6.99 (d, *J* = 7.9 Hz, 1 H), 7.31–7.33 (m, 1 H), 7.37–7.40 (m, 2 H), 7.42–7.43 (m, 2 H).

^{13}C NMR and DEPT (150 MHz, $CDCl_3$): δ = 12.87 (3 CH), 15.62 (CH_3), 17.91 (6 CH_3), 56.11 (CH_3), 69.73 (CH_2), 100.94 (CH), 108.51 (CH), 112.64 (CH), 113.31 (2 CH), 118.43 (C), 127.09 (2 CH), 127.66 (CH), 128.45 (2 CH), 130.96 (CH), 136.66 (C), 137.44 (C), 143.90 (C), 146.21 (C), 146.36 (C), 157.52 (C).

MS (EI): *m*/*z* (%) = 491 (41, [M$^+$]), 433 (57), 342 (14), 327 (17), 314 (11), 91 (100).

UV (MeOH): λ = 285 nm.

Anal. Calcd for $C_{30}H_{41}NO_3Si$: C, 73.28; H, 8.40; N, 2.85. Found: C, 73.34; H, 8.61; N, 2.93.

2-Benzyloxy-6-methoxy-3-methyl-7-(triisopropylsilyloxy)-9*H*-carbazole (25)

A mixture of the diarylamine **24** (100 mg, 0.203 mmol), $Pd(OAc)_2$ (6.80 mg, 30.5 µmol), $Cu(OAc)_2$ (92.3 mg, 0.508 mmol), and AcOH (1 mL) was heated at 130 °C under air by microwave irradiation (300 W) for 1 h. The mixture was cooled to r.t., diluted with EtOAc, and washed with sat. aq K_2CO_3 and brine several times. The aqueous layers were extracted with EtOAc and the combined organic layers were dried ($MgSO_4$). Removal of the solvent under vacuum and flash chromatography (silica gel, isohexane–EtOAc, 20:1) of the crude product provided **25** as a colorless solid; yield: 70.5 mg (71%); mp 154–156 °C.

IR (ATR): 3367, 3061, 3031, 2942, 2864, 1624, 1478, 1454, 1432, 1390, 1361, 1283, 1222, 1164, 1122, 1074, 1042, 1005, 978, 919, 881, 837, 818, 780, 737, 683, 652, 626 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.13 (d, *J* = 7.6 Hz, 18 H), 1.27–1.35 (m, 3 H), 2.43 (s, 3 H), 3.90 (s, 3 H), 5.13 (s, 2 H), 6.84 (s, 1 H), 6.91 (s, 1 H), 7.32–7.34 (m, 1 H), 7.39–7.41 (m, 3 H), 7.48–7.49 (m, 2 H), 7.63 (br s, 1 H), 7.69 (s, 1 H).

^{13}C NMR and DEPT (150 MHz, $CDCl_3$): δ = 12.89 (3 CH), 16.85 (CH_3), 17.96 (6 CH_3), 56.32 (CH_3), 70.20 (CH_2), 94.30 (CH), 102.50 (CH), 102.78 (CH), 116.69 (C), 117.08 (C), 119.20 (C), 120.61 (CH), 127.04 (2 CH), 127.67 (CH), 128.48 (2 CH), 134.08 (C), 137.59 (C), 139.05 (C), 144.41 (C), 146.20 (C), 155.30 (C).

MS (EI): *m*/*z* (%) = 489 (37, [M$^+$]), 431 (100), 345 (13), 78 (12), 43 (12).

UV (MeOH): λ = 212, 237, 267, 316, 328 (sh), 341 (sh) nm.

Fluorescence (MeOH): λ_{ex} = 267 nm, λ_{em} = 371 nm.

Anal. Calcd for $C_{30}H_{39}NO_3Si$: C, 73.58; H, 8.03; N, 2.86. Found: C, 73.30; H, 8.15; N, 2.93.

2-Hydroxy-6-methoxy-3-methyl-7-triisopropylsilyloxy-9*H*-carbazole (26)

A mixture of carbazole **25** (679 mg, 1.39 mmol) and 10% Pd/C (204 mg) in EtOAc (35 mL) was stirred at r.t. for 19 h under a H_2 atmosphere at normal pressure. The mixture was filtered over Celite (EtOAc) and the solvent was removed under vacuum to afford **26** as a colorless-light pink solid; yield: 492 mg (89%); mp 177–178 °C.

IR (ATR): 3701, 3626, 3571, 3339, 2942, 2865, 1698, 1623, 1479, 1435, 1388, 1358 1296, 1225, 1206, 1177, 1154, 1140, 1116, 1071, 1004, 974, 921, 869, 832, 767, 724, 708, 685, 644 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 1.12 (d, *J* = 7.5 Hz, 18 H), 1.25–1.34 (m, 3 H), 2.39 (s, 3 H), 3.90 (s, 3 H), 4.78 (br s, 1 H), 6.77 (s, 1 H), 6.89 (s, 1 H), 7.37 (s, 1 H), 7.59 (br s, 1 H), 7.64 (s, 1 H).

^{13}C NMR and DEPT (150 MHz, $CDCl_3$): δ = 12.89 (3 CH), 16.11 (CH_3), 17.95 (6 CH_3), 56.39 (CH_3), 96.59 (CH), 102.50 (CH), 102.90 (CH), 115.76 (C), 116.62 (C), 117.82 (C), 120.73 (CH), 134.24 (C), 139.39 (C), 144.57 (C), 146.20 (C), 151.94 (C).

MS (EI): *m*/*z* (%) = 399 (21, [M^+]), 341 (100), 255 (25), 43 (22).

UV (MeOH): λ = 213, 235, 267, 318, 329 (sh), 342 (sh) nm.

Fluorescence (MeOH): λ_{ex} = 267 nm, λ_{em} = 367 nm.

Anal. Calcd for $C_{23}H_{33}NO_3Si$: C, 69.13; H, 8.32; N, 3.51. Found: C, 69.00; H, 8.31; N, 3.49.

8-Methoxy-3,3,5-trimethyl-9-(triisopropylsilyloxy)pyrano[3,2-*a*]carbazole (27)

Prenal (48.3 µL, 0.500 mmol) was added to a solution of the carbazole **26** (100 mg, 0.250 mmol) in toluene (5 mL) and then, Ti(O*i*-Pr)$_4$ (0.30 mL, 1.00 mmol) was added in one portion. The reaction mixture was stirred at r.t. for 15.5 h. Removal of the solvent under vacuum and flash chromatography (silica gel, isohexane–EtOAc, 25:1) of the crude product afforded **27** as a colorless solid; yield: 76.0 mg (65%); mp 135–137 °C.

IR (ATR): 3347, 2942, 2865, 2056, 1629, 1577, 1559, 1541, 1491, 1471, 1459, 1433, 1400, 1357, 1283, 1233, 1207, 1165, 1127, 1057, 1015, 941, 915, 884, 843, 797, 769, 738, 681, 616 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 1.12 (d, *J* = 7.5 Hz, 18 H), 1.26–1.35 (m, 3 H), 1.47 (s, 6 H), 2.32 (s, 3 H), 3.89 (s, 3 H), 5.68 (d, *J* = 9.7 Hz, 1 H), 6.59 (d, *J* = 9.7 Hz, 1 H), 6.93 (s, 1 H), 7.34 (s, 1 H), 7.54 (br s, 1 H), 7.61 (br s, 1 H).

^{13}C NMR and DEPT (150 MHz, $CDCl_3$): δ = 12.87 (3 CH), 16.02 (CH_3), 17.95 (6 CH_3), 27.46 (2 CH_3), 56.33 (CH_3), 75.62 (C), 102.68 (CH), 102.79 (CH), 104.62 (C), 117.14 (C), 117.32 (C, CH), 118.13 (C), 120.14 (CH), 129.41 (CH), 134.14 (C), 134.90 (C), 144.40 (C), 146.31 (C), 148.66 (C).

MS (EI): *m*/*z* (%) = 465 (18, [M^+]), 450 (100), 392 (24), 306 (29), 43 (19).

UV (MeOH): λ = 223, 238 (sh), 290 (sh), 300, 329, 360 (sh) nm.

Fluorescence (MeOH): λ_{ex} = 300 nm, λ_{em} = 370 nm.

Anal. Calcd for $C_{28}H_{39}NO_3Si$: C, 72.21; H, 8.44; N, 3.01. Found: C, 72.07; H, 8.49; N, 3.34.

Koenigine (4a)

A 1 M solution of TBAF in THF (0.650 mL, 0.650 mmol) was added slowly to a solution of the pyrano[3,2-*a*]carbazole **27** (202 mg, 0.434 mmol) in THF (12 mL) at 0 °C. The solution was stirred for 10 min at 0 °C and H_2O was added. The mixture was extracted with EtOAc (2 ×) and the combined organic layers were dried ($MgSO_4$). Removal of the solvent under vacuum and flash chromatography (silica gel, isohexane–EtOAc, 3:1) of the crude product provided koenigine (**4a**) as a light yellow solid; yield: 126 mg (94%); mp 182–183 °C (Lit.[5,6] 183–185 °C).

IR (ATR): 3501, 3410, 3309, 3041, 2973, 2930, 2050, 1727, 1629, 1593, 1557, 1542, 1474, 1458, 1430, 1374, 1357, 1342, 1279, 1248, 1204, 1159, 1126, 1056, 1030, 1012, 980, 941, 882, 844, 767, 738, 716, 694, 652, 621 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.48 (s, 6 H), 2.32 (s, 3 H), 3.99 (s, 3 H), 5.69 (d, *J* = 9.7 Hz, 1 H), 5.80 (s, 1 H), 6.60 (dd, *J* = 9.7, 1.5 Hz, 1 H), 6.96 (s, 1 H), 7.35 (s, 1 H), 7.53 (s, 1 H), 7.66 (br s, 1 H).

^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 16.05 (CH_3), 27.52 (2 CH_3), 56.63 (CH_3), 75.66 (C), 96.68 (CH), 101.27 (CH), 104.60 (C), 115.91 (C), 117.23 (C), 117.28 (CH), 118.17 (C), 119.94 (CH), 129.45 (CH), 134.35 (C), 134.66 (C), 141.89 (C), 144.45 (C), 148.63 (C).

MS (EI): *m*/*z* (%) = 309 (37, [M^+]), 294 (100), 279 (39).

UV (MeOH): λ = 223, 237 (sh), 289 (sh), 300, 344, 359 (sh) nm.

Fluorescence (MeOH): λ_{ex} = 300 nm, λ_{em} = 376 nm.

Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53. Found: C, 73.76; H, 5.94; N, 4.61.

Koenigicine (Koenimbidine, Koenidine, 4b)

Me_2SO_4 (63 µL, 0.663 mmol) was added to a solution of koenigine (**4a**; 41.0 mg, 0.133 mmol) and K_2CO_3 powder (36.6 mg, 0.266 mmol) in acetone (3.5 mL) at 56 °C. The mixture was stirred for 18.5 h at 56 °C and H_2O was added. The mixture was extracted with EtOAc (2 ×) and the combined organic layers were dried ($MgSO_4$). Removal of the solvent under vacuum and flash chromatography (silica gel, isohexane–EtOAc, 3:1) of the crude product provided koenigicine (**4b**) as a light brown solid; yield: 40 mg (93%); mp 223–224 °C (Lit.[5,6] [koenidine] 224–225 °C, Lit.[8] [koenigicine] 224–225 °C, Lit.[11] [koenimbidine] 225 °C).

IR (ATR): 3424, 2977, 2939, 2833, 1734, 1697, 1626, 1492, 1471, 1443, 1400, 1375, 1359, 1274, 1241, 1207, 1192, 1158, 1116, 1056, 1029, 994, 945, 871, 826, 780, 767, 740, 722, 699, 682, 662, 614 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.48 (s, 6 H), 2.33 (s, 3 H), 3.93 (s, 3 H), 3.98 (s, 3 H), 5.68 (d, *J* = 9.7 Hz, 1 H), 6.60 (d, *J* = 9.7 Hz, 1 H), 6.90 (s, 1 H), 7.38 (s, 1 H), 7.55 (br s, 1 H), 7.74 (br s, 1 H).

^1H NMR (500 MHz, CD_2Cl_2): δ = 1.47 (s, 6 H), 2.30 (s, 3 H), 3.90 (s, 3 H), 3.91 (s, 3 H), 5.72 (d, *J* = 9.7 Hz, 1 H), 6.64 (d, *J* = 9.7 Hz, 1 H), 6.95 (s, 1 H), 7.38 (s, 1 H), 7.54 (br s, 1 H), 7.85 (br s, 1 H).

^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 16.07 (CH_3), 27.52 (2 CH_3), 56.16 (CH_3), 56.51 (CH_3), 75.67 (C), 94.58 (CH), 102.10 (CH), 104.61 (C), 115.99 (C), 117.20 (C), 117.26 (CH), 118.29 (C), 120.10 (CH), 129.45 (CH), 133.97 (C), 134.66 (C), 144.29 (C), 148.07 (C), 148.63 (C).

^{13}C NMR and DEPT (125 MHz, CD_2Cl_2): δ = 16.15 (CH_3), 27.64 (2 CH_3), 56.44 (CH_3), 56.85 (CH_3), 76.08 (C), 95.19 (CH), 102.84 (CH), 105.01 (C), 116.17 (C), 117.49 (C), 117.53 (CH), 118.53 (C), 120.32 (CH), 129.89 (CH), 134.45 (C), 135.06 (C), 144.92 (C), 148.85 (C), 149.01 (C).

MS (EI): *m*/*z* (%) = 323 (42, [M^+]), 308 (100), 292 (23), 154 (11).

UV (MeOH): λ = 223, 237, 289 (sh), 298, 341, 357 (sh) nm.

Fluorescence (MeOH): λ_{ex} = 298 nm, λ_{em} = 376 nm.

Anal. Calcd for $C_{20}H_{21}NO_3$: C, 74.28; H, 6.55; N, 4.33. Found: C, 74.23; H, 6.79; N, 4.47.

X-ray Crystallographic Data[35]

$C_{20}H_{21}NO_3$, M = 323.38 g mol^{-1}, crystal size: 0.37 × 0.10 × 0.09 mm^3, orthorhombic, space group: $P2_12_12_1$, a = 7.496(2), b = 10.345(2), c = 21.658(4) Å, V = 1679.5(6) Å^3, Z = 4, ρ_{calcd} = 1.279 g cm^{-3}, μ = 0.086 mm^{-1}, λ = 0.71073 Å, T = 198(2) K, θ range = 3.31–28.99°, reflections collected: 63725, independent reflections: 4461 (R_{int} = 0.0465), 226 parameters. The structure was solved by direct methods and refined by full-matrix least squares on F^2; final R indices [I >2σ(I)]: R_1 = 0.0379; wR_2 = 0.0868; max. residual electron density: 0.203 e Å^{-3}.

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1560359.

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