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Palladium(II)-Catalyzed Synthesis of the Formylcarbazole Alkaloids Murrayaline A–C, 7-Methoxymukonal, and 7-Methoxy-*O*-methylmukonal[‡]

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We describe the synthesis of the naturally occurring 2,7-dioxygenated formylcarbazole alkaloids 7-methoxymukonal, 7-methoxy-*O*-methylmukonal, and the murrayalines A–C. The carbazole framework was constructed by a Buchwald–Hartwig amination and a subsequent palladium(II)-catalyzed oxidative cyclization.

Introduction

Over the past decade, numerous carbazole alkaloids have been obtained from various natural sources. Their biological activities as well as approaches towards their total syntheses have been the focus of scientific research.[1] Naturally occurring tricyclic carbazoles have been classified on the basis of their oxygenation pattern.[1f,1p] Herein, we report the total syntheses of the five 2,7-dioxygenated carbazolecarbaldehydes 7-methoxymukonal (**1**), 7-methoxy-*O*-methylmukonal (**2**), and the murrayalines A–C (**3**–**5**) (see Figure 1). 7-Methoxymukonal (**1**) was first isolated in 1988 by Pummangura and co-workers from the root bark of *Clausena harmandiana* Pierre, which was collected in Thailand (see Figure 1).[2] These plants are used in folk medicine for the treatment of stomach aches and fever. The structure of **1** was assigned on the basis of its spectroscopic data. In addition, 7-methoxymukonal (**1**) was isolated from the stem bark of *Clausena excavata* Burm. F by Ito et al.,[3] from *Clausena vestita* D. D. Tao by Zhao et al.,[4] and from *Clausena wallichii by* Laphookhieo et al.[5] In 1990, Lange et al. reported the first isolation of the corresponding methyl ether, 7-methoxy-*O*-methylmukonal (**2**), from the roots of *Murraya siamensis*, which was collected in Thailand.[6] Subsequently, compound **2** was also isolated from *Clausena excavata* by Wu et al.,[7] from *Clausena vestita* D. D. Tao by Zhao et al.,[4] and from the roots of *Clausena wallichii* by Laphookhieo and co-workers.[5] A variety of biological activities has been reported for 7-methoxymukonal (**1**) and 7-methoxy-*O*-methylmukonal (**2**). In 1996, Wu and co-workers identified **1** as an inhibitor of rabbit platelet aggregation.[8] Kongkathip and co-workers observed that 7-methoxymukonal (**1**) displays weak antimycobacterial activity against the $H_{37}Ra$ strain and weak antifungal activity against *Candida albicans*.[9] Furthermore, cytotoxicity against the MCF-7 cell line (breast cancer) and the KB cell line (oral human epidermal carcinoma),[5,10] antimalarial activity,[10a] weak antioxidant activity, and an inhibition of lipid peroxidation have been described for **1**.[11] In 2005, Kongkathip and co-workers reported anti-HIV activity for 7-methoxy-*O*-methylmukonal (**2**).[12]

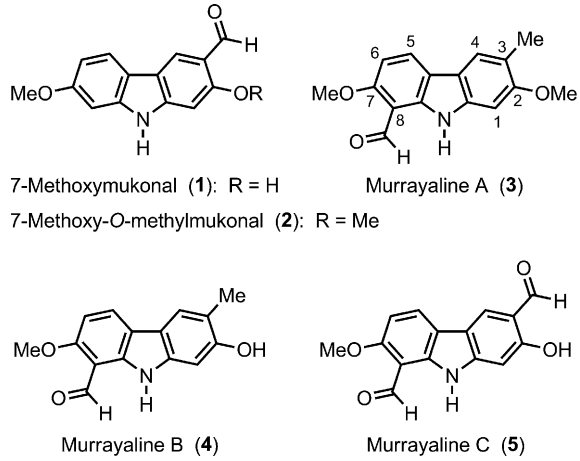

Figure 1. Naturally occurring 2,7-dioxygenated carbazolecarbaldehydes **1**–**5**.

Previously, we described the first total synthesis of 7-methoxy-*O*-methylmukonal (**2**) by using an iron-mediated route (three steps, 38% overall yield).[13] We also reported the palladium-catalyzed synthesis of 7-hydroxy-*O*-methylmukonal (four steps, 51% overall yield), a regioisomer of the natural product 7-methoxymukonal (**1**).[14] However, no total synthesis of **1** has been reported so far.

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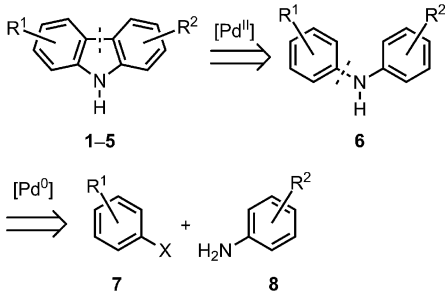
In 1986, the carbazole-8-carbaldehyde murrayaline A (**3**) was first isolated by Furukawa et al. from the stem bark of *Murraya euchrestifolia* Hayata, which was collected in Taiwan.[15] Its structure was determined by spectroscopic data and confirmed by total synthesis (no experimental details and yields were given).[15] In 1991, the murrayalines B (**4**) and C (**5**) were both isolated by Furukawa et al. from the acetone extract of the stem bark of *Murraya euchrestifolia* Hayata, which was collected in Taiwan.[16] No syntheses have yet been reported for the murrayalines B and C (**4** and **5**).

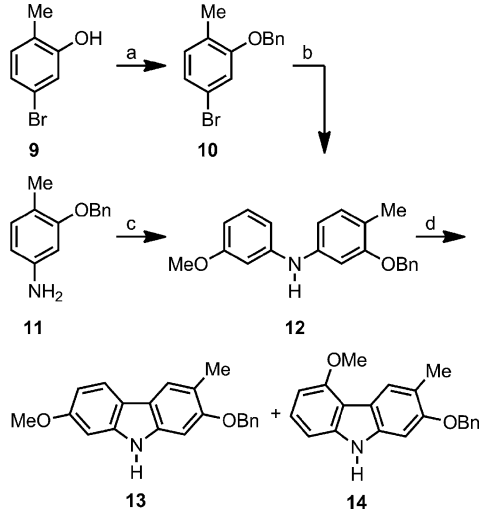
Results and Discussion

We devised an approach to the 2,7-dioxygenated carbazolecarbaldehydes **1**–**5** by using our palladium(II)-catalyzed synthesis for carbazole alkaloids (see Scheme 1).[1i,17] The key step of this approach is the oxidative cyclization of diarylamine **6** through a double C–H bond activation by using catalytic amounts of palladium(II) acetate. In 1994, we demonstrated that this process, originally described by Åkermark in 1975 using stoichiometric amounts of a palladium(II) salt,[18] becomes catalytic with regard to the palladium through the reoxidation of palladium(0), which is formed during the reaction.[17a] The required diarylamine **6** is most conveniently prepared through a Buchwald–Hartwig coupling reaction between an appropriately substituted aryl halide **7** and an arylamine **8**.[19]



Scheme 1. Palladium-catalyzed approach to carbazole alkaloids **1**–**5**.

For the synthesis of 7-methoxymukonal (**1**), we first prepared diarylamine **12** by the Buchwald–Hartwig coupling reaction of bromoarene **10** and *meta*-anisidine with a catalytic amount of SPhos[19c] as ligand (see Scheme 2). Alternatively, under the same reaction conditions, compound **12** was available in a similar high yield through the coupling of the arylamine **11** and *meta*-bromoanisole. Compound **11** was prepared by the *O*-benzylation of 2-methyl-5-nitrophenol and subsequent reduction reaction (two steps, 99% yield).[20] An oxidative cyclization of diarylamine **12** by heating in pivalic acid in the presence of a catalytic amount of palladium(II) acetate and a stoichiometric amount of cupric acetate provided the desired carbazole **13** along with the undesired, sterically more hindered isomer **14** in a ratio of 18:1 and 96% combined yield (see Table 1). The formation of the sterically more hindered 4-oxygenated carbazoles has been previously observed and can be explained by a directed palladation that results from the coordination of palladium(II) to the oxygen atom of the methoxy group.[14,21] Oxidative cyclization in the absence of cupric acetate with smaller amounts of palladium acetate in the presence of potassium carbonate led exclusively to the desired regioisomer **13**.



Scheme 2. Synthesis of the 2,7-dioxygenated carbazole **13**. Reagents and conditions: (a) BnBr (1.2 equiv.), K_2CO_3 (2.0 equiv.), acetone, reflux, 17 h, 97%; (b) *m*-anisidine (1.3 equiv.), $Pd(OAc)_2$ (5 mol-%), 2-dicyclohexylphosphino-2′,6′-dimethoxybiphenyl (SPhos, 10 mol-%), Cs_2CO_3 (1.4 equiv.), toluene, 100 °C, 18 h, 97%; (c) *m*-bromoanisole (1.0 equiv.), **11** (1.3 equiv.), $Pd(OAc)_2$ (5 mol-%), SPhos (10 mol-%), Cs_2CO_3 (1.4 equiv.), toluene, 100 °C, 22 h, 94%; (d) $Pd(OAc)_2$ (8 mol-%), K_2CO_3 (10 mol-%), pivalic acid (PivOH), 100 °C, 24 h, air, 95% (for **13**).

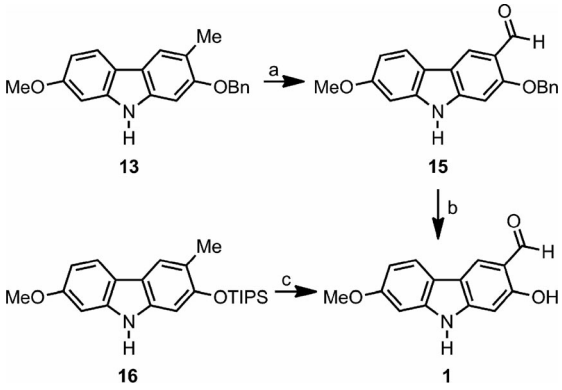
Table 1. Palladium(II)-catalyzed oxidative cyclization of the diarylamine **12**.

$Pd(OAc)_2$ [mol-%]	Additive (equiv.)	Conditions	Yield [%] **13**	**14**
15	$Cu(OAc)_2$ (2.5)	PivOH, 110 °C, MW,[a] 4 h, air	91	5
11	$Cu(OAc)_2$ (0.1), K_2CO_3 (0.15)	PivOH, 100 °C, 29 h, air	72	3
8	K_2CO_3 (0.1)	PivOH, 100 °C, 24 h, air	95	–

[a] MW = microwave.

The carbazole **13** was converted into carbazole-3-carbaldehyde **15** by treatment with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in a mixture of methanol, tetrahydrofuran (THF), and water (see Scheme 3).[22] The removal of the benzyl group to gain access to 7-methoxymukonal (**1**) proceeded with low yields under most conditions and often was accompanied by benzylation at C-1 of the carbazole framework. Finally, cleavage of the benzyl ether was achieved by using overstoichiometric amounts of zinc bromide and 2,6-dimethoxytoluene as a benzyl scavenger to provide 7-methoxymukonal (**1**) in 77% yield. Alternatively, **1** was accessible in two steps from TIPS-protected carbazole **16** (TIPS = triisopropylsilyl), which served as an intermediate in our syntheses of the pyrayafolines A–E.[17e] The oxidation of compound **16** by treatment with DDQ followed by desilylation afforded 7-methoxymukonal (**1**), al-

beit in only 26% yield over both steps. The spectroscopic data of synthetic **1** are in full agreement with those reported for the natural product.[2] The structure of 7-methoxymukonal (**1**) was also confirmed by single-crystal X-ray analysis (see Figure 2). Our palladium-catalyzed approach completes the first total synthesis of 7-methoxymukonal (**1**) and provides the natural product in five steps and 60% overall yield based on the bromophenol **9**.



Scheme 3. Synthesis of 7-methoxymukonal (**1**). Reagents and conditions: (a) DDQ (2.5 equiv.), MeOH/THF/H_2O (6:3:1), room temp., 37 min, 87%; (b) $ZnBr_2$ (15.0 equiv.), 2,6-dimethoxytoluene (3.1 equiv.), 1,2-dichloroethane, 70 °C to reflux, 30 h, 77%; (c) (1) DDQ (2.2 equiv.), MeOH/THF/H_2O (10:5:1), room temp., 1.5 h, 39%; (2) tetra-*n*-butylammonium fluoride (TBAF, 1.5 equiv.), *N*,*N*-dimethylformamide (DMF), –15 °C to room temp., 13 min, 67%. For the synthesis of compound **16**, see ref.[17e]

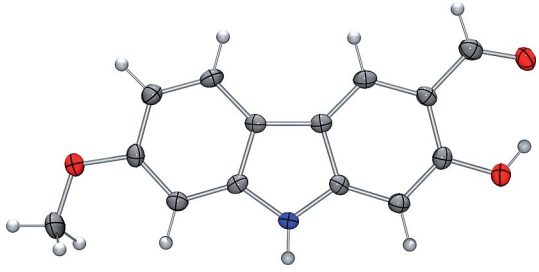
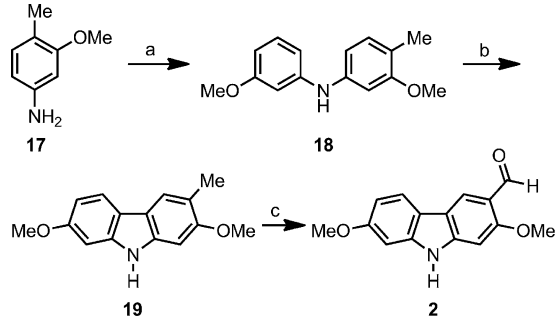


Figure 2. Molecular structure of 7-methoxymukonal (**1**) in the crystal. ORTEP plot showing thermal ellipsoids at 50% probability level.

An improved approach was developed for the synthesis of 7-methoxy-*O*-methylmukonal (**2**) by following a similar route. A Buchwald–Hartwig coupling reaction of *meta*-bromoanisole and commercially available 3-methoxy-4-methylaniline (**17**) using (±)-2,2′-bis(diphenylphosphino)-1,1′-binaphthalene (*rac*-BINAP) as ligand provided diarylamine **18** (see Scheme 4). The oxidative cyclization of compound **18** by treatment with a stoichiometric amount of palladium(II) acetate in acetic acid at 90 °C provided the desired carbazole **19** in 55% yield (see Table 2). We then investigated a number of reagents for the re-oxidation of the palladium(0) species. Using 10 mol-% of palladium(II) acetate and either 1,4-benzoquinone or *tert*-butyl hydroperoxide as a co-oxidant led only to decomposition. Employing our original conditions for the palladium(II)-catalyzed oxidative cyclization, 10 mol-% palladium(II) acetate in the presence of 2.5 equiv. of cupric acetate in air,[17a] provided carbazole **19** in 62% yield. This yield could be improved further by reducing the amount of cupric acetate to 10 mol-%. Thus, using catalytic amounts of palladium(II) acetate and cupric acetate (10 mol-% each) under air provided carbazole **19** in 67% yield. Replacing cupric acetate by manganese(III) acetate dihydrate led to almost identical results.[17c] The oxidative cyclization under oxygen, instead of air, provided carbazole **19** in 55% yield when 10 mol-% of palladium(II) acetate and cupric acetate were used. However, under an oxygen atmosphere, the catalyst loading could be further reduced to 5 mol-% of palladium(II) acetate and cupric acetate without a significant decrease in the yield. A further decrease of the amount of palladium(II) acetate to 1 mol-% provided carbazole **19** in 45% yield (equivalent to a turnover number of 45). The absence of any co-oxidant resulted in a sharp decrease in the yield (23%). Without a palladium(II) source, no cyclization, but partial decomposition, was observed. Finally, the oxidation of diarylamine **19** by treatment with DDQ afforded 7-methoxy-*O*-methylmukonal (**2**). In conclusion, our palladium(II)-catalyzed approach provides 7-methoxy-*O*-methylmukonal (**2**) in three steps and 42% overall yield and is superior to our iron-mediated synthesis of **2** (three steps and 38% yield).[13]



Scheme 4. Synthesis of 7-methoxy-*O*-methylmukonal (**2**). Reagents and conditions: (a) *m*-bromoanisole (1.0 equiv.), **17** (1.25 equiv.), $Pd(OAc)_2$ (6 mol-%), *rac*-BINAP (5 mol-%), Cs_2CO_3 (1.2 equiv.), toluene, reflux, 24 h, 85%; (b) $Pd(OAc)_2$ (10 mol-%), $Cu(OAc)_2$ (10 mol-%), AcOH, 90 °C, air, 5 h, 67%; (c) DDQ (4.2 equiv.), MeOH/H_2O (10:1), room temp., 80 min, 73%, see ref.[13b]

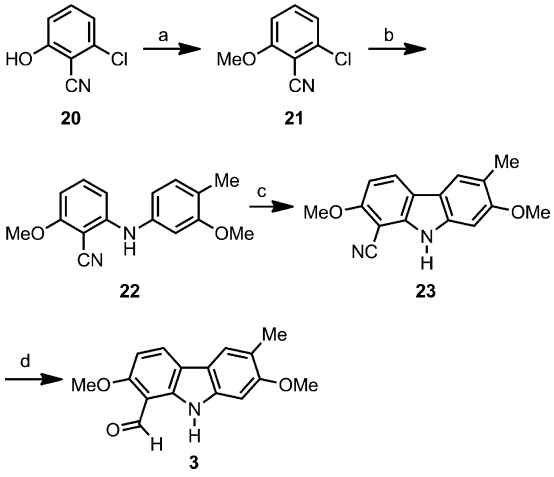
Table 2. Palladium(II)-catalyzed oxidative cyclization of the diarylamine **18**.

$Pd(OAc)_2$ [mol-%]	Co-oxidant (equiv.)	Conditions[a]	Yield [%] **19**
120	–	argon, 2 h	55
10	benzoquinone (2.5)	air, 3 h	decomp.
10	*t*BuOOH (2.5)	air, 3 h	decomp.
10	$Cu(OAc)_2$ (2.5)	air, 2 d	62
10	$Cu(OAc)_2$ (0.1)	air, 5 h	67
10	$Mn(OAc)_3$ (0.1)	air, 6 h	65
10	$Cu(OAc)_2$ (0.1)	oxygen, 6 h	55
5	$Cu(OAc)_2$ (0.05)	oxygen, 8 h	54
1	$Cu(OAc)_2$ (0.05)	oxygen, 20 h	45
10	–	oxygen, 12 h	23
–	$Cu(OAc)_2$ (0.1)	oxygen, 24 h	–[b]

[a] Acetic acid, 90 °C. [b] Isolation of 77% of starting material.

Our approach to the murrayalines A–C (**3**–**5**) relies on a late-stage reduction of a cyano group to introduce the for-

myl group at C-8. This strategy has already been applied to generate the formyl group at C-3 in our synthesis of 7-hydroxy-*O*-methylmukonal.[14] Thus, we first prepared benzonitrile **21** from commercially available 2-chloro-6-hydroxybenzonitrile (**20**) by *O*-methylation with methyl iodide (see Scheme 5). The Buchwald–Hartwig coupling of **21** with aniline **17** led to diarylamine **22**. The palladium(II)-catalyzed oxidative cyclization of **22** by heating at 120 °C in pivalic acid in air and in the presence of a catalytic amount of palladium(II) acetate and potassium carbonate provided carbazolecarbonitrile **23** in 87% yield. In comparison to our standard conditions,[17] we had to increase the amount of palladium(II) catalyst slightly to achieve an efficient oxidative cyclization of diarylamine **22**. The reduction of the cyano group by treatment with diisobutylaluminium hydride (DIBAL-H)[23] in dichloromethane at low temperature provided murrayaline A (**3**) in four steps and 54% overall yield. All spectroscopic data of **3** matched with those reported for the natural product.[15] The structure of **3** was also confirmed by single-crystal X-ray analysis (see Figure 3).



Scheme 5. Synthesis of murrayaline A (**3**). Reagents and conditions: (a) MeI (6.0 equiv.), K_2CO_3 (5.1 equiv.), DMF, reflux, 19 h, 87%; (b) **17** (1.27 equiv.), $Pd(OAc)_2$ (6 mol-%), SPhos (13 mol-%), Cs_2CO_3 (1.8 equiv.), toluene, reflux, 19.5 h, 100%; (c) $Pd(OAc)_2$ (23 mol-%), K_2CO_3 (25 mol-%), PivOH, 120 °C, 15.5 h, air, 87%; (d) DIBAL-H (2.5 equiv.), CH_2Cl_2, –55 to –25 °C, 4 h, 72%.

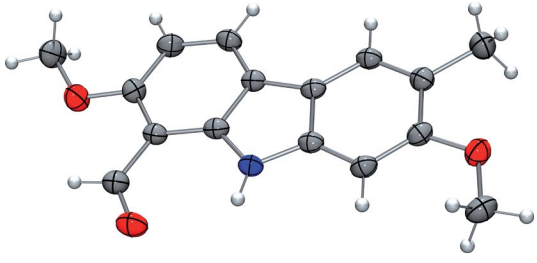
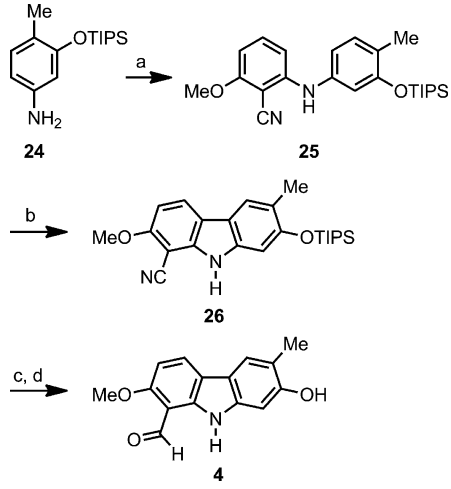


Figure 3. Molecular structure of murrayaline A (**3**) in the crystal. ORTEP plot showing thermal ellipsoids at 50% probability level.

The *O*-silyl-protected *m*-aminophenol **24** served as the starting material for the synthesis of murrayaline B (**4**) (see Scheme 6). Compound **24** was already used as a precursor in our syntheses of pyrayafolines A–E.[17e] The palladium(0)-catalyzed coupling of **24** with benzonitrile **21** provided diarylamine **25** in 85% yield. The structure of compound **25** was confirmed by an X-ray crystal structure analysis (see Figure 4). The palladium(II)-catalyzed oxidative cyclization of **25** afforded carbazolecarbonitrile **26** in 87% yield. The reduction of the cyano group by treatment with DIBAL-H to give a formyl group followed by cleavage of the silyl ether with tetra-*n*-butylammonium fluoride provided murrayaline B (**4**). The spectroscopic data of our synthetic **4** were identical to those reported for the natural product.[16] The single-crystal X-ray structure determination of murrayaline B (**4**) unambiguously confirmed the compound assignment (see Figure 5). The present route constitutes the first total synthesis of murrayaline B (**4**) and provides the natural product in six steps and 66% overall yield.



Scheme 6. Synthesis of murrayaline B (**4**). Reagents and conditions: (a) **21** (1.0 equiv.), **24** (1.2 equiv.), $Pd(OAc)_2$ (5 mol-%), SPhos (10 mol-%), Cs_2CO_3 (1.4 equiv.), toluene, reflux, 18 h, 85%; (b) $Pd(OAc)_2$ (22 mol-%), $Cu(OAc)_2$ (21 mol-%), K_2CO_3 (26 mol-%), PivOH, 100 °C, air, 18.5 h, 87%; (c) DIBAL-H (3.0 equiv.), CH_2Cl_2, –40 to –30 °C, 4 h; (d) TBAF (1.5 equiv.), DMF, –15 °C to room temp., 10 min, 89% (two steps).

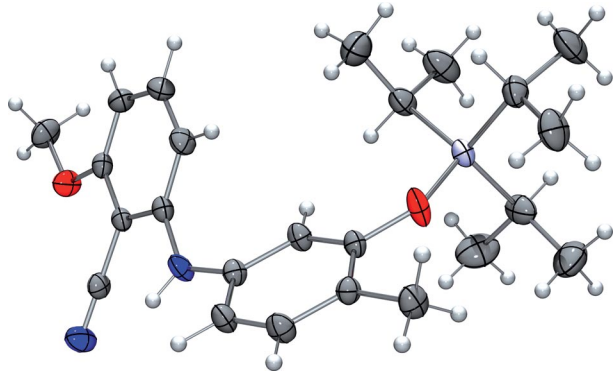


Figure 4. Molecular structure of diarylamine **25** in the crystal. ORTEP plot showing thermal ellipsoids at 50% probability level.

For our first attempt towards the synthesis of murrayaline C (**5**), we envisaged an oxidation of the C-3 methyl

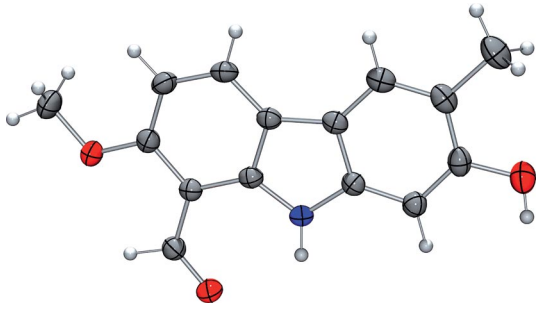
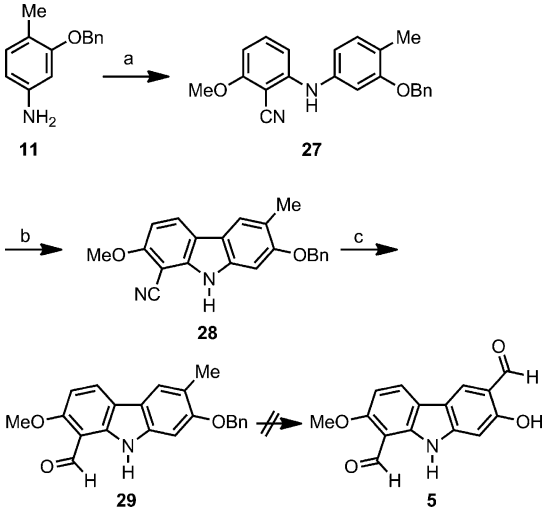


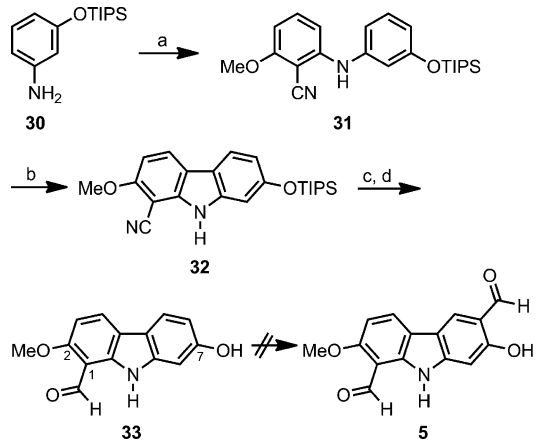
Figure 5. Molecular structure of murrayaline B (**4**) in the crystal. ORTEP plot showing thermal ellipsoids at 50% probability level.

group of the benzyl-protected carbazole **28** to give a formyl group (see Scheme 7). Benzyl protection was preferred to silyl protection (as used for carbazole **26** in the synthesis of **4**), as we previously learned from our synthesis of 7-methoxymukonal (**1**) that DDQ oxidation of a methyl group *ortho* to a bulky silyl ether is difficult (cf. Scheme 3, oxidation of **16** to **1**). A Buchwald–Hartwig coupling of compound **21** and aniline **11** followed by the palladium(II)-catalyzed oxidative cyclization of diarylamine **27** afforded carbazole **28** in 94% yield over both steps. Reduction of the cyano into a formyl group by using DIBAL-H at low temperature afforded benzyl-protected carbazolecarbaldehyde **29**. Unfortunately, all efforts to convert **29** into dialdehyde **5** failed and led only to decomposition.



Scheme 7. First approach to murrayaline C (**5**). Reagents and conditions: (a) **21** (1.0 equiv.), **11** (1.25 equiv.), $Pd(OAc)_2$ (5 mol-%), SPhos (10 mol-%), Cs_2CO_3 (1.4 equiv.), toluene, reflux, 20.5 h, 96%; (b) $Pd(OAc)_2$ (20 mol-%), K_2CO_3 (19 mol-%), PivOH, 110 °C, air, 2 d, 98%; (c) DIBAL-H (3.5 equiv.), CH_2Cl_2, –40 to –30 °C, 4 h, 56%.

In our second approach to murrayaline C (**5**), we proposed a Vilsmeier–Haack formylation of hydroxycarbazole **33** (see Scheme 8). Compound **33** was prepared by a Buchwald–Hartwig coupling of aniline **30** with compound **21** to give diarylamine **31**, which by palladium(II)-catalyzed cyclization gave carbazole **32**. Subsequent DIBAL-H reduction of the cyano group and cleavage of the silyl ether afforded carbazolecarbaldehyde **33** in 55% yield over four steps. The structure of **33** was confirmed by single-crystal X-ray analysis (see Figure 6). The formylation of compound **33** was expected to occur preferentially at the 6-position of the more electron-rich benzene ring. However, several attempts to achieve the formylation of **33** resulted in decomposition.



Scheme 8. Second approach to murrayaline C (**5**). Reagents and conditions: (a) **21** (1.25 equiv.), $Pd(OAc)_2$ (5 mol-%), SPhos (10 mol-%), Cs_2CO_3 (1.4 equiv.), toluene, reflux, 23 h, 100%; (b) $Pd(OAc)_2$ (9 mol-%), Cs_2CO_3 (10 mol-%), PivOH, 110 °C, air, 50 h, 76%; (c) DIBAL-H (3.0 equiv.), CH_2Cl_2, –78 to –30 °C, 4 h; (d) TBAF (1.5 equiv.), DMF, –8 °C to room temp., 10 min, 73% (two steps).

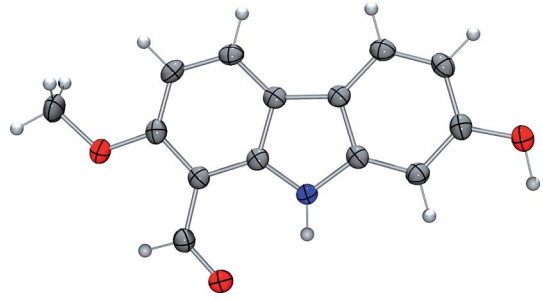
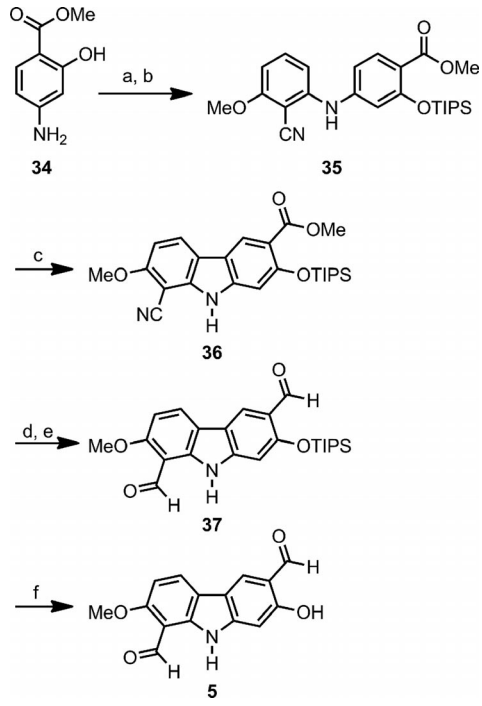


Figure 6. Molecular structure of 7-hydroxy-2-methoxycarbazole-1-carbaldehyde (**33**) in the crystal. ORTEP plot showing thermal ellipsoids at 50% probability level.

Finally, we decided to generate the C-3 formyl group of murrayaline C (**5**) by reduction of an ester group. Thus, carbazole **36** was prepared from commercially available methyl 4-aminosalicylate (**34**) (see Scheme 9). Protection of the hydroxy group and Buchwald–Hartwig amination led to the diarylamine **35**. The palladium(II)-catalyzed oxidative cyclization of **35** under microwave conditions (110 °C) provided carbazole **36** in 77% yield. Although both aryl rings of diarylamine **35** contained an electron-withdrawing group, with the appropriate reaction conditions, the oxidative cyclization was achieved in high yield by using only 7 mol-% of the palladium(II) catalyst. The DIBAL-H reduction of **36** led to a 3-hydroxymethylcarbazole-8-carbaldehyde, which was directly oxidized by using manganese(IV) oxide to afford the carbazole-3,8-dicarbaldehyde **37**. Cleavage of the silyl ether by treatment with TBAF pro-

vided synthetic murrayaline C (**5**) in six steps and 20% overall yield based on methyl 4-aminosalicylate (**34**). The spectroscopic data of our synthetic murrayaline C (**5**) were in full agreement with those reported for the natural product.[16]



Scheme 9. Synthesis of murrayaline C (**5**). Reagents and conditions: (a) imidazole (ImH, 4.0 equiv.), TIPSCl (3.0 equiv.), DMF, 50 °C, 4 d, 65%; (b) **21** (1.2 equiv.), $Pd(OAc)_2$ (5 mol-%), SPhos (10 mol-%), Cs_2CO_3 (1.4 equiv.), toluene, reflux, 18 h, 85%; (c) $Pd(OAc)_2$ (7 mol-%), K_2CO_3 (10 mol-%), $Cu(OAc)_2$ (2.5 equiv.), PivOH, microwave, 110 °C, air, 5 h, 77%; (d) DIBAL-H (4.5 equiv.), CH_2Cl_2, –78 to –35 °C, 4 h; (e) MnO_2 (20 equiv.), CH_2Cl_2, room temp., 6 d; (f) TBAF (1.5 equiv.), DMF, –10 °C to room temp., 10 min, 48% (three steps).

Conclusions

We have developed the palladium(II)-catalyzed total syntheses of five naturally occurring 2,7-dioxygenated carbazolecarbaldehydes. 7-Methoxymukonal (**1**) and 7-methoxy-*O*-methylmukonal (**2**) were obtained in five steps and 60% overall yield and three steps and 42% overall yield, respectively. It has been shown that acceptor-substituted carbazoles can be efficiently prepared through palladium(II)-catalyzed oxidative cyclizations of diarylamines that contain electron-withdrawing groups. Carbazolecarbaldehydes **3**–**5** were obtained from cyano-substituted diarylamines through short synthetic routes, which thus provided murrayaline A (**3**) in four steps and 54% overall yield, murrayaline B (**4**) in six steps and 66% overall yield, and murrayaline C (**5**) in six steps and 20% overall yield. 7-Methoxymukonal (**1**), murrayaline B (**4**), and murrayaline C (**5**) were obtained by total synthesis for the first time.

Experimental Section

General Methods: All reactions were carried out in oven-dried glassware under argon and with dry solvents unless stated otherwise. Tetrahydrofuran was dried using a solvent purification system (MBraun-SPS). Other chemicals were used as received from their commercial sources. Flash chromatography was performed on a Büchi Sepacore system that was equipped with an UV monitor, and silica gel from Acros Organics (0.035–0.070 mm) was used. Thin layer chromatography was performed with TLC plates from Merck (60 F_{254}), and UV light was used for the visualizations. Melting points were measured with a Gallenkamp MPD 350 melting point apparatus. Ultraviolet spectra were recorded with a Perkin–Elmer 25 UV/Vis spectrometer. Infrared spectra were recorded with a Thermo Nicolet Avatar 360 FTIR spectrometer using the ATR method (attenuated total reflectance). The NMR spectroscopic data were recorded with Bruker Avance III 600 and DRX 500 spectrometers. Chemical shifts (δ) are reported in parts per million with the nondeuterated residual solvent as the internal standard. The abbreviations that are used to report the data are s (singlet), d (doublet), t (triplet), sept (septet), m (multiplet), and br. (broad). Mass spectrometry data were recorded with a Finnigan MAT-95 spectrometer (electron impact, 70 eV) or through GC–MS coupling with an Agilent Technologies 6890 N GC System equipped with a 5973 mass selective detector (electron impact, 70 eV). Elemental analyses were determined with a EuroVector EuroEA3000 elemental analyzer. X-ray crystal structure analyses were performed with a Bruker-Nonius Kappa CCD that was equipped with a 700 series Cryostream low temperature device from Oxford Cryosystems. SHELXS-97,[24] SADABS version 2.10,[25] SHELXL-97,[26] POV-Ray for Windows version 3.6.2.msvc9.win64, and ORTEP-3 for Windows[27] were used for processing and visualization.

2-Benzyloxy-4-bromotoluene (10): Benzyl bromide (2.28 mL, 3.28 g, 19.2 mmol) was added dropwise to a solution of 5-bromo-2-methylphenol (**9**, 2.99 g, 16.0 mmol) and potassium carbonate (4.43 g, 32.1 mmol) in acetone (40 mL), and the mixture was stirred and heated at reflux for 17 h. The mixture was diluted with ethyl acetate, and the resulting solution was washed with water and brine several times. The aqueous layers were extracted with ethyl acetate. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (petroleum ether/diethyl ether, gradient from 1:0 to 5:1) provided 2-benzyloxy-4-bromotoluene (**10**, 4.30 g, 97% yield) as a colorless oil. UV (MeOH): λ = 277, 283 nm. IR (ATR): $\tilde{\nu}$ = 3088, 3064, 3031, 2922, 2853, 1592, 1486, 1457, 1419, 1397, 1378, 1304, 1238, 1189, 1125, 1083, 1015, 913, 877, 834, 799, 733, 694, 630 cm^{-1}. ^1H NMR (500 MHz, [D_6]acetone): δ = 2.19 (s, 3 H), 5.17 (s, 2 H), 7.03 (dd, J = 7.9, 1.7 Hz, 1 H), 7.11 (d, J = 7.9 Hz, 1 H), 7.17 (d, J = 1.7 Hz, 1 H), 7.34 (t, J = 7.5 Hz, 1 H), 7.41 (t, J = 7.5 Hz, 2 H), 7.51 (d, J = 7.5 Hz, 2 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D_6]acetone): δ = 16.09 (CH_3), 70.71 (CH_2), 115.70 (CH), 120.06 (C), 124.11 (CH), 126.82 (C), 128.22 (2 CH), 128.71 (CH), 129.34 (2 CH), 132.66 (CH), 138.06 (C), 158.55 (C) ppm. MS (EI, 70 eV): *m*/*z* (%) = 278 (46), 276 (44) $[M]^+$, 197 (22), 181 (21), 91 (100). HRMS: calcd. for $C_{14}H_{13}BrO$ $[M]^+$ 276.0150; found 276.0126.

3-Benzyloxy-*N*-(3-methoxyphenyl)-4-methylaniline (12):

Method A: To a suspension of *m*-anisidine (174 mg, 1.41 mmol), palladium acetate (12.1 mg, 53.9 µmol), SPhos (44.8 mg, 0.109 mmol), and cesium carbonate (493 mg, 1.51 mmol) in toluene (10 mL) was added dropwise over a period of 2 h a solution of 2-benzyloxy-4-bromotoluene (**10**, 300 mg, 1.08 mmol) in toluene

(10 mL) at 100 °C, and the mixture was stirred at 100 °C for 16 h (total reaction time: 18 h). After cooling to room temperature, the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (pentane/ethyl acetate, gradient from 1:0 to 7:1) provided 3-benzyloxy-*N*-(3-methoxyphenyl)-4-methylaniline (**12**, 337 mg, 97% yield) as a colorless solid; m.p. 82 °C. UV (MeOH): λ = 283 nm. IR (ATR): $\tilde{\nu}$ = 3413, 3392, 3055, 3025, 2999, 2922, 2850, 2826, 1591, 1510, 1490, 1473, 1456, 1395, 1366, 1336, 1262, 1203, 1169, 1154, 1127, 1079, 1037, 995, 975, 932, 860, 839, 826, 808, 745, 686, 630, 613 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.34 (s, 3 H), 3.82 (s, 3 H), 5.08 (s, 2 H), 5.58 (br. s, 1 H), 6.54 (dd, J = 8.1, 2.0 Hz, 1 H), 6.63 (br. d, J = 8.1 Hz, 1 H), 6.65 (t, J = 2.0 Hz, 1 H), 6.70 (dd, J = 7.9, 2.0 Hz, 1 H), 6.76 (d, J = 2.0 Hz, 1 H), 7.13 (d, J = 7.9 Hz, 1 H), 7.21 (t, J = 8.1 Hz, 1 H), 7.40 (t, J = 7.2 Hz, 1 H), 7.44–7.51 (m, 4 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 15.89 (CH_3), 55.18 (CH_3), 69.75 (CH_2), 102.66 (CH), 103.55 (CH), 105.69 (CH), 109.48 (CH), 111.30 (CH), 120.35 (C), 127.14 (2 CH), 127.80 (CH), 128.58 (2 CH), 130.16 (CH), 131.12 (CH), 137.38 (C), 141.50 (C), 145.29 (C), 157.42 (C), 160.75 (C). GC–MS (70 eV): m/z (%) = 319 (57) $[M]^+$, 228 (10), 200 (8), 91 (100). $C_{21}H_{21}NO_2$ (319.40): calcd. C 78.97, H 6.63, N 4.39; found C 78.89, H 6.82, N 4.24.

Method B: To a mixture of 3-benzyloxy-4-methylaniline (**11**, 3.43 g, 16.1 mmol), palladium acetate (139 mg, 0.619 mmol), SPhos (508 mg, 1.24 mmol), and cesium carbonate (5.71 g, 17.5 mmol) in toluene (70 mL) was added dropwise over a period of 18 h a solution of *m*-bromoanisole (2.31 g, 12.4 mmol) in toluene (10 mL) at 100 °C, and the mixture was stirred at 100 °C for 4 h (total reaction time: 22 h). The mixture was diluted with ethyl acetate, and the resulting solution was washed with water and brine several times. The aqueous layers were extracted with ethyl acetate. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (pentane/ethyl acetate, gradient from 50:1 to 15:1) provided 3-benzyloxy-*N*-(3-methoxyphenyl)-4-methylaniline (**12**, 3.71 g, 94% yield) as a colorless solid.

2-Benzyloxy-7-methoxy-3-methylcarbazole (13): To a mixture of diarylamine **12** (1.01 g, 3.16 mmol), potassium carbonate (44.3 mg, 0.321 mmol), and pivalic acid (3.1 g) in a 25 mL test tube under air was added palladium acetate (36.2 mg, 0.161 mmol) at 100 °C. The mixture was heated and vigorously stirred at 100 °C for 15 h, and then an additional portion of palladium acetate (21.8 mg, 97.1 μmol) was added. The stirring was continued at 100 °C for 9 h (total reaction time: 24 h). The mixture was cooled to room temperature, diluted with ethyl acetate, and the resulting solution was washed with a saturated solution of potassium carbonate and brine several times. The aqueous layers were extracted with ethyl acetate. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (pentane/ethyl acetate, gradient from 12:1 to 1:2) provided 2-benzyloxy-7-methoxy-3-methylcarbazole (**13**, 957 mg, 95% yield) as a brown solid; m.p. 252–253 °C. UV (MeOH): λ = 236, 261, 312, 320 nm. Fluorescence (MeOH): λ_{ex} = 261 nm, λ_{em} = 354 nm. IR (ATR): $\tilde{\nu}$ = 3402, 3064, 3028, 2992, 2942, 2836, 1619, 1500, 1469, 1450, 1389, 1339, 1308, 1264, 1233, 1216, 1197, 1179, 1160, 1138, 1018, 945, 911, 880, 853, 822, 803, 752, 736, 696, 632 cm^{-1}. ^1H NMR (500 MHz, [D$_6$]acetone): δ = 2.37 (s, 3 H), 3.83 (s, 3 H), 5.19 (s, 2 H), 6.75 (dd, J = 8.5, 2.3 Hz, 1 H), 6.96 (d, J = 2.3 Hz, 1 H), 7.08 (s, 1 H), 7.33 (t, J = 7.4 Hz, 1 H), 7.41 (m, 2 H), 7.54 (m, 2 H), 7.74 (s, 1 H), 7.83 (d, J = 8.5 Hz, 1 H), 9.98 (br. s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D$_6$]acetone): δ = 17.05 (CH_3), 55.68 (CH_3), 70.60 (CH_2), 95.16 (CH), 95.52 (CH), 108.27 (CH), 117.41 (C), 117.98 (C), 119.13 (C), 120.51 (CH), 121.35 (CH), 128.10 (2 CH), 128.45 (CH), 129.28 (2 CH), 138.90 (C), 140.55 (C), 142.11 (C), 156.22 (C), 158.97 (C) ppm. MS (EI, 70 eV): m/z (%) = 317 (23) $[M]^+$, 226 (100), 91 (11). HRMS: calcd. for $C_{21}H_{19}NO_2$ $[M]^+$ 317.1416; found 317.1427. $C_{21}H_{19}NO_2$ (317.39): calcd. C 79.47, H 6.03, N 4.41; found C 78.92, H 6.14, N 4.36.

2-Benzyloxy-5-methoxy-3-methylcarbazole (14): A 10 mL microwave tube was charged with diarylamine **12** (300 mg, 0.939 mmol), palladium acetate (32.2 mg, 0.143 mmol), cupric acetate (427 mg, 2.35 mmol), and pivalic acid (1.5 g) under air. The tube was irradiated in a microwave reactor at 110 °C and 300 W for 4 h. After cooling to room temperature, the mixture was diluted with ethyl acetate, and the resulting solution was washed with a saturated solution of potassium carbonate and brine several times. The aqueous layers were extracted with ethyl acetate. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (pentane/ethyl acetate, gradient from 10:1 to 2:5) provided 2-benzyloxy-7-methoxy-3-methylcarbazole (**13**, 271 mg, 91% yield, for spectroscopic data see above) and the less polar 2-benzyloxy-5-methoxy-3-methylcarbazole (**14**, 15.9 mg, 5% yield) as a brown solid; m.p. 191–192 °C. UV (MeOH): λ = 240, 284 (sh), 294, 317, 330 nm. Fluorescence (MeOH): λ_{ex} = 240 nm, λ_{em} = 340, 352 nm. IR (ATR): $\tilde{\nu}$ = 3377, 3058, 3035, 2942, 2908, 2863, 2833, 2030, 2007, 1970, 1947, 1631, 1604, 1580, 1504, 1475, 1457, 1434, 1401, 1342, 1313, 1272, 1216, 1163, 1143, 1097, 1020, 969, 894, 815, 781, 740, 725, 697, 615 cm^{-1}. ^1H NMR (500 MHz, [D$_6$]acetone): δ = 2.38 (s, 3 H), 4.04 (s, 3 H), 5.20 (s, 2 H), 6.66 (d, J = 8.0 Hz, 1 H), 7.03 (d, J = 8.0 Hz, 1 H), 7.10 (s, 1 H), 7.20 (t, J = 8.0 Hz, 1 H), 7.33 (t, J = 7.3 Hz, 1 H), 7.41 (m, 2 H), 7.55 (m, 2 H), 8.00 (s, 1 H), 10.12 (br. s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D$_6$]-acetone): δ = 17.11 (CH_3), 55.57 (CH_3), 70.53 (CH_2), 94.62 (CH), 100.58 (CH), 104.54 (CH), 113.15 (C), 116.60 (C), 119.10 (C), 124.71 (CH), 125.76 (CH), 128.12 (2 CH), 128.45 (CH), 129.28 (2 CH), 138.85 (C), 139.79 (C), 142.19 (C), 156.33 (C), 156.44 (C) ppm. MS (ESI, +25 V): m/z = 318.2 $[M + H]^+$, 340.3 $[M + Na]^+$, 635.5 $[2M + H]^+$. MS (ESI, –25 V): m/z = 224.8 $[M – C_7H_7]^-$. MS (EI, 70 eV): m/z (%) = 317 (55) $[M]^+$, 226 (100), 91 (10). HRMS: calcd. for $C_{21}H_{19}NO_2$ $[M]^+$ 317.1416; found 317.1428.

2-Benzyloxy-7-methoxycarbazole-3-carbaldehyde (15): DDQ (484 mg, 2.13 mmol) was added to a solution of 2-benzyloxy-7-methoxy-3-methylcarbazole (**13**, 271 mg, 0.854 mmol) in a mixture of methanol (150 mL), THF (75 mL), and water (25 mL), and the resulting mixture was vigorously stirred at room temperature for 37 min. Diethyl ether was added, and the mixture was washed with aqueous potassium hydroxide (2 M) and brine several times. The aqueous layers were extracted with diethyl ether. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (pentane/ethyl acetate, gradient from 6:1 to 2:3) provided 2-benzyloxy-7-methoxycarbazole-3-carbaldehyde (**15**, 247 mg, 87% yield) as yellow crystals; m.p. 196–199 °C. UV (MeOH): λ = 240, 299, 346 nm. Fluorescence (MeOH): λ_{ex} = 299 nm, λ_{em} = 357, 519 nm. IR (ATR): $\tilde{\nu}$ = 3322, 2921, 2873, 2843, 1659, 1633, 1601, 1577, 1541, 1506, 1456, 1409, 1388, 1346, 1311, 1270, 1246, 1225, 1211, 1149, 1032, 1019, 976, 936, 903, 864, 843, 820, 792, 730, 694, 626 cm^{-1}. ^1H NMR (500 MHz, [D$_6$]acetone): δ = 3.86 (s, 3 H), 5.34 (s, 2 H), 6.85 (dd, J = 8.6, 2.3 Hz, 1 H), 7.03 (d, J = 2.3 Hz, 1 H), 7.22 (s, 1 H), 7.36 (t, J = 7.4 Hz, 1 H), 7.43 (m, 2 H), 7.58 (m, 2 H), 8.01 (d, J = 8.6 Hz, 1 H), 8.41 (s, 1 H), 10.53 (br. s, 1 H), 10.54 (s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D$_6$]acetone): δ = 55.79 (CH_3), 71.34 (CH_2), 95.33 (CH),

96.13 (CH), 109.55 (CH), 117.87 (C), 118.55 (C), 119.79 (C), 120.24 (CH), 121.58 (CH), 128.41 (2 CH), 128.83 (CH), 129.43 (2 CH), 137.92 (C), 142.95 (C), 146.44 (C), 160.09 (C), 160.71 (C), 188.65 (CHO) ppm. MS (ESI, +75 V): *m/z* = 332.2 $[M + H]^+$, 347.3 $[M + NH_4]^+$, 354.1 $[M + Na]^+$, 685.2 $[2M + Na]^+$. MS (ESI, –10 V): *m/z* = 329.9 $[M - H]^-$, 660.8 $[2M - H]^-$. MS (EI, 70 eV): *m/z* (%) = 331 (51) $[M]^+$, 240 (100), 91 (28). HRMS: calcd. for $C_{21}H_{17}NO_3$ $[M]^+$ 331.1208; found 331.1222. $C_{21}H_{17}NO_3$ (331.37): calcd. C 76.12, H 5.17, N 4.23; found C 75.81, H 5.45, N 4.27.

Crystal Data for 15: $C_{21}H_{17}NO_3$, crystal size: $0.35 \times 0.12 \times 0.08$ mm^3, M = 313.36 g mol^{-1}, triclinic, space group: $P\bar{1}$, a = 8.1299(5) Å, b = 8.3239(5) Å, c = 12.4639(7) Å, α = 103.061(3)°, β = 98.540(3)°, γ = 97.992(3)°, V = 799.39(8) Å^3, Z = 2, $\rho_{calcd.}$ = 1.377 g cm^{-3}, μ = 0.092 mm^{-1}, T = 150(2) K, λ = 0.71073 Å, θ range: 1.71–28.00°, 38008 reflections collected, 3830 independent reflections (R_{int} = 0.0640), 231 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 = 0.0382, wR_2 = 0.0926, maximal residual electron density: 0.247 e Å^{-3}. CCDC-988852) contains the supplementary crystallographic data for **15**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

7-Methoxymukonal (1):

Method A: A mixture of 2-benzyloxy-7-methoxycarbazole-3-carbaldehyde (**15**, 50.2 mg, 0.151 mmol), zinc bromide (512 mg, 2.27 mmol), and 2,6-dimethoxytoluene (70.2 mg, 0.461 mmol) in 1,2-dichloroethane (10 mL) was heated at 70 °C for 2 h and then at reflux for 28 h. After cooling to room temperature, the mixture was diluted with ethyl acetate, and the solution was washed with water and brine several times. The aqueous layers were extracted with ethyl acetate. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (pentane/ethyl acetate, gradient from 4:1 to 5:2) provided 7-methoxymukonal (**1**, 28.2 mg, 77% yield) as yellow crystals, m.p. 222 °C; ref.[2] m.p. 226–227 °C. UV (MeOH): λ = 223, 237, 300, 338 nm. Fluorescence (MeOH): λ_{ex} = 299 nm, λ_{em} = 361 nm. IR (ATR): $\tilde{\nu}$ = 3254, 3015, 2920, 2850, 1699, 1609, 1540, 1508, 1452, 1394, 1311, 1243, 1218, 1180, 1152, 1102, 1025, 944, 895, 842, 813, 762, 725, 701, 645 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 3.83 (s, 3 H), 6.79 (dd, J = 8.5, 2.3 Hz, 1 H), 6.85 (s, 1 H), 6.94 (d, J = 2.3 Hz, 1 H), 7.93 (d, J = 8.5 Hz, 1 H), 8.32 (s, 1 H), 10.12 (s, 1 H), 10.91 (br. s, 1 H), 11.42 (br. s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D$_6$]-DMSO): δ = 55.35 (CH$_3$), 95.37 (CH), 96.33 (CH), 108.34 (CH), 115.68 (C), 116.40 (C), 117.07 (C), 120.67 (CH), 123.09 (CH), 142.07 (C), 145.95 (C), 158.49 (C), 159.32 (C), 192.51 (CHO) ppm. GC–MS (70 eV): *m/z* (%) = 241 (100) $[M]^+$, 226 (63), 198 (30), 140 (9). MS (EI, 70 eV): *m/z* (%) = 241 (100) $[M]^+$, 226 (45), 198 (16). HRMS: calcd. for $C_{14}H_{11}NO_3$ $[M]^+$ 241.0739; found 241.0732.

Crystal Data for 1: $C_{14}H_{11}NO_3$, M = 241.24 g mol^{-1}, crystal size: $0.35 \times 0.03 \times 0.03$ mm^3, orthorhombic, space group: $Pna2_1$, a = 12.424(1) Å, b = 17.649(2) Å, c = 5.084(1) Å, V = 1114.8(3) Å^3, Z = 4, $\rho_{calcd.}$ = 1.437 g cm^{-3}, μ = 0.102 mm^{-1}, T = 150(2) K, λ = 0.71073 Å, θ range: 2.00–29.29°, 8197 reflections collected, 3010 independent reflections (R_{int} = 0.0771), 172 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 = 0.0417, wR_2 = 0.0557, maximal residual electron density: 0.186 e Å^{-3}. CCDC-988849 contains the supplementary crystallographic data for **1**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Method B: DDQ (65.0 mg, 0.286 mmol) was added to a solution of 7-methoxy-3-methyl-2-triisopropylsilyloxycarbazole (**16**, 50.6 mg, 0.132 mmol) in a mixture of methanol (10 mL), THF (5 mL), and water (1 mL), and the mixture was vigorously stirred at room temperature for 90 min. Ethyl acetate was added, and the mixture was washed with aqueous potassium hydroxide (2 M) and brine several times. The aqueous layers were extracted with ethyl acetate. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (pentane/ethyl acetate, 10:1) provided 7-methoxy-2-triisopropylsilyloxycarbazole-3-carbaldehyde (20.7 mg, 39% yield) as a yellow solid. ^{1}H NMR (500 MHz, [D$_6$]acetone): δ = 1.18 (d, J = 7.6 Hz, 18 H), 1.45 (sept, J = 7.6 Hz, 3 H), 3.86 (s, 3 H), 6.85 (dd, J = 8.5, 2.3 Hz, 1 H), 7.03 (d, J = 2.3 Hz, 1 H), 7.04 (s, 1 H), 8.00 (d, J = 8.5 Hz, 1 H), 8.38 (s, 1 H), 10.40 (br. s, 1 H), 10.56 (s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D$_6$]-acetone): δ = 13.75 (3 CH), 18.37 (6 CH$_3$), 55.81 (CH$_3$), 96.21 (CH), 101.02 (CH), 109.47 (CH), 117.85 (C), 119.35 (C), 120.13 (CH), 121.31 (C), 121.65 (CH), 143.25 (C), 146.45 (C), 158.13 (C), 160.21 (C), 189.01 (CHO) ppm. To a solution of 7-methoxy-2-(triisopropylsilyloxy)carbazole-3-carbaldehyde (71.8 mg, 0.181 mmol) in DMF (8 mL) was added TBAF (1 M in THF, 0.27 mL, 0.27 mmol) at –15 °C. The cooling bath was removed, and the mixture was stirred for 13 min and then diluted with ethyl acetate. The resulting mixture was washed with water, a saturated aqueous solution of ammonium chloride, and brine. The aqueous layers were extracted with ethyl acetate. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (pentane/ethyl acetate, gradient from 4:1 to 5:2) provided 7-methoxymukonal (**1**, 29.0 mg, 67% yield) as a yellow solid. For spectroscopic data of **1**, see above.

3-Methoxy-*N*-(3-methoxyphenyl)-4-methylaniline (18): A solution of *m*-bromoanisole (1.51 g, 8.07 mmol) in toluene (20 mL) was added over a period of 10 h to a refluxing mixture of 3-methoxy-4-methylaniline (**17**, 1.39 g, 10.1 mmol), cesium carbonate (3.18 g, 9.76 mmol), palladium acetate (110 mg, 0.490 mmol), and *rac*-BINAP (251 mg, 0.403 mmol) in toluene, and the mixture was heated at reflux for 14 h (total reaction time: 24 h). The suspension was cooled to room temperature and then filtered through Celite® (diethyl ether), and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (petroleum ether/acetone, 25:1) provided diarylamine **18** (1.67 g, 85% yield) as a red oil. UV (MeOH): λ = 283, 303 (sh) nm. IR (ATR): $\tilde{\nu}$ = 3386, 2998, 2936, 2835, 1593, 1508, 1491, 1461, 1391, 1318, 1268, 1209, 1151, 1126, 1035, 995, 966, 829, 806, 759, 741, 687, 855 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]acetone): δ = 2.10 (s, 3 H), 3.74 (s, 3 H), 3.77 (s, 3 H), 6.39 (m, 1 H), 6.64–6.68 (m, 3 H), 6.72 (d, J = 1.7 Hz, 1 H), 6.99 (d, J = 7.9 Hz, 1 H), 7.11 (t, J = 8.4 Hz, 1 H), 7.27 (br. s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D$_6$]acetone): δ = 15.70 (CH$_3$), 55.27 (CH$_3$), 55.47 (CH$_3$), 102.24 (CH), 102.84 (CH), 105.90 (CH), 109.90 (CH), 110.72 (CH), 119.07 (C), 130.69 (CH), 131.48 (CH), 143.38 (C), 146.63 (C), 159.20 (C), 161.73 (C) ppm. MS (EI, 70 eV): *m/z* (%) = 243 (100) $[M]^+$, 184 (45), 154 (16). HRMS: calcd. for $C_{15}H_{17}NO_2$ $[M]^+$ 243.1259; found 243.1254. $C_{15}H_{17}NO_2$ (243.30): calcd. C 74.05, H 7.04, N 5.76; found C 74.21, H 7.14, N 5.77.

2,7-Dimethoxy-3-methylcarbazole (19): A mixture of diarylamine **18** (294 mg, 1.21 mmol), palladium acetate (27.0 mg, 0.120 mmol), and cupric acetate (22.5 mg, 0.124 mmol) in acetic acid (7.5 mL)

was heated at 90 °C and vigorously stirred under air for 5 h. The mixture was cooled to room temperature and then filtered through Celite® (diethyl ether), and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (petroleum ether/ethyl acetate, 4:1) provided 2,7-dimethoxy-3-methylcarbazole (**19**, 195 mg, 67% yield) as a colorless solid; m.p. 243–244 °C. For spectroscopic data and the transformation into 7-methoxy-*O*-methylmukonal (**2**), see ref.[13b]

2-Chloro-6-methoxybenzonitrile (21): A mixture of 2-chloro-6-hydroxybenzonitrile (**20**, 2.00 g, 13.0 mmol) and potassium carbonate (9.23 g, 66.8 mmol) in DMF (30 mL) was heated at reflux. Methyl iodide (4.05 mL, 9.23 g, 65.1 mmol) was added dropwise at that temperature over a period of 13 h. The mixture was heated at reflux for an additional 4 h, and an additional portion of methyl iodide (0.81 mL, 1.85 g, 13.0 mmol) was added. The mixture was heated at reflux for an additional 2 h (total reaction time: 19 h). The reaction mixture was cooled to room temperature and then diluted with ethyl acetate, and the resulting solution was washed several times with water, dilute hydrochloric acid, and brine. The aqueous layers were extracted with ethyl acetate. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (pentane/dichloromethane, gradient from 3:1 to 3:2) provided 2-chloro-6-methoxybenzonitrile (**21**, 1.90 g, 87% yield) as colorless crystals; m.p. 114 °C. UV (MeOH): λ = 239, 246, 304 nm. IR (ATR): $\tilde{\nu}$ = 3106, 2992, 2956, 2847, 2232, 1591, 1572, 1470, 1450, 1434, 1286, 1212, 1190, 1156, 1074, 1031, 973, 890, 858, 785, 772, 725, 645 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.94 (s, 3 H), 6.88 (d, J = 8.4 Hz, 1 H), 7.06 (dd, J = 8.4, 0.6 Hz, 1 H), 7.45 (t, J = 8.4 Hz, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 56.62 (CH_3), 103.25 (C), 109.49 (CH), 113.73 (C), 121.82 (CH), 134.43 (CH), 138.14 (C), 162.72 (C) ppm. GC–MS (70 eV): m/z (%) = 167 (100) [M]$^+$, 139 (67), 138 (98), 124 (59), 100 (18), 88 (21),75 (22), 63 (23).

Crystal Data for 21: C_8H_6ClNO, crystal size: 0.20 × 0.09 × 0.04 mm^3, M = 167.59 g mol^{-1}, orthorhombic, space group: $P2_12_12_1$, a = 3.948(1) Å, b = 6.902(1) Å, c = 28.272(4) Å, V = 770.4(2) Å^3, Z = 4, $\rho_{calcd.}$ = 1.445 g cm^{-3}, μ = 0.429 mm^{-1}, T = 198(2) K, λ = 0.71073 Å, θ range: 3.04–25.39°, 17088 reflections collected, 1371 independent reflections (R_{int} = 0.0743), 101 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 = 0.0608, wR_2 = 0.1695, maximal residual electron density: 0.630 e Å^{-3}. CCDC-988853 contains the supplementary crystallographic data for **21**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

2-Methoxy-6-(3-methoxy-4-methylphenylamino)benzonitrile (22): A solution of 2-chloro-6-methoxybenzonitrile (**21**, 913 mg, 5.45 mmol) in toluene (10 mL) was added dropwise over a period of 5 h to a solution of 3-methoxy-4-methylaniline (**17**, 946 mg, 6.90 mmol), palladium acetate (77.6 mg, 0.346 mmol), SPhos (285 mg, 0.693 mmol), and cesium carbonate (3.21 g, 9.84 mmol) in degassed toluene (60 mL) at reflux. The mixture was then heated at reflux for an additional 14.5 h (total reaction time: 19.5 h). The reaction mixture was cooled to room temperature, and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (petroleum ether/dichloromethane/ethyl acetate, gradient from 60:5:1 to 45:5:1) provided diarylamine **22** (1.47 g, 100% yield) as a colorless solid; m.p. 160–163 °C. UV (MeOH): λ = 262, 284 (sh), 340 nm. IR (ATR): $\tilde{\nu}$ = 3315, 3081, 3020, 3002, 2957, 2928, 2851, 2214, 1593, 1577, 1504, 1473, 1450, 1435, 1397, 1375, 1303, 1267, 1203, 1193, 1181, 1158, 1128, 1087, 1033, 988, 973, 846, 815, 772, 730, 651 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]acetone): δ = 2.14 (s, 3 H), 3.80 (s, 3 H), 3.91 (s, 3 H), 6.53 (d, J = 8.4 Hz, 1 H), 6.77 (dd, J = 7.9, 1.7 Hz, 1 H), 6.80 (d, J = 8.4 Hz, 1 H), 6.87 (d, J = 1.7 Hz, 1 H), 7.08 (d, J = 7.9 Hz, 1 H), 7.32 (br. s, 1 H), 7.35 (t, J = 8.4 Hz, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D$_6$]acetone): δ = 15.83 (CH_3), 55.61 (CH_3), 56.49 (CH_3), 89.64 (C), 102.00 (CH), 105.58 (CH), 108.02 (CH), 114.18 (CH), 115.49 (C), 122.18 (C), 131.50 (CH), 135.34 (CH), 140.78 (C), 150.34 (C), 159.26 (C), 163.42 (C) ppm. GC–MS (70 eV): m/z (%) = 268 (100) [M]$^+$, 237 (7), 225 (16). $C_{16}H_{16}N_2O_2$ (268.31): calcd. C 71.62, H 6.01, N 10.44; found C 71.90, H 6.18, N 10.27.

2,7-Dimethoxy-6-methylcarbazole-1-carbonitrile (23): To a mixture of diarylamine **22** (135 mg, 0.503 mmol), potassium carbonate (17.4 mg, 0.126 mmol), and pivalic acid (442 mg) in a 10 mL test tube was added palladium acetate (25.5 mg, 0.114 mmol) at 120 °C, and the mixture was heated at 120 °C for 15.5 h and vigorously stirred under air. The mixture was cooled to room temperature and then diluted with ethyl acetate, and the solution was washed with a saturated solution of potassium carbonate and brine several times. The aqueous layers were extracted with ethyl acetate. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (petroleum ether/ethyl acetate, gradient from 9:1 to 2:3) provided 2,7-dimethoxy-6-methylcarbazole-1-carbonitrile (**23**, 116 mg, 87% yield) as a pale yellow solid; m.p. 280–282 °C. UV (MeOH): λ = 219, 240, 286, 347 nm. Fluorescence (MeOH): λ_{ex} = 286 nm, λ_{em} = 414 nm. IR (ATR): $\tilde{\nu}$ = 3281, 2988, 2965, 2939, 2841, 2223, 1613, 1588, 1507, 1478, 1447, 1395, 1354, 1308, 1281, 1241, 1196, 1168, 1144, 1087, 1064, 1014, 999, 956, 890, 820, 804, 766, 735, 661 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]-acetone): δ = 2.30 (s, 3 H), 3.91 (s, 3 H), 4.01 (s, 3 H), 6.96 (d, J = 8.7 Hz, 1 H), 7.11 (s, 1 H), 7.79 (s, 1 H), 8.16 (d, J = 8.7 Hz, 1 H), 10.65 (br. s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D$_6$]acetone): δ = 16.84 (CH_3), 55.81 (CH_3), 57.01 (CH_3), 83.73 (C), 94.08 (CH), 103.54 (CH), 115.48 (C), 116.37 (C), 119.17 (C), 120.45 (C), 121.74 (CH), 125.54 (CH), 141.15 (C), 142.69 (C), 158.24 (C), 160.46 (C) ppm. GC–MS (70 eV): m/z (%) = 266 (90) [M]$^+$, 251 (100), 236 (12), 208 (17), 179 (12). $C_{16}H_{14}N_2O_2$ (266.30): calcd. C 72.16, H 5.30, N 10.52; found C 71.74, H 5.44, N 10.24.

Murrayaline A (3): To a solution of carbonitrile **23** (121 mg, 0.454 mmol) in degassed dichloromethane (20 mL) was added diisobutylaluminium hydride (1 M in toluene, 1.13 mL, 1.13 mmol) slowly at –78 °C, and the mixture was stirred for 4 h and then gradually warmed from –55 to –25 °C. The excess amount of reagent was quenched by the addition of ethyl acetate (1 mL) at –25 °C. The mixture was warmed to room temperature and then diluted with ethyl acetate. The resulting solution was washed several times with water, dilute hydrochloric acid, and brine. The aqueous layers were extracted with ethyl acetate. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (petroleum ether/dichloromethane/ethyl acetate, gradient from 90:10:1 to 20:10:1) provided murrayaline A (**3**, 88.4 mg, 72% yield) as yellow crystals, m.p. 271–272 °C; ref.[15] m.p. 248–250 °C. UV (MeOH): λ = 223, 238 (sh), 255, 302, 380 nm. Fluorescence (MeOH): λ_{ex} = 302 nm, λ_{em} = 417 nm. IR (ATR): $\tilde{\nu}$ = 3370, 2979, 2942, 2848, 1647, 1632, 1591, 1576, 1508, 1477, 1451, 1389, 1357, 1317, 1263, 1233, 1187, 1166, 1138, 1076, 1018, 999, 960, 918, 882, 824, 808, 772, 737, 683, 635 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.35 (s, 3 H), 3.92 (s, 3 H), 4.00 (s, 3 H), 6.75 (d, J = 8.5 Hz, 1 H), 6.93 (s, 1 H), 7.69 (s, 1 H), 8.05 (d, J = 8.5 Hz, 1 H), 10.32 (br. s, 1 H), 10.61 (s, 1 H) ppm. ^{13}C NMR and DEPT (150 MHz,

$CDCl_3$): δ = 16.88 (CH_3), 55.75 (CH_3), 56.41 (CH_3), 93.34 (CH), 102.24 (CH), 108.76 (C), 114.99 (C), 118.68 (C), 120.32 (C), 121.02 (CH), 127.37 (CH), 139.84 (C), 139.98 (C), 157.23 (C), 160.87 (C), 191.14 (CHO) ppm. GC–MS (70 eV): *m/z* (%) = 269 (100) $[M]^+$, 254 (74), 226 (21), 211 (14), 183 (27), 154 (13). $C_{16}H_{15}NO_3$ (269.30): calcd. C 71.36, H 5.61, N 5.20; found C 71.14, H 5.69, N 5.38.

Crystal Data for 3: $C_{16}H_{15}NO_3$, M = 269.29 g mol^{-1}, crystal size: 0.22 × 0.15 × 0.10 mm^3, monoclinic, space group: $P2_1/c$, a = 10.962(1) Å, b = 15.532(1) Å, c = 7.776(2) Å, β = 90.94(1)°, V = 1323.8(4) Å^3, Z = 4, $\rho_{calcd.}$ = 1.351 g cm^{-3}, μ = 0.094 mm^{-1}, T = 198(2) K, λ = 0.71073 Å, θ range: 3.21–28.00°, 42436 reflections collected, 3182 independent reflections (R_{int} = 0.1095), 188 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 = 0.0464, wR_2 = 0.0941, maximal residual electron density: 0.241 e Å^{-3}. CCDC-988850 contains the supplementary crystallographic data for **3**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

2-Methoxy-6-[4-methyl-3-(triisopropylsilyloxy)phenylamino]benzonitrile (25): 4-Methyl-3-(triisopropylsilyloxy)aniline (**24**, 1.00 g, 3.58 mmol), palladium acetate (34.2 mg, 0.152 mmol), SPhos (127 mg, 0.309 mmol), and cesium carbonate (1.37 g, 4.20 mmol) were dissolved in degassed toluene (15 mL), and the mixture was heated at reflux. A solution of 2-chloro-6-methoxybenzonitrile (**21**, 502 mg, 3.00 mmol) in toluene (20 mL) was added dropwise over a period of 15 h, and the mixture was heated at reflux for 3 h (total reaction time: 18 h). The reaction mixture was cooled to room temperature, and the solvent was evaporated. The residue was purified by chromatography on a silica gel column (petroleum ether/dichloromethane/ethyl acetate, gradient from 60:5:1 to 45:5:1) to provide compound **25** (1.04 g, 85% yield) as colorless crystals; m.p. 142–143 °C. UV (MeOH): λ = 215, 259, 281 (sh), 340 nm. IR (ATR): $\tilde{\nu}$ = 3355, 2939, 2864, 2214, 1590, 1505, 1475, 1403, 1385, 1362, 1331, 1274, 1205, 1176, 1131, 1087, 1011, 995, 981, 948, 918, 880, 845, 815, 777, 723, 697, 678, 661, 615 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]acetone): δ = 1.12 (d, J = 7.5 Hz, 18 H), 1.32 (m, 3 H), 2.21 (s, 3 H), 3.91 (s, 3 H), 6.53 (d, J = 8.3 Hz, 1 H), 6.75–6.80 (m, 3 H), 7.11 (d, J = 7.8 Hz, 1 H), 7.35 (t, J = 8.4 Hz, 1 H), 7.43 (br. s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D$_6$]acetone): δ = 13.67 (3 CH), 16.69 (CH_3), 18.39 (6 CH_3), 56.49 (CH_3), 89.96 (C), 102.14 (CH), 108.18 (CH), 112.55 (CH), 115.21 (CH), 115.46 (C), 124.20 (C), 132.04 (CH), 135.18 (CH), 140.72 (C), 150.31 (C), 155.59 (C), 163.50 (C) ppm. GC–MS (70 eV): *m/z* (%) = 410 (49) $[M]^+$, 367 (100). $C_{24}H_{34}N_2O_2Si$ (410.63): calcd. C 70.20, H 8.35, N 6.82; found C 70.05, H 8.62, N 6.82.

Crystal Data for 25: $C_{24}H_{34}N_2O_2Si$, M = 410.62 g mol^{-1}, crystal size: 0.36 × 0.10 × 0.07 mm^3, monoclinic, space group: $C2/c$, a = 24.940(5) Å, b = 7.632(2) Å, c = 26.616(5) Å, β = 115.65(3)°, V = 4566.9(17) Å^3, Z = 8, $\rho_{calcd.}$ = 1.194 g cm^{-3}, μ = 0.125 mm^{-1}, T = 198(2) K, λ = 0.71073 Å, θ range: 3.08–27.00°, 65253 reflections collected, 4990 independent reflections (R_{int} = 0.0890), 274 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 = 0.0422, wR_2 = 0.0948, maximal residual electron density: 0.258 e Å^{-3}. CCDC-988854 contains the supplementary crystallographic data for **25**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

2-Methoxy-6-methyl-7-(triisopropylsilyloxy)carbazole-1-carbonitrile (26): Diarylamine **25** (205 mg, 0.499 mmol), potassium carbonate (18.0 mg, 0.130 mmol), cupric acetate (19.4 mg, 0.107 mmol), and pivalic acid (470 mg) were placed in a 10 mL test tube, and the mixture was heated at 100 °C. Palladium acetate (24.2 mg, 0.108 mmol) was added, and the mixture was vigorously stirred at that temperature for 18.5 h under air. The mixture was cooled to room temperature and then diluted with ethyl acetate, and the resulting solution was washed with a saturated solution of potassium carbonate and brine several times. The aqueous layers were extracted with ethyl acetate. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (pentane/dichloromethane/ethyl acetate, gradient from 60:5:1 to 45:5:1) provided carbazolecarbonitrile **26** (177 mg, 87% yield) as pale yellow crystals; m.p. 211 °C. UV (MeOH): λ = 221, 240 (sh), 286, 326 (sh), 349 nm. Fluorescence (MeOH): λ_{ex} = 286 nm, λ_{em} = 403 nm. IR (ATR): $\tilde{\nu}$ = 3294, 3018, 2941, 2864, 2219, 1614, 1505, 1473, 1396, 1351, 1312, 1282, 1253, 1236, 1169, 1142, 1096, 1055, 996, 910, 883, 848, 789, 766, 733, 715, 672, 656 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.15 (d, J = 7.5 Hz, 18 H), 1.37 (m, 3 H), 2.38 (s, 3 H), 3.99 (s, 3 H), 6.75 (d, J = 8.6 Hz, 1 H), 6.90 (s, 1 H), 7.68 (s, 1 H), 7.96 (d, J = 8.6 Hz, 1 H), 8.41 (br. s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 13.19 (3 CH), 17.71 (CH_3), 18.22 (6 CH_3), 56.67 (CH_3), 83.15 (C), 100.40 (CH), 102.70 (CH), 115.53 (C), 116.46 (C), 118.35 (C), 121.20 (CH), 122.66 (C), 124.72 (CH), 139.15 (C), 142.18 (C), 153.76 (C), 159.62 (C) ppm. GC–MS (70 eV): *m/z* (%) = 408 (100) $[M]^+$, 365 (72), 337 (30), 263 (26), 154 (25). $C_{24}H_{32}N_2O_2Si$ (408.62): calcd. C 70.55, H 7.89, N 6.86; found C 70.18, H 7.99, N 6.80.

Crystal Data for 26: $C_{24}H_{32}N_2O_2Si$, crystal size: 0.38 × 0.22 × 0.20 mm^3, M = 408.61 g mol^{-1}, triclinic, space group: $P\bar{1}$, a = 8.1619(4) Å, b = 8.5757(4) Å, c = 18.5198(9) Å, α = 81.623(2)°, β = 82.958(3)°, γ = 64.754(2)°, V = 1157.30(10) Å^3, Z = 2, $\rho_{calcd.}$ = 1.173 g cm^{-3}, μ = 0.123 mm^{-1}, T = 150(2) K, λ = 0.71073 Å, θ range: 1.11–26.00°, 28247 reflections collected, 4480 independent reflections (R_{int} = 0.0334), 274 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 = 0.0360, wR_2 = 0.0885, maximal residual electron density: 0.425 e Å^{-3}. CCDC-988855 contains the supplementary crystallographic data for **26**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Murrayaline B (4): To a solution of carbazolecarbonitrile **26** (100 mg, 0.245 mmol) in dry, degassed dichloromethane (12 mL) was slowly added diisobutylaluminium hydride (1 M in hexane, 0.734 mL, 0.734 mmol) at –78 °C. The reaction mixture was stirred at –40 to –30 °C for 4 h and then quenched with ethyl acetate (1 mL) at that temperature. The mixture was washed with water, dilute hydrochloric acid, and brine. The aqueous layers were extracted with ethyl acetate. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. The crude product was dried under high vacuum to provide 2-methoxy-6-methyl-7-(triisopropylsilyloxy)carbazole-1-carbaldehyde as yellow crystals; m.p. 211 °C. UV (MeOH): λ = 225, 257, 303, 382 nm. IR (ATR): $\tilde{\nu}$ = 3386, 2961, 2942, 2865, 1647, 1631, 1606, 1575, 1509, 1472, 1392, 1355, 1319, 1256, 1232, 1179, 1138, 1083, 1069, 996, 937, 883, 852, 807, 768, 739, 716, 677, 636 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]acetone): δ = 1.16 (d, J = 7.5 Hz, 18 H), 1.43 (sept, J = 7.5 Hz, 3 H), 2.38 (s, 3 H), 4.02 (s, 3 H), 6.91 (d, J = 8.5 Hz, 1 H), 7.35 (s, 1 H), 7.79 (s, 1 H), 8.19 (d, J = 8.5 Hz, 1 H), 10.58 (s, 1 H), 10.99 (br. s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D$_6$]acetone): δ = 13.76 (3 CH), 17.79 (CH_3), 18.49 (6 CH_3), 56.82 (CH_3), 102.08 (CH), 103.10 (CH), 109.46 (C), 116.73 (C), 119.45 (C), 121.57 (CH), 122.24 (C), 128.04 (CH), 140.34 (C), 141.36 (C),

153.90 (C), 161.76 (C), 190.17 (CHO) ppm. GC–MS (70 eV): *m*/*z* (%) = 411 (100) $[M]^+$, 368 (55), 340 (22), 266 (15), 156 (18). $C_{24}H_{33}NO_3Si$ (411.62): calcd. C 70.03, H 8.08, N 3.40; found C 70.14, H 8.21, N 3.50. The crude 2-methoxy-6-methyl-7-(triisopropylsilyloxy)carbazole-1-carbaldehyde was dissolved in degassed DMF (10 mL), and TBAF (1 M in THF, 0.37 mL, 0.37 mmol) was added at –15 °C. The reaction was warmed to room temperature and then stirred for 10 min. Water (10 mL) was added, and the mixture was diluted with diethyl ether. The resulting solution was washed with water and brine, and the aqueous layers were extracted with diethyl ether. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. Purification of the residue by column chromatography (pentane/ethyl acetate, gradient from 6:1 to 3:1) provided murrayaline B (**4**, 55.6 mg, 89% yield) as yellow crystals, m.p. 248–250 °C; ref.[17] m.p. 240–242 °C. UV (MeOH): λ = 223, 259, 272 (sh), 303, 383 nm. Fluorescence (MeOH): λ_{ex} = 303 nm, λ_{em} = 354, 418 nm. IR (ATR): $\tilde{\nu}$ = 3448, 3360, 2969, 2916, 2848, 1648, 1626, 1580, 1506, 1485, 1454, 1385, 1350, 1319, 1234, 1216, 1167, 1140, 1110, 1081, 1061, 982, 923, 882, 803, 766, 729, 682, 622 cm^{-1}. ^1H NMR (500 MHz, [D$_6$]acetone): δ = 2.33 (s, 3 H), 4.01 (s, 3 H), 6.88 (d, J = 8.5 Hz, 1 H), 7.20 (s, 1 H), 7.73 (s, 1 H), 8.15 (d, J = 8.5 Hz, 1 H), 8.38 (s, 1 H), 10.57 (s, 1 H), 10.80 (br. s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D$_6$]-acetone): δ = 16.73 (CH_3), 56.80 (CH_3), 98.38 (CH), 102.94 (CH), 109.43 (C), 115.73 (C), 118.93 (C), 119.72 (C), 121.63 (CH), 127.66 (CH), 140.19 (C), 141.50 (C), 155.35 (C), 161.49 (C), 190.22 (CHO) ppm. GC–MS (70 eV): *m*/*z* (%) = 255 (100) $[M]^+$, 240 (38), 212 (22), 184 (34). $C_{15}H_{13}NO_3$ (255.27): calcd. C 70.58, H 5.13, N 5.49; found C 70.31, H 5.17, N 5.54.

Crystal Data for 2-Methoxy-6-methyl-7-(triisopropylsilyloxy)-carbazole-1-carbaldehyde: $C_{24}H_{33}NO_3Si$, crystal size: 0.74 × 0.23 × 0.21 mm^3, M = 411.60 $g\,mol^{-1}$, triclinic, space group: $P\bar{1}$, a = 7.928(1) Å, b = 15.421(1) Å, c = 19.187(3) Å, α = 86.95(1)°, β = 81.90(1)°, γ = 86.56(1)°, V = 2315.8(5) $Å^3$, Z = 4, $\rho_{calcd.}$ = 1.181 $g\,cm^{-3}$, μ = 0.125 mm^{-1}, T = 198(2) K, λ = 0.71073 Å, θ range: 3.13–27.00°, 87761 reflections collected, 9931 independent reflections (R_{int} = 0.0805), 529 parameters. The structure was solved by direct methods and refined by full-matrix least-squares on F^2, final R indices [$I > 2\sigma(I)$]: R_1 = 0.0490, wR_2 = 0.1008, maximal residual electron density: 0.305 e $Å^{-3}$. CCDC-988856 contains the supplementary crystallographic data for 2-methoxy-6-methyl-7-(triisopropylsilyloxy)carbazole-1-carbaldehyde. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Crystal Data for 4·Me$_2$CO: $C_{18}H_{19}NO_4$, M = 313.34 $g\,mol^{-1}$, crystal size: 0.41 × 0.27 × 0.21 mm^3, triclinic, space group: $P\bar{1}$, a = 7.853(1) Å, b = 10.277(2) Å, c = 11.504(1) Å, α = 65.21(1)°, β = 79.16(1)°, γ = 69.55(1)°, V = 788.8(2) $Å^3$, Z = 2, $\rho_{calcd.}$ = 1.319 $g\,cm^{-3}$, μ = 0.093 mm^{-1}, T = 198(2) K, λ = 0.71073 Å, θ range: 3.01–25.40°, 22791 reflections collected, 2907 independent reflections (R_{int} = 0.0489), 221 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 = 0.0420, wR_2 = 0.0930, maximal residual electron density: 0.167 e $Å^{-3}$. CCDC-988851 contains the supplementary crystallographic data for **4**·Me$_2$CO. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

2-[3-(Benzyloxy)-4-methylphenylamino]-6-methoxybenzonitrile (27): A suspension of 3-benzyloxy-4-methylaniline (**11**, 1.70 g, 7.97 mmol), 2-chloro-6-methoxybenzonitrile (**21**, 1.07 g, 6.38 mmol), palladium acetate (71.3 mg, 0.318 mmol), SPhos (265 mg, 0.646 mmol), and cesium carbonate (2.91 g, 8.93 mmol) in toluene (20 mL) was stirred and heated at reflux for 20.5 h. The mixture was cooled to room temperature and then diluted with ethyl acetate. The resulting solution was washed several times with water, a saturated aqueous solution of ammonium chloride (containing a small portion of dilute hydrochloric acid), a saturated aqueous solution of potassium carbonate, and brine. The aqueous layers were extracted with ethyl acetate. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (pentane/dichloromethane/ethyl acetate, gradient from 34:5:1 to 24:5:1) provided diarylamine **27** (2.12 g, 96% yield) as a colorless solid. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.28 (s, 3 H), 3.90 (s, 3 H), 5.07 (s, 2 H), 6.28 (br. s, 1 H), 6.30 (d, J = 8.2 Hz, 1 H), 6.54 (d, J = 8.5 Hz, 1 H), 6.70 (d, J = 2.1 Hz, 1 H), 6.71 (br. s, 1 H), 7.13 (d, J = 8.6 Hz, 1 H), 7.18 (t, J = 8.4 Hz, 1 H), 7.35 (m, 1 H), 7.38–7.44 (m, 4 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 16.12 (CH_3), 56.14 (CH_3), 69.92 (CH_2), 87.84 (C), 100.50 (CH), 106.00 (CH), 106.97 (CH), 114.89 (CH), 115.72 (C), 123.67 (C), 127.16 (2 CH), 127.96 (CH), 128.72 (2 CH), 131.31 (CH),134.60 (CH), 137.17 (C), 138.41 (C), 149.33 (C), 157.41 (C), 162.50 (C) ppm.

7-Benzyloxy-2-methoxy-6-methylcarbazole-1-carbonitrile (28): To a mixture of diarylamine **27** (1.00 g, 2.90 mmol), potassium carbonate (75.5 mg, 0.546 mmol), and pivalic acid (5.0 g) in a 25 mL test tube was added palladium acetate (32.6 mg, 0.145 mmol) at 110 °C, and the mixture was vigorously stirred at 110 °C under air. Additional palladium acetate was added after 9 h (33.4 mg, 0.149 mmol), after 24 h (32.4 mg, 0.144 mmol), and after 32 h (32.7 mg, 0.146 mmol). After a total reaction time of 48 h, the mixture was cooled to room temperature and then diluted with ethyl acetate. The resulting solution was washed several times with water, a saturated aqueous solution of potassium carbonate, and brine. The aqueous layers were extracted with ethyl acetate. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (pentane/ethyl acetate/ethanol, gradient from 100:1:1 to 66:16:1) provided carbazolecarbonitrile **28** (975 mg, 98% yield) as a brown solid. ^1H NMR (500 MHz, [D$_6$]acetone): δ = 2.38 (s, 3 H), 4.01 (s, 3 H), 5.23 (s, 2 H), 6.96 (d, J = 8.7 Hz, 1 H), 7.20 (s, 1 H), 7.34 (t, J = 7.5 Hz, 1 H), 7.42 (t, J = 7.5 Hz, 2 H), 7.55 (d, J = 7.5 Hz, 2 H), 7.83 (s, 1 H), 8.18 (d, J = 8.7 Hz, 1 H), 10.68 (br. s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D$_6$]acetone): δ = 17.04 (CH_3), 57.02 (CH_3), 70.65 (CH_2), 95.63 (CH), 103.58 (CH), 115.45 (C), 116.70 (C), 119.10 (C), 120.83 (C), 121.85 (CH), 125.63 (CH), 128.18 (2 CH), 128.57 (CH), 129.33 (2 CH), 136.32 (C), 138.58 (C), 140.88 (C), 142.63 (C), 157.19 (C), 160.54 (C) ppm. MS (ESI, +10 V): *m*/*z* = 343.1 $[M + H]^+$. MS (ESI, –10 V): *m*/*z* = 340.9 $[M - H]^-$.

7-Benzyloxy-2-methoxy-6-methylcarbazole-1-carbaldehyde (29): To a solution of carbonitrile **28** (174 mg, 0.508 mmol) in degassed dichloromethane (20 mL) was added diisobutylaluminium hydride (1 M in hexane, 1.78 mL, 1.78 mmol) slowly at –78 °C, and the mixture was stirred for 4 h and then gradually warmed from –40 to –30 °C. The excess amount of reagent was quenched by the addition of ethyl acetate (2 mL) at –30 °C. The mixture was warmed to room temperature and then diluted with ethyl acetate, and the resulting solution was washed several times with water, a saturated solution of aqueous ammonium chloride, dilute hydrochloric acid, and brine. The aqueous layers were extracted with ethyl acetate. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (petroleum ether/dichloromethane/ethyl acetate, gradient from 500:4:1 to 15:4:1) provided carbaldehyde **29** (98.2 mg, 56% yield) as a colorless solid. ^1H NMR

(500 MHz, [D$_6$]acetone): δ = 2.38 (s, 3 H), 4.03 (s, 3 H), 5.22 (s, 2 H), 6.93 (d, J = 8.5 Hz, 1 H), 7.33 (t, J = 7.5 Hz, 1 H), 7.40 (s, 1 H), 7.42 (m, 2 H), 7.55 (d, J = 7.5 Hz, 2 H), 7.81 (s, 1 H), 8.21 (d, J = 8.5 Hz, 1 H), 10.59 (s, 1 H), 10.94 (br. s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D$_6$]acetone): δ = 17.08 (CH$_3$), 56.86 (CH$_3$), 70.59 (CH$_2$), 96.22 (CH), 103.29 (CH), 109.49 (C), 115.99 (C), 119.36 (C), 120.65 (C), 121.57 (CH), 128.06 (CH), 128.23 (2 CH), 128.54 (CH), 129.30 (2 CH), 138.64 (C), 140.12 (C), 141.31 (C), 156.87 (C), 161.72 (C), 190.25 (CHO) ppm. MS (ESI, +25 V): m/z = 346.2 [M + H]$^+$.

3-(Triisopropylsilyloxy)aniline (30): Chlorotriisopropylsilane (4.59 g, 23.8 mmol) was added to a solution of 3-aminophenol (2.01 g, 18.4 mmol) and imidazole (2.49 g, 36.6 mmol) in THF (18 mL), and the reaction mixture was stirred at room temperature for 20 h. The mixture was diluted with diethyl ether, and the solution was washed with water and brine several times. The aqueous layers were extracted with diethyl ether. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (pentane/dichloromethane/ethyl acetate, gradient from 80:5:1 to 35:5:1) provided 3-(triisopropylsilyloxy)aniline (**30**, 4.72 g, 97% yield) as a light red oil. ^{1}H NMR (500 MHz, CDCl$_3$): δ = 1.10 (d, J = 7.4 Hz, 18 H), 1.25 (m, 3 H), 3.75 (br. s, 2 H), 6.26 (t, J = 2.1 Hz, 1 H), 6.30 (dt, J = 2.1, 7.9 Hz, 2 H), 6.98 (t, J = 7.9 Hz, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, CDCl$_3$): δ = 12.81 (3 CH), 18.08 (6 CH$_3$), 107.27 (CH), 108.50 (CH), 110.68 (CH), 130.00 (CH), 147.43 (C), 157.21 (C) ppm. GC–MS (70 eV): m/z (%) = 265 (63) [M]$^+$, 222 (100), 194 (50), 166 (60), 152 (47).

2-Methoxy-6-[3-(triisopropylsilyloxy)phenylamino]benzonitrile (31): A mixture of 3-(triisopropylsilyloxy)aniline (**30**, 1.01 g, 3.80 mmol), 2-chloro-6-methoxybenzonitrile (**21**, 508 mg, 3.03 mmol), palladium acetate (34.4 mg, 0.153 mmol), SPhos (124 mg, 0.302 mmol), and cesium carbonate (1.38 g, 4.24 mmol) in degassed toluene (14 mL) was heated at reflux for 23 h. The mixture was cooled to room temperature and then diluted with diethyl ether. The resulting mixture was filtered through Celite® (ethyl acetate), and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (pentane/dichloromethane/ethyl acetate, gradient from 140:5:1 to 70:5:1) provided diarylamine **31** (1.21 g, 100% yield) as a colorless solid; m.p. 94 °C. UV (MeOH): λ = 214, 258, 281, 338 nm. IR (ATR): $\tilde{\nu}$ = 3325, 2944, 2865, 2216, 1593, 1578, 1508, 1492, 1470, 1439, 1398, 1293, 1265, 1181, 1159, 1089, 988, 942, 880, 830, 769, 720, 683, 612 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]-acetone): δ = 1.11 (d, J = 7.4 Hz, 18 H), 1.29 (sept, J = 7.4 Hz, 3 H), 3.92 (s, 3 H), 6.59 (d, J = 8.4 Hz, 1 H), 6.63 (m, 1 H), 6.85–6.89 (m, 3 H), 7.21 (t, J = 8.1 Hz, 1 H), 7.40 (dt, J = 8.4, 0.8 Hz, 1 H), 7.51 (br. s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D$_6$]-acetone): δ = 13.34 (3 CH), 18.25 (6 CH$_3$), 56.54 (CH$_3$), 90.89 (C), 102.86 (CH), 108.96 (CH), 113.16 (CH), 114.63 (CH), 115.33 (C), 115.47 (CH), 130.87 (CH), 135.25 (CH), 143.52 (C), 149.62 (C), 157.81 (C), 163.51 (C) ppm. GC–MS (70 eV): m/z (%) = 396 (28) [M]$^+$, 353 (100), 281 (8), 267 (10), 253 (10), 223 (18), 126 (13). C$_{23}$H$_{32}$N$_2$O$_2$Si (396.60): calcd. C 69.95, H 8.13, N 7.06; found C 69.97, H 8.44, N 7.12.

2-Methoxy-7-(triisopropylsilyloxy)carbazole-1-carbonitrile (32): To a mixture of diarylamine **31** (319 mg, 0.804 mmol), cesium carbonate (26 mg, 80 µmol), and pivalic acid (510 mg) in a 10 mL test tube was added palladium acetate (5.8 mg, 26 µmol) at 110 °C, and the mixture was vigorously stirred at 110 °C under air. Additional palladium acetate was added after 14 h (3.4 mg, 15 µmol), after 25 h (3.6 mg, 16 µmol), and after 39 h (3.6 mg, 16 µmol). After a total reaction time of 50 h, the mixture was cooled to room temperature and then diluted with ethyl acetate. The resulting solution was washed with a saturated aqueous solution of potassium carbonate and brine several times. The aqueous layers were extracted with ethyl acetate. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (pentane/dichloromethane/ethyl acetate, gradient from 60:5:1 to 40:5:1) provided carbazole-1-carbonitrile **32** (241 mg, 76% yield) as a pale yellow solid; m.p. 197 °C. UV (MeOH): λ = 221, 234 (sh), 282, 321 (sh), 348 nm. Fluorescence (MeOH): λ_{ex} = 282 nm, λ_{em} = 386 nm. IR (ATR): $\tilde{\nu}$ = 3338, 2943, 2889, 2866, 2218, 1612, 1586, 1542, 1507, 1456, 1441, 1391, 1366, 1309, 1285, 1264, 1243, 1219, 1160, 1119, 1091, 1071, 1013, 994, 970, 952, 898, 881, 849, 837, 801, 774, 722, 683, 653, 606 cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): δ = 1.13 (d, J = 7.4 Hz, 18 H), 1.31 (sept, J = 7.4 Hz, 3 H), 4.00 (s, 3 H), 6.78 (d, J = 8.7 Hz, 1 H), 6.84 (dd, J = 8.4, 2.1 Hz, 1 H), 6.96 (d, J = 2.1 Hz, 1 H), 7.77 (d, J = 8.4 Hz, 1 H), 8.00 (d, J = 8.7 Hz, 1 H), 8.39 (br. s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, CDCl$_3$): δ = 12.84 (3 CH), 18.10 (6 CH$_3$), 56.73 (CH$_3$), 83.34 (C), 102.16 (CH), 102.98 (CH), 114.38 (CH), 115.36 (C), 117.07 (C), 118.33 (C), 120.39 (CH), 124.95 (CH), 140.90 (C), 142.33 (C), 155.42 (C), 159.87 (C) ppm. GC–MS (70 eV): m/z (%) = 394 (100) [M]$^+$, 351 (90), 323 (45), 295 (58), 281 (42), 249 (35), 147 (48). C$_{23}$H$_{30}$N$_2$O$_2$Si (394.59): calcd. C 70.01, H 7.66, N 7.10; found C 69.82, H 7.68, N 6.88.

7-Hydroxy-2-methoxycarbazole-1-carbaldehyde (33): To a solution of carbazolecarbonitrile **32** (119 mg, 0.302 mmol) in dichloromethane (11 mL) was added diisobutylaluminium hydride (1 M in hexane, 0.907 mL, 0.907 mmol) slowly at –78 °C. The reaction mixture was stirred at –40 to –30 °C for 4 h and then quenched at –30 °C by the addition of ethyl acetate (1 mL). The mixture was warmed to room temperature and then diluted with ethyl acetate. The resulting solution was washed several times with water, a saturated aqueous solution of ammonium chloride (containing a small portion of dilute hydrochloric acid), and brine. The aqueous layers were extracted with ethyl acetate. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. The crude product was dried under high vacuum to provide 2-methoxy-7-(triisopropylsilyloxy)carbazole-1-carbaldehyde (133 mg) as a yellow solid of sufficient purity, m.p. 204–206 °C. UV (MeOH): λ = 225, 237 (sh), 256 (sh), 280, 378 nm. Fluorescence (MeOH): λ_{ex} = 225 nm, λ_{em} = 345 nm. IR (ATR): $\tilde{\nu}$ = 3387, 2941, 2889, 2864, 1649, 1607, 1575, 1542, 1498, 1453, 1394, 1357, 1320, 1236, 1183, 1145, 1119, 1084, 1015, 994, 957, 932, 880, 858, 844, 804, 782, 743, 722, 673, 629, 606 cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): δ = 1.13 (d, J = 7.4 Hz, 18 H), 1.31 (sept, J = 7.4 Hz, 3 H), 4.00 (s, 3 H), 6.75 (d, J = 8.5 Hz, 1 H), 6.83 (dd, J = 8.4, 2.1 Hz, 1 H), 6.97 (d, J = 2.1 Hz, 1 H), 7.77 (d, J = 8.4 Hz, 1 H), 8.06 (d, J = 8.5 Hz, 1 H), 10.30 (br. s, 1 H), 10.61 (s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, CDCl$_3$): δ = 12.85 (3 CH), 18.11 (6 CH$_3$), 56.40 (CH$_3$), 102.30 (CH), 102.35 (CH), 108.73 (C), 114.17 (CH), 116.35 (C), 118.67 (C), 120.15 (CH), 127.53 (CH), 140.46 (C), 141.48 (C), 155.04 (C), 161.04 (C), 191.10 (CHO) ppm. GC–MS (70 eV): m/z (%) = 397 (100) [M]$^+$, 354 (64), 326 (34), 298 (25), 284 (21), 252 (14), 224 (21), 149 (22). C$_{23}$H$_{31}$NO$_3$Si (397.59): calcd. C 69.48, H 7.86, N 3.52; found C 69.34, H 7.98, N 3.62. To a solution of the carbazolecarbaldehyde in DMF (10 mL) was added TBAF (1 M in THF, 0.454 mL, 0.454 mmol) at –10 °C, and the cooling bath was removed. The mixture was stirred for 10 min, and water (10 mL) was added. The mixture was diluted with diethyl ether, and the resulting solution was washed with water and brine several times. The aqueous layers were extracted with diethyl ether. The combined organic layers were dried with sodium sulfate, and the solvent

was evaporated. Purification of the residue by chromatography on a silica gel column (pentane/ethyl acetate, gradient from 3:1 to 2:1) provided 7-hydroxy-2-methoxycarbazole-1-carbaldehyde (**33**, 53.4 mg, 73% yield) as yellow crystals; m.p. 265–267 °C. UV (MeOH): λ = 223, 237 (sh), 255, 298, 378 nm. Fluorescence (MeOH): λ_{ex} = 298 nm, λ_{em} = 350, 405 nm. IR (ATR): $\tilde{\nu}$ = 3443, 3318, 3023, 2921, 2850, 1639, 1616, 1581, 1525, 1498, 1451, 1387, 1345, 1310, 1205, 1184, 1170, 1145, 1125, 1079, 948, 922, 821, 805, 767, 733, 680, 631 cm^{-1}. ^1H NMR (500 MHz, [D$_6$]acetone): δ = 4.02 (s, 3 H), 6.78 (dd, J = 8.4, 2.2 Hz, 1 H), 6.91 (d, J = 8.5 Hz, 1 H), 7.20 (d, J = 2.2 Hz, 1 H), 7.84 (d, J = 8.4 Hz, 1 H), 8.18 (d, J = 8.5 Hz, 1 H), 8.45 (s, 1 H), 10.58 (s, 1 H), 10.90 (br. s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D$_6$]acetone): δ = 56.83 (CH_3), 98.86 (CH), 103.21 (CH), 109.49 (C), 110.42 (CH), 115.96 (C), 119.69 (C), 120.98 (CH), 127.78 (CH), 140.38 (C), 143.31 (C), 157.29 (C), 161.61 (C), 190.26 (CHO) ppm. GC–MS (70 eV): m/z (%) = 241 (100) $[M]^+$, 226 (42), 198 (17), 170 (39). $C_{14}H_{11}NO_3$ (241.25): calcd. C 69.70, H 4.60, N 5.81; found C 69.93, H 4.42, N 5.15.

Crystal Data for 33: $C_{14}H_{11}NO_3$, M = 241.24 g mol^{-1}, crystal size: 0.57 × 0.21 × 0.16 mm^3, monoclinic, space group: $P2_1/c$, a = 10.859(1) Å, b = 14.173(2) Å, c = 7.067(1) Å, β = 94.762(9)°, V = 1083.9(2) $Å^3$, Z = 4, $\rho_{calcd.}$ = 1.478 g cm^{-3}, μ = 0.105 mm^{-1}, T = 198(2) K, λ = 0.71073 Å, θ range: 3.23–25.40°, 19319 reflections collected, 1993 independent reflections (R_{int} = 0.0714), 168 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 = 0.0453, wR_2 = 0.1013, maximal residual electron density: 0.216 e $Å^{-3}$. CCDC-988857 contains the supplementary crystallographic data for **33**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Methyl 4-Amino-2-(triisopropylsilyloxy)benzoate: To a degassed solution of methyl 4-amino-2-hydroxybenzoate (**34**, 2.00 g, 12.0 mmol) and imidazole (3.27 g, 48.0 mmol) in DMF (50 mL) was added chlorotriisopropylsilane (4.70 mL, 4.23 g, 21.9 mmol) at 50 °C, and the mixture was stirred at 50 °C for 3 d. A second batch of chlorotriisopropylsilane (3.00 mL, 2.70 g, 14.0 mmol) was added, and the mixture was stirred for 1 d (total reaction time 4 d). The mixture was cooled to room temperature and then diluted with diethyl ether. The resulting solution was washed several times with water, dilute hydrochloric acid, and brine. The aqueous layers were extracted with diethyl ether. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (pentane/dichloromethane/ethyl acetate, gradient from 45:5:1 to 35:5:1) provided methyl 4-amino-2-(triisopropylsilyloxy)benzoate (2.50 g, 65% yield) as a slightly red oil. UV (MeOH): λ = 212 (sh), 233, 280, 300 (sh) nm. Fluorescence (MeOH): λ_{ex} = 280 nm, λ_{em} = 335 nm. IR (ATR): $\tilde{\nu}$ = 3473, 3368, 3230, 2945, 2866, 1699, 1677, 1653, 1599, 1565, 1506, 1453, 1397, 1345, 1319, 1278, 1247, 1209, 1139, 1083, 992, 963, 920, 881, 839, 772, 681, 642, 612 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.11 (d, J = 7.4 Hz, 18 H), 1.30 (m, 3 H), 3.80 (s, 3 H), 4.40 (br. s, 2 H), 6.15 (d, J = 2.2 Hz, 1 H), 6.28 (dd, J = 8.5, 2.2 Hz, 1 H), 7.69 (d, J = 8.5 Hz, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 13.33 (3 CH), 18.10 (6 CH_3), 51.46 (CH_3), 106.27 (CH), 107.99 (CH), 112.58 (C), 134.14 (CH), 150.73 (C), 158.06 (C), 167.16 (C=O) ppm. GC-MS (70 eV): m/z (%) = 280 (100) $[M – C_3H_7]^+$, 194 (8). $C_{17}H_{29}NO_3Si$ (323.51): calcd. C 63.12, H 9.04, N 4.33; found C 63.06, H 9.27, N 4.60.

Methyl 4-[(2-Cyano-3-methoxyphenyl)amino]-2-(triisopropylsilyloxy)benzoate (35): A suspension of methyl 4-amino-2-(triisopropylsilyloxy)benzoate (555 mg, 1.72 mmol), 2-chloro-6-methoxybenzonitrile (**21**, 344 mg, 2.05 mmol), palladium acetate (19.0 mg, 84.6 µmol), SPhos (72.0 mg, 0.175 mmol), and cesium carbonate (779 mg, 2.39 mmol) in toluene (12 mL) was stirred and heated at reflux for 18 h. The reaction mixture was cooled to room temperature and then filtered through Celite® (ethyl acetate), and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (pentane/dichloromethane/ethyl acetate, gradient from 35:5:1 to 25:5:1) provided diarylamine **35** (660 mg, 85% yield) as a pale yellow solid; m.p. 131–132 °C. UV (MeOH): λ = 231 (sh), 272, 299, 326 (sh), 341 nm. IR (ATR): $\tilde{\nu}$ = 3299, 3183, 3091, 3025, 2943, 2864, 2221, 1771, 1724, 1699, 1684, 1651, 1612, 1579, 1518, 1475, 1455, 1401, 1335, 1312, 1260, 1235, 1207, 1148, 1075, 1008, 969, 946, 921, 882, 847, 829, 814, 774, 708, 686, 663, 610 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.11 (d, J = 7.4 Hz, 18 H), 1.29 (m, 3 H), 3.85 (s, 3 H), 3.93 (s, 3 H), 6.37 (br. s, 1 H), 6.46 (d, J = 8.4 Hz, 1 H), 6.62 (d, J = 2.1 Hz, 1 H), 6.72 (dd, J = 8.5, 2.1 Hz, 1 H), 6.91 (d, J = 8.4 Hz, 1 H), 7.33 (t, J = 8.4 Hz, 1 H), 7.79 (d, J = 8.5 Hz, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 13.25 (3 CH), 18.05 (6 CH_3), 51.80 (CH_3), 56.28 (CH_3), 90.54 (C), 102.78 (CH), 108.38 (CH), 110.76 (CH), 112.13 (CH), 115.22 (C), 116.88 (C), 133.67 (CH), 134.53 (CH), 145.04 (C), 146.77 (C), 157.49 (C), 162.66 (C), 166.84 (C=O) ppm. GC–MS (70 eV): m/z (%) = 411 (100) $[M – C_3H_7]^+$, 309 (3), 205 (4). $C_{25}H_{34}N_2O_4Si$ (454.64): calcd. C 66.05, H 7.54, N 6.16; found C 66.36, H 7.75, N 6.17.

Methyl 8-Cyano-7-methoxy-2-(triisopropylsilyloxy)carbazole-3-carboxylate (36): A 10 mL microwave tube was charged with diarylamine **35** (101 mg, 0.222 mmol), palladium acetate (3.4 mg, 15 µmol), potassium carbonate (3.1 mg, 22 µmol), cupric acetate (101 mg, 0.556 mmol), and pivalic acid (400 mg) under air. The tube was irradiated in a microwave reactor at 110 °C and 300 W for 5 h. The mixture was cooled to room temperature and then diluted with ethyl acetate. The resulting solution was washed with a saturated solution of potassium carbonate and brine several times. The aqueous layers were extracted with ethyl acetate. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (pentane/dichloromethane/ethyl acetate, 28:5:1) provided methyl carbazole-3-carboxylate **36** (77.2 mg, 77% yield) as a colorless solid; m.p. 227 °C. UV (MeOH): λ = 217, 249, 287, 326, 331, 347 nm. Fluorescence (MeOH): λ_{ex} = 287 nm, λ_{em} = 378 nm. IR (ATR): $\tilde{\nu}$ = 3300, 2942, 2863, 2222, 1734, 1689, 1612, 1570, 1507, 1459, 1433, 1396, 1349, 1318, 1283, 1240, 1170, 1087, 1050, 1015, 978, 905, 883, 817, 782, 735 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.15 (d, J = 7.5 Hz, 18 H), 1.38 (m, 3 H), 3.91 (s, 3 H), 4.01 (s, 3 H), 6.82 (d, J = 8.7 Hz, 1 H), 6.93 (s, 1 H), 8.03 (d, J = 8.7 Hz, 1 H), 8.42 (s, 1 H), 8.62 (br. s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 13.29 (3 CH), 18.11 (6 CH_3), 52.02 (CH_3), 56.78 (CH_3), 83.74 (C), 101.99 (CH), 103.70 (CH), 115.08 (C), 116.60 (C), 116.75 (C), 118.12 (C), 124.04 (CH), 125.45 (CH), 142.93 (C), 143.09 (C), 155.24 (C), 160.32 (C), 167.87 (C=O) ppm. GC–MS (70 eV): m/z (%) = 409 (100) $[M – C_3H_7]^+$, 307 (5), 279 (6), 264 (5). $C_{25}H_{32}N_2O_4Si$ (452.62): calcd. C 66.34, H 7.13, N 6.19; found C 66.33, H 7.26, N 6.17.

6-(Hydroxymethyl)-2-methoxy-7-(triisopropylsilyloxy)carbazole-1-carbaldehyde: To a solution of methyl 8-cyano-7-methoxy-2-triisopropylsilyloxy-9*H*-carbazole-3-carboxylate (**36**, 100 mg, 0.221 mmol) in dichloromethane (20 mL) was slowly added diisobutylaluminium hydride (1 M in toluene, 0.99 mL, 0.99 mmol) at –78 °C, and the mixture was stirred at –40 to –35 °C for 4 h. The reaction was quenched at low temperature with ethyl acetate (1 mL) and then diluted with diethyl ether, and the resulting mixture was

washed several times with water, a saturated aqueous solution of ammonium chloride (containing a small portion of dilute hydrochloric acid), and brine. The aqueous layers were extracted with diethyl ether. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. The residue was dried under high vacuum to provide crude 6-(hydroxymethyl)-2-methoxy-7-(triisopropylsilyloxy)carbazole-1-carbaldehyde (94.5 mg, 100% yield); m.p. 145–146 °C. UV (MeOH): λ = 228, 257 (sh), 302, 352 (sh), 380 nm. Fluorescence (MeOH): λ_{ex} = 228 nm, λ_{em} = 392 nm. IR (ATR): $\tilde{\nu}$ = 3384, 2942, 2865, 1650, 1631, 1606, 1575, 1508, 1472, 1436, 1389, 1355, 1319, 1255, 1232, 1145, 1087, 995, 948, 882, 851, 798, 773, 722, 677 cm^{-1}. ^{1}H NMR (600 MHz, [D$_6$]acetone): δ = 1.16 (d, J = 7.6 Hz, 18 H), 1.44 (m, 3 H), 3.93 (t, J = 6.0 Hz, 1 H), 4.04 (s, 3 H), 4.84 (d, J = 6.0 Hz, 2 H), 6.94 (d, J = 8.5 Hz, 1 H), 7.36 (s, 1 H), 8.06 (s, 1 H), 8.24 (d, J = 8.5 Hz, 1 H), 10.59 (s, 1 H), 11.04 (br. s, 1 H) ppm. ^{13}C NMR and DEPT (150 MHz, [D$_6$]-acetone): δ = 13.76 (3 CH), 18.50 (6 CH$_3$), 56.87 (CH$_3$), 61.16 (CH$_2$), 101.89 (CH), 103.31 (CH), 109.56 (C), 116.66 (C), 119.10 (CH), 119.69 (C), 126.95 (C), 128.11 (CH), 140.44 (C), 141.77 (C), 152.83 (C), 161.83 (C), 190.19 (CHO) ppm. MS (ESI, +25 V): m/z = 410.3 [M – OH]$^+$, 877.6 [2M + Na]$^+$. MS (ESI, –25 V): m/z = 425.9 [M – H]$^-$. MS (EI, 70 eV): m/z (%) = 427 (100) [M]$^+$, 424 (35), 384 (77), 381 (37), 342 (33), 314 (32), 311 (28), 280 (40), 253 (24). HRMS: calcd. for $C_{24}H_{33}NO_4Si$ [M]$^+$ 427.2179; found 427.2163.

2-Methoxy-7-(triisopropylsilyloxy)carbazole-1,6-dicarbaldehyde (37): A suspension of the crude hydroxymethylcarbazole and manganese dioxide (191 mg, 2.20 mmol) in degassed dichloromethane (12 mL) was stirred at room temperature for 3 d. A second batch of manganese dioxide (191 mg, 2.20 mmol) was added, and the mixture was stirred for an additional 3 d (total reaction time 6 d). The mixture was filtered through Celite® (ethyl acetate), and the solvent was evaporated. The residue was dried under high vacuum to provide crude 2-methoxy-7-(triisopropylsilyloxy)carbazole-1,6-dicarbaldehyde (**37**, 94.1 mg, 100% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.17 (d, J = 7.5 Hz, 18 H), 1.42 (m, 3 H), 4.02 (s, 3 H), 6.83 (d, J = 8.6 Hz, 1 H), 6.89 (s, 1 H), 8.11 (d, J = 8.6 Hz, 1 H), 8.44 (s, 1 H), 10.46 (br. s, 1 H), 10.58 (s, 1 H), 10.59 (s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 13.20 (3 CH), 18.18 (6 CH$_3$), 56.49 (CH$_3$), 100.86 (CH), 103.66 (CH), 109.06 (C), 117.11 (C), 118.45 (C), 120.36 (CH), 121.70 (C), 128.29 (CH), 141.26 (C), 145.59 (C), 158.53 (C), 161.65 (C), 190.18 (CHO), 191.13 (CHO) ppm. MS (ESI, +25 V): m/z = 426.4 [M + H]$^+$. MS (ESI, –50 V): m/z = 424.0 [M – H]$^-$.

Murrayaline C (5): Without further purification, dicarbaldehyde **37** was dissolved in degassed DMF (15 mL), and TBAF (1 M in THF, 0.33 mL, 0.33 mmol) was added at –10 °C. The reaction was warmed to room temperature and then stirred for 10 min. Water (5 mL) was added, and the mixture was diluted with diethyl ether. The resulting mixture was washed with water and brine several times. The aqueous layers were extracted with ethyl acetate. The combined organic layers were dried with sodium sulfate, and the solvent was evaporated. Purification of the residue by chromatography on a silica gel column (pentane/ethyl acetate, gradient from 5:1 to 7:2) provided murrayaline C (**5**, 28.3 mg, 48% yield) as a yellow solid, m.p. 273 °C; ref.[17] no m.p. (yellow powder). UV (MeOH): λ = 257, 266 (sh), 305 (sh), 327, 330 nm. Fluorescence (MeOH): λ_{ex} = 266 nm, λ_{em} = 358 nm. IR (ATR): $\tilde{\nu}$ = 3357, 2921, 2850, 1735, 1700, 1658, 1643, 1594, 1509, 1462, 1432, 1394, 1327, 1253, 1230, 1183, 1082, 932, 880, 822, 798, 719, 678, 631 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]acetone): δ = 4.07 (s, 3 H), 7.06 (d, J = 8.6 Hz, 1 H), 7.21 (s, 1 H), 8.33 (d, J = 8.6 Hz, 1 H), 8.42 (s, 1 H), 10.02 (s, 1 H), 10.58 (s, 1 H), 11.36 (br. s, 1 H), 11.40 (s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D$_6$]acetone): δ = 57.03 (CH$_3$), 99.05 (CH), 104.99 (CH), 110.00 (C), 117.04 (C), 117.32 (C), 118.87 (C), 127.53 (CH), 128.60 (CH), 141.53 (C), 147.85 (C), 161.55 (C), 162.53 (C), 190.28 (CHO), 196.91 (CHO) ppm. GC–MS (70 eV): m/z (%) = 269 (100) [M]$^+$, 254 (27), 226 (12), 198 (23). $C_{15}H_{11}NO_4$ (269.26): calcd. C 66.91, H 4.12, N 5.20; found C 67.15, H 4.45, N 4.84.

Supporting Information (see footnote on the first page of this article): Copies of the ^{1}H and ^{13}C NMR spectra of all compounds and data for the X-ray crystal structure analyses of 2-methoxy-6-methyl-7-(triisopropylsilyloxy)carbazole-1-carbaldehyde and compounds **15**, **21**, and **26**.

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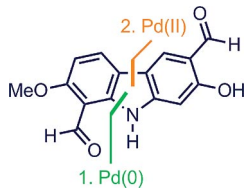
Total Synthesis

We describe the synthesis of the naturally occurring 2,7-dioxygenated formylcarbazole alkaloids 7-methoxymukonal, 7-methoxy-*O*-methylmukonal, and the murrayalines A–C. The carbazole framework was constructed by a Buchwald–Hartwig amination and a subsequent palladium(II)-catalyzed oxidative cyclization.



Keywords: Natural products / Alkaloids / Nitrogen heterocycles / C–H activation / Cyclization / Palladium

