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TRANSITION METALS IN ORGANIC SYNTHESIS, PART 84.[1] APPLICATION OF IRON- AND NICKEL-MEDIATED COUPLING REACTIONS TO THE TOTAL SYNTHESIS OF THE NEURONAL CELL PROTECTING SUBSTANCE (±)-CARQUINOSTATIN A**

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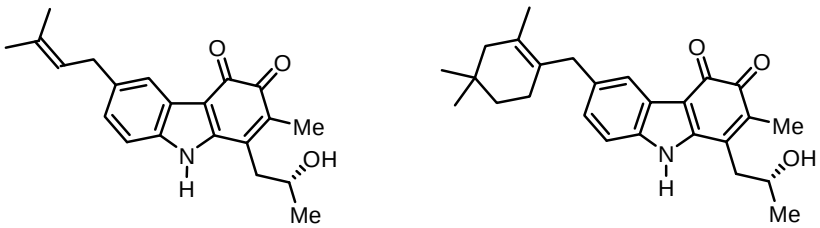
Abstract – Using iron- and nickel-mediated coupling reactions as key steps a convergent and highly efficient total synthesis of the potent neuronal cell protecting alkaloid (±)-carquinostatin A has been accomplished.

INTRODUCTION

A wide range of structurally diverse carbazole alkaloids with useful biological activities has been isolated from different natural sources. Therefore, several research groups developed novel strategies for the total synthesis of carbazole natural products.[2] Carbazole alkaloids isolated from *Streptomyces* exhibit quite often antibiotic, antifungal, or antioxidant and neuronal cell protecting activities. Many of these compounds have a 3,4-dioxygenated carbazole framework. In 1993, on their screening for substances with neuronal cell protecting activities, Seto and co-workers from the University of Tokyo isolated carquinostatin A (**1**) from *Streptomyces exfoliatus* 2419-SVT2 (Figure 1).[3]



1 carquinostatin A **2** lavanduquinocin

Figure 1. Carquinostatin A and Lavanduquinocin.

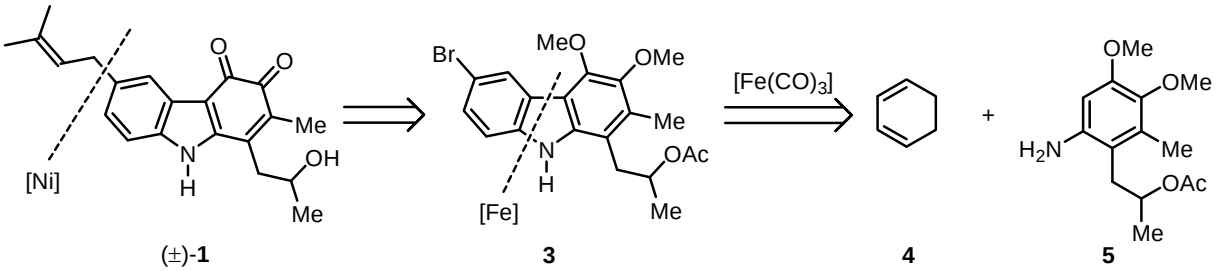
Carquinostatin A represented the first example of a carbazole-3,4-quinone alkaloid and proved to be a free radical scavenger.[3] It is well known that oxygen-derived free radicals play a pivotal role in the

** Dedicated to Professor Ekkehard Winterfeldt on the occasion of his 75th birthday.

initiation of a variety of diseases. Thus, free radical scavengers are thought to represent potential therapeutic agents for such diseases.[4] Two years later, Seto *et al*. isolated another structurally unique carbazole-3,4-quinone alkaloid, lavanduquinocin (**2**), from *Streptomyces viridochromogenes* 2942-AVS3.[5] Lavanduquinocin (**2**) has a monoterpenoid β-cyclolavandulyl side chain at C-6 and shows strong neuronal cell protecting activity. We are developing novel transition metal-mediated and -catalyzed methods for the total synthesis of pharmacologically active carbazole alkaloids.[6] Herein, we report full details on our total synthesis of (±)-carquinostatin A ((±)-**1**) by using an iron-mediated oxidative coupling of cyclohexadiene with a fully functionalized arylamine for construction of the carbazole framework and a subsequent nickel-mediated prenylation.[7-9]

RESULTS AND DISCUSSION

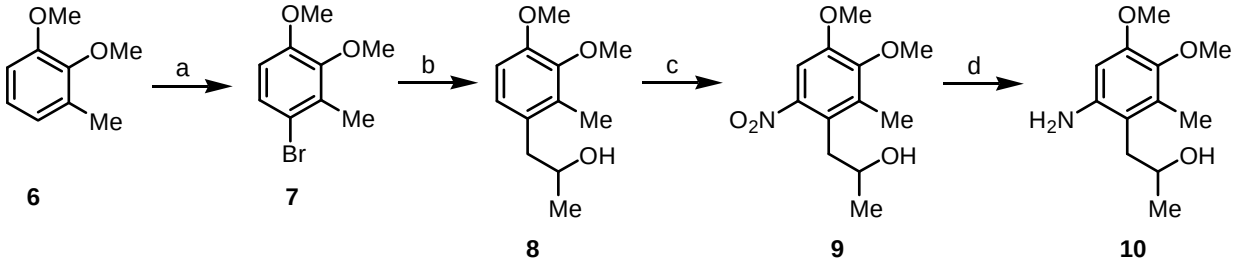
We devised a highly convergent synthesis of 3,4-dioxygenated carbazole alkaloids *via* a consecutive iron-mediated C–C and C–N bond formation, which has been applied to the total synthesis of the antibiotic carbazomycins.[10-13] The iron-mediated oxidative cyclization to the carbazole framework can also be achieved by oxidation with air in protic medium.[14] This procedure was exploited for a direct construction of the carbazole nucleus by a one-pot C–C and C–N bond formation and has been applied to the total syntheses of carbazoquinocin C,[15] the carbazomycins A and B,[16] carquinostatin A,[7,9] lavanduquinocin,[17] and neocarazostatin B.[18] The iron-mediated carbazole construction and the nickel-mediated prenylation were envisaged as key-steps for the total synthesis of (±)-carquinostatin A ((±)-**1**). According to our synthetic plan, (±)-carquinostatin A ((±)-**1**) should be available by regioselective prenylation of the bromocarbazole **3**, which is prepared from cyclohexadiene (**4**) and the arylamine **5** (Scheme 1).



Scheme 1. Retrosynthetic analysis of (±)-carquinostatin A ((±)-**1**).

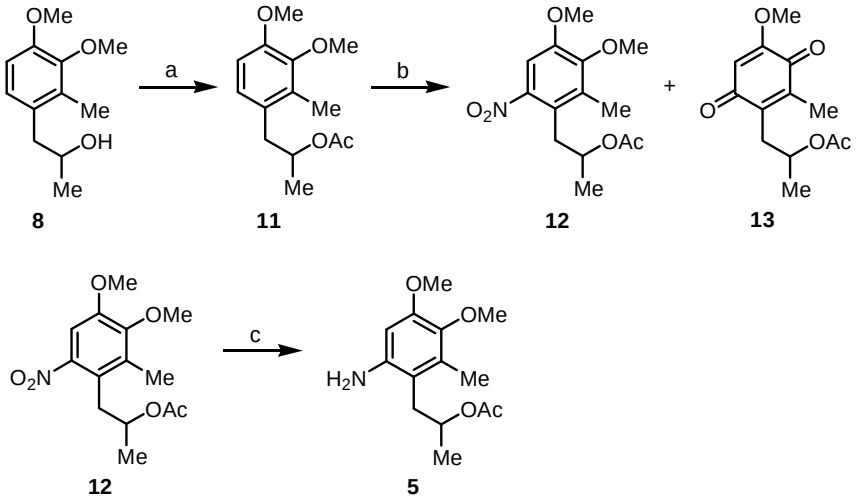
Initially, we planned to prepare the fully functionalized arylamine without protection of the hydroxy group (Scheme 2). Regioselective bromination of commercial 3-methylveratrole (**6**) led to the corresponding bromo derivative **7**.[9,19] A halogen–metal exchange with *n*-butyllithium and subsequent reaction of the intermediate aryl lithium compound with (±)-propene oxide afforded the carbinol **8**.

Nitration of **8** with fuming nitric acid and acetic acid in dichloromethane afforded regioselectively the nitro derivative **9**. The regioselectivity of the nitration was confirmed by comparison with previous results.[15] Catalytic hydrogenation of the nitro derivative **9** over 10% palladium on activated carbon provided the arylamine **10** in 93% yield. The arylamine **10** was available in four steps and 37% overall yield based on the veratrole **6**.



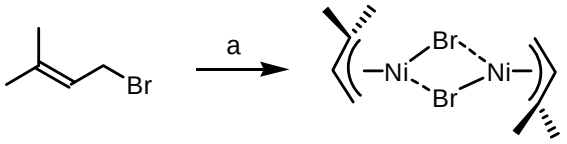
Scheme 2. Synthesis of the arylamine **10**. Reagents and conditions. (a) NBS, MeCN, rt, 27 h, 96%; (b) BuLi, THF, –78 °C, 15 min, (±)-propene oxide, –78 °C to rt, 18 h, 89%; (c) 100% HNO_3, HOAc, CH_2Cl_2, 0 °C to rt, 2 h, 47%; (d) H_2, 10% Pd/C, MeOH, rt, 1.5 h, 93%.

The drawback of the sequence described above is the moderate yield of the nitration to the desired nitro derivative **9** (47%), which limits the overall yield of the arylamine **10**. Therefore, we developed an alternative route by protection of the hydroxy group as an acetate prior to nitration. Acetylation of the carbinol **8** to the *O*-acetyl derivative **11** followed by nitration with fuming nitric acid in a mixture of acetic anhydride and acetic acid afforded the desired nitroaryl derivative **12** as the major product (89% yield) along with the quinone **13** (6% yield). Finally, catalytic hydrogenation of the nitro derivative **12** provided the arylamine **5** in 94% yield (Scheme 3). The route depicted in Scheme 3 afforded the arylamine **5** in five steps and 69% overall yield based on the veratrole **6**.



Scheme 3. Synthesis of the arylamine **5**. *Reagents and conditions*: (a) Ac_2O, Et_3N, DMAP, CH_2Cl_2, rt, 1 h, 97%; (b) 100% HNO_3, Ac_2O, HOAc, CH_2Cl_2, 0 °C, 1.5 h, 89% **12**, 6% **13**; (c) H_2, 10% Pd/C, MeOH, rt, 5 h, 94%.

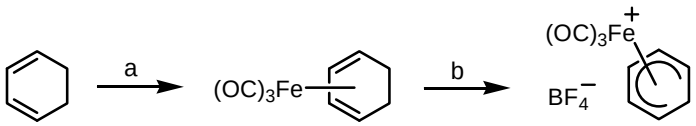
For the projected nickel-mediated prenylation we required bis[(μ-bromo(η^3-1,1-dimethylallyl)nickel] (**15**). This dimeric nickel complex represents a useful reagent for introduction of prenyl groups by reaction with organic halides in the presence of a range of functional groups.[20] Complex **15** is readily prepared by treatment of prenyl bromide (**14**) with 3 equivalents of nickeltetracarbonyl in benzene at 60 °C (Scheme 4).



14 **15**

Scheme 4. Synthesis of the dimeric π-prenylnickel bromide complex **15**. *Reagents and conditions*: (a) 3 equiv. $Ni(CO)_4$, C_6H_6, 60 °C.

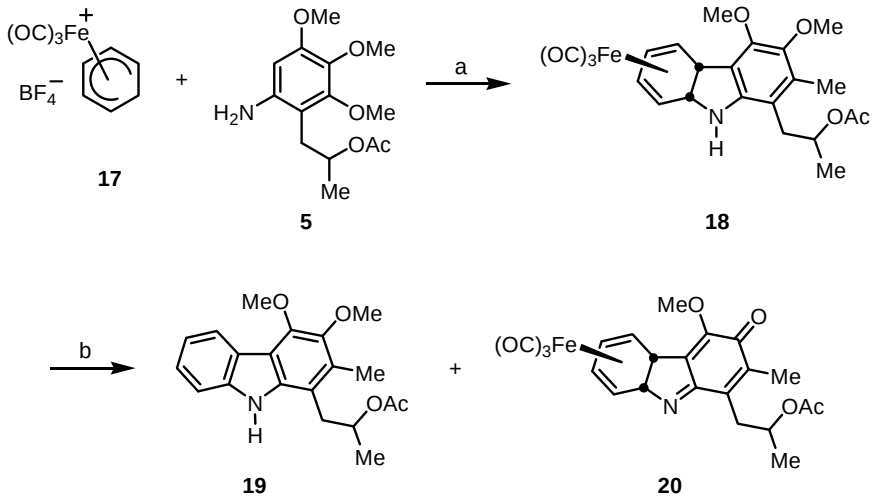
The iron complex salt **17** was obtained on large scale in almost quantitative overall yield by a 1-azadiene-catalyzed complexation of cyclohexa-1,3-diene (**4**) with pentacarbonyliron[21] followed by hydride abstraction of tricarbonyl(η^4-cyclohexa-1,3-diene)iron (**16**) using triphenylcarbenium tetrafluoroborate[22] (Scheme 5).



4 **16** **17**

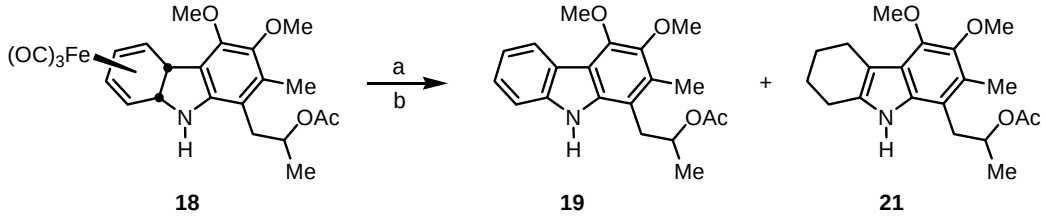
Scheme 5. Synthesis of the iron complex salt **17**. *Reagents and conditions*: (a) 1-(4-$MeOC_6H_4$)-4-C_6H_5-1-azabuta-1,3-diene, $Fe(CO)_5$, dioxane, 101 °C, 45 h, 99%; (b) $Ph_3C^+BF_4^-$, CH_2Cl_2, 99%.

The one-pot constuction of the carbazole framework was achieved by an iron-mediated oxidative coupling of the arylamine **5** using conditions described previously.[15] Reaction of the iron complex salt **17** with the arylamine **5** (ratio 1:2) in a solution of acetonitrile afforded after seven days at room temperature the tricarbonyl(η^4-4a,9a-dihydro-9*H*-carbazole)iron complex **18** as a 1:1 mixture of diastereoisomers (Scheme 6). Based on our previous studies, we envisaged a direct transformation of the iron complex **18** to the carbazole **19** by aromatization with concomitant demetalation.[10c,23] However, oxidation of complex **18** using very active manganese dioxide[24] in the presence of Alox B at room temperature afforded carbazole **19** only in 50% yield along with the tricarbonyliron-coordinated dihydrocarbazolone **20** (31% yield). This sequence provided carbazole **19** in two steps and 44% overall yield based on the iron complex salt **17**.



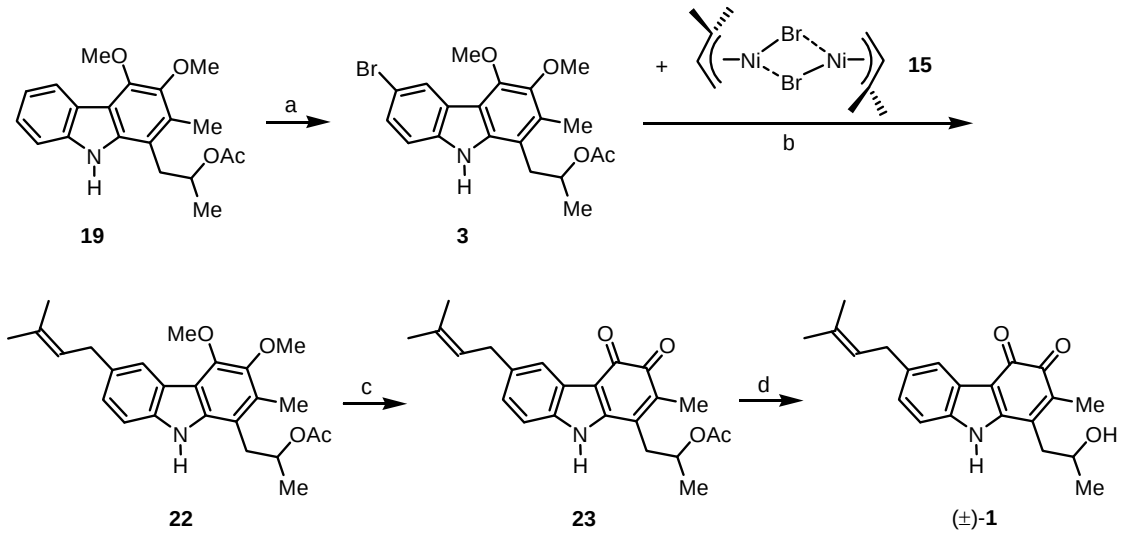
Scheme 6. Synthesis of the *O*-acetylcarbazole **19**. *Reagents and conditions*: (a) MeCN, air, rt, 7 d, 88%; (b) very active MnO_2, Alox B, CH_2Cl_2, rt, 4.5 h, 50% **19** and 31% **20**.

In order to improve the overall yield, we applied an alternative route via selective demetalation of the tricarbonyliron-coordinated 4a,9a-dihydrocarbazole followed by catalytic dehydrogenation to the aromatized carbazole. Demetalation of complex **18** using trimethylamine *N*-oxide in acetone[25,26] at reflux and subsequent aromatization by catalytic dehydrogenation with 10% palladium on activated carbon in boiling *o*-xylene[27] provided the carbazole **19** in 82% yield along with the tetrahydrocarbazole **21** (6% yield) (Scheme 7). This route leads to carbazole **19** in three steps and 72% overall yield based on the iron complex salt **17**.



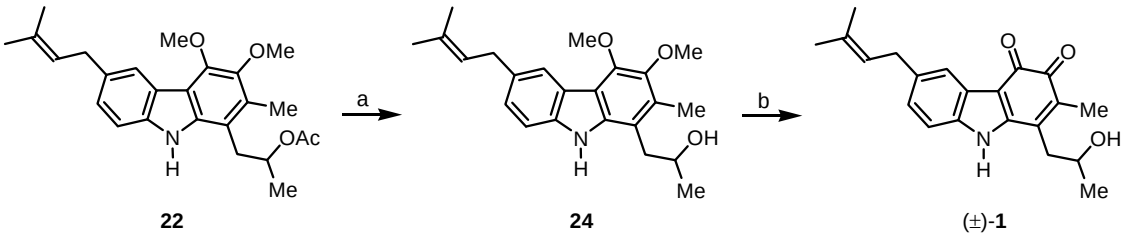
Scheme 7. Synthesis of the carbazole **19**. *Reagents and Conditions*: (a) Me_3NO, acetone, 56 °C, 5.5 h; (b) 10% Pd/C, *o*-xylene, 145 °C, 4 h, 82% **19** and 6% **21**.

Regioselective bromination by electrophilic substitution of the carbazole **19** with *N*-bromosuccinimide in tetrachloromethane at reflux provided the 6-bromocarbazole **3** in 93% yield. The nickel-mediated prenylation of **3** by reaction with two equivalents of the dimeric π-prenylnickel bromide complex **15** in dry and degassed *N*,*N*-dimethylformamide at 65 °C led to the 6-prenylcarbazole **22** in 81% yield along with the hydrodebromination product (carbazole **19**) in 7% yield. Oxidation of the 6-prenylcarbazole **22** with ceric ammonium nitrate (CAN)[28] in acetonitrile and water at 0°C afforded (±)-*O*-acetylcarquinostatin A (**23**) in 62% yield. Transformation to the natural product (±)-**1** was achieved in 61% yield by reduction of compound **23** with lithium aluminum hydride (Scheme 8).



Scheme 8. Synthesis of (±)-carquinostatin ((±)-**1**). *Reagents and Conditions*: (a) NBS, CCl_4, 77 °C, 30 min, 93%; (b) DMF, 65 °C, 15 h, 81%; (c) CAN, MeCN/H_2O, 0 °C, 30 min, 62%; (d) $LiAH_4$, THF, rt, 22.5 h, 61%.

Due to the low yield of the ester cleavage in (±)-*O*-acetylcarquinostatin A (**23**), we reversed the sequence of oxidation and deprotection. Thus, the acetyl protecting group in **22** was removed by reaction of the acetate with potassium hydroxide in methanol and water at room temperature to afford the carbinol **24** in 95% yield. Finally, oxidation of **24** with ceric ammonium nitrate (CAN) in acetonitrile and water at 0 °C provided (±)-carquinostatin A ((±)-**1**) (Scheme 9).



Scheme 9. Synthesis of (±)-carquinostatin ((±)-**1**). *Reagents and Conditions*: (a) KOH, MeOH/H_2O, rt, 3 h, 95%; (b) CAN, MeCN/H_2O, 0 °C, 30 min, 64%.

In conclusion, the optimized synthetic route *via* the carbazole **24** provides (±)-carquinostatin A ((±)-**1**) in seven steps and 33% overall yield based on the iron complex salt **17**. The spectroscopic data of (±)-**1** were in full agreement with those reported for the natural product.[3] Our convergent synthesis of (±)-carquinostatin A emphasizes the high efficiency of the iron-mediated carbazole construction.

EXPERIMENTAL

All reactions were carried out using dry and degassed solvents under an argon atmosphere unless otherwise stated. Flash chromatography: Merck silica gel (0.03–0.06 mm). Melting points: Büchi 535

(uncorrected). UV spectra: Perkin–Elmer Lambda 2 (UV/VIS spectrometer). IR spectra: Bruker IFS 88 (FT–IR). ^{1}H NMR and ^{13}C NMR spectra: Bruker AC-250, Bruker AM-400, and Bruker DRX-500; internal standard: TMS or the signal of the deuterated solvent; δ in ppm; coupling constants (*J*) in Hz. MS: Finnigan MAT-90; ionization potential: 70 eV. Elemental analyses: Heraeus CHN-Rapid.

4-Bromo-3-methylveratrole (7)

To a stirred solution of 3-methylveratrole (**6**) (15.38 g, 101 mmol) in MeCN (100 mL) at rt was added portionwise *N*-bromosuccinimide (NBS) (18.88 g, 106.1 mmol). The resulting mixture was stirred for an additional 27 h at rt. During this time the reaction mixture became almost colorless and succinimide precipitated. The solvent was evaporated, tetrachloromethane (50 mL) was added to the residue, and the succinimide was separated by filtration. After removal of the solvent, the residue was crystallized from cold methanol to afford 4-bromo-3-methylveratrole (**7**), yield: 22.45 g (96%). Colorless crystals; mp 59–60 °C (lit.,[19] 55 °C). IR (KBr): ν = 3081, 3006, 2968, 2938, 2840, 1574, 1463, 1297, 1268, 1227, 1080, 1012, 827, 810, 802, 693 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.34 (s, 3 H), 3.78 (s, 3 H), 3.84 (s, 3 H), 6.66 (d, *J* = 8.8 Hz, 1 H), 7.24 (d, *J* = 8.8 Hz, 1 H).

1-(3,4-Dimethoxy-2-methylphenyl)propan-2-ol (8)

A solution of *n*-BuLi in hexane (1.6 M, 24.4 mL, 39.0 mmol) was added dropwise over a period of 15 min to a solution of 4-bromo-3-methylveratrole (**7**) (6.0 g, 25.96 mmol) in THF (75 mL) at –78 °C. After stirring for 15 min at –78 °C, (±)-propene oxide (4.51 g, 5.43 mL, 77.7 mmol) was added. Stirring was continued for 18 h and the resulting suspension was allowed to warm to rt. After removal of the solvent, Et_2O was added, the mixture was poured into a saturated aqueous solution of NH_4Cl (100 mL) and extracted with Et_2O (2 × 50 mL). The combined organic layers were dried over sodium sulfate and the solvent was evaporated. Flash chromatography (hexane/EtOAc, 4:3) of the residue on silica gel provided compound **8** as a colorless oil, yield: 4.83 g (89%). UV (MeOH): λ = 200, 277 nm. IR (neat): ν = 3415, 2965, 2934, 2836, 1603, 1492, 1274, 1087, 1004, 939, 802 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.22 (d, *J* = 6.1 Hz, 3 H), 2.08 (br s, 1 H), 2.23 (s, 3 H), 2.63–2.74 (m, 2 H), 3.77 (s, 3 H), 3.82 (s, 3 H), 3.91–3.96 (m, 1 H), 6.70 (d, *J* = 8.4 Hz, 1 H), 6.86 (d, *J* = 8.4 Hz, 1 H). ^{13}C NMR and DEPT (100 MHz, $CDCl_3$): δ = 12.07 (CH_3), 22.85 (CH_3), 42.79 (CH_2), 55.60 (CH_3), 60.12 (CH_3), 67.81 (CH), 109.39 (CH), 125.55 (CH), 130.08 (C), 130.84 (C), 147.41 (C), 151.28 (C). MS (EI): *m/z* = 210 (36) [M$^+$], 166 (28), 165 (100), 151 (24), 135 (8), 91 (5). HRMS: *m/z* calcd for $C_{12}H_{18}O_3$ [M$^+$]: 210.1256; found 210.1273.

1-(3,4-Dimethoxy-2-methyl-6-nitrophenyl)propan-2-ol (9)

A solution of 100% HNO_3 (130 μL, 3.1 mmol) in CH_2Cl_2 (1 mL) was added over a period of 5 min to a solution of compound **8** (392 mg, 1.86 mmol) and HOAc/CH_2Cl_2 (5:2, 7 mL) at 0 °C. After stirring for 1 h at 0 °C, the reaction mixture was additionally stirred for 1 h at rt and subsequently ice-water (10 mL) and a conc. aqueous solution of ammonia (4 mL) were added. After separation of the organic layer, the aqueous layer was extracted twice with CH_2Cl_2 (2 × 20 mL). The combined organic layers were washed with a saturated aqueous solution of $NaHCO_3$ (2 × 20 mL) and H_2O (20 mL), and dried over sodium sulfate. Removal of the solvent and flash chromatography (hexane/EtOAc, 2:1) of the residue on silica gel provided the nitro derivative **9** as a light red solid, yield: 225 mg (47%). Recrystallization from hexane/$CHCl_3$ (3:1) afforded light yellow crystals, mp 77–78 °C. UV (MeOH): λ = 198, 216 (sh), 240 (sh), 290 nm. IR (KBr): ν = 3344, 3265, 2974, 1515, 1317, 1237, 1105, 1002, 855, 782 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.29 (d, *J* = 6.1 Hz, 3 H), 2.06 (d, *J* = 5.3 Hz, 1 H), 2.33 (s, 3 H), 2.95–3.08 (m, 2 H), 3.84 (s, 3 H), 3.89 (s, 3 H), 3.99–4.05 (m, 1 H), 7.28 (s, 1 H). ^{13}C NMR and DEPT (100 MHz, $CDCl_3$): δ = 12.96 (CH_3), 23.97 (CH_3), 37.31 (CH_2), 55.92 (CH_3), 60.37 (CH_3), 68.19 (CH), 106.51 (CH), 125.89 (C), 133.27 (C), 146.61 (C), 150.78 (C), 150.88 (C). MS (EI): *m/z* = 255 (7) [M^+], 194 (100), 45 (4). HRMS: *m/z* calcd for $C_{12}H_{17}NO_5$ [M^+]: 255.1107; found: 255.1093. Anal. Calcd for $C_{12}H_{17}NO_5$: C 56.46, H 6.71, N 5.49. Found: C 56.44, H 6.68, N 5.64%.

1-(6-Amino-3,4-dimethoxy-2-methylphenyl)propan-2-ol (10)

Palladium on carbon (10%, 15 mg) was added to a solution of the nitrobenzene **9** (98 mg, 0.39 mmol) in MeOH (10 mL). The mixture was vigorously stirred at rt under an hydrogen atmosphere (1.1 atm) for 1.5 h. The reaction mixture was filtered over a short path of Celite, which was subsequently washed with MeOH. Evaporation of the solvent *in vacuo* and trituration of the crude product with Et_2O afforded the arylamine **10** as light red crystals, yield: 80 mg (93%). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.31 (d, *J* = 6.2 Hz, 3 H), 2.19 (s, 3 H), 2.60–2.69 (m, 2 H), 3.26 (br s, 2 H), 3.70 (s, 3 H), 3.80 (s, 3 H), 3.98–4.07 (m, 1 H), 6.19 (s, 1 H). ^{13}C NMR and DEPT (100 MHz, $CDCl_3$): δ = 12.41 (CH_3), 23.76 (CH_3), 36.88 (CH_2), 55.56 (CH_3), 60.48 (CH_3), 69.00 (CH), 99.10 (CH), 115.55 (C), 131.45 (C), 140.48 (C), 141.75 (C), 151.53 (C).

1-(3,4-Dimethoxy-2-methylphenyl)propan-2-yl acetate (11)

Acetic anhydride (2.24 g, 2.07 mL, 21.9 mmol) was added over a period of 10 min to a stirred solution of compound **8** (4.18 g, 19.9 mmol), Et_3N (2.42 g, 24 mmol) and DMAP (100 mg, 0.82 mmol) in CH_2Cl_2 (25 mL) at rt. After stirring for 1 h at rt, the solvent was evaporated *in vacuo*. The residue was subjected to flash chromatography (hexane/EtOAc, 2:1) on silica gel to provide the acetate **11** as a colorless oil,

yield: 4.85 g (97%). UV (MeOH): λ = 200, 223, 276 nm. IR (neat): ν = 2936, 2837, 1736, 1493, 1245, 1086, 956, 803 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.22 (d, *J* = 6.5 Hz, 3 H), 1.99 (s, 3 H), 2.27 (s, 3 H), 2.66 (dd, *J* = 13.9, 6.5 Hz, 1 H), 2.92 (dd, *J* = 13.9, 6.5 Hz, 1 H), 3.77 (s, 3 H), 3.83 (s, 3 H), 5.06 (sext., *J* = 6.5 Hz, 1 H), 6.69 (d, *J* = 8.4 Hz, 1 H), 6.84 (d, *J* = 8.4 Hz, 1 H). ^{13}C NMR and DEPT (100 MHz, $CDCl_3$): δ = 12.06 (CH_3), 19.57 (CH_3), 21.33 (CH_3), 39.26 (CH_2), 55.59 (CH_3), 60.14 (CH_3), 71.03 (CH), 109.25 (CH), 125.60 (CH), 129.14 (C), 130.98 (C), 147.27 (C), 151.31 (C), 170.54 (C=O). MS (EI): *m/z* = 252 (15) [M^+], 192 (100), 165 (59), 43 (20). HRMS: *m/z* calcd for $C_{14}H_{20}O_4$ [M^+]: 252.1362; found: 252.1352.

1-(3,4-Dimethoxy-2-methyl-6-nitrophenyl)propan-2-yl acetate (12) and 1-(4-Methoxy-6-methyl-2,5-dioxo-3,6-cyclohexadienyl)propan-2-yl acetate (13)

A solution of 100% HNO_3 (1.17 mL, 28.2 mmol) in HOAc/Ac_2O (4:1, 5 mL) was added over a period of 75 min to a solution of compound **11** (3.57 g, 14.1 mmol) in HOAc/Ac_2O (4:1, 15 mL) at 0 °C. After stirring for 15 min at 0 °C, ice (30 g) and a conc. aqueous solution of NH_3 (25 mL) were added to the reaction mixture. The aqueous layer was extracted twice with Et_2O (2 × 40 mL). The combined organic layers were washed twice with a saturated aqueous solution of $NaHCO_3$ (2 × 40 mL) and dried over sodium sulfate. Removal of the solvent and flash chromatography (hexane/EtOAc, 2:1) of the residue on silica gel provided 3.75 g (89%) of the nitro derivative **12** (less polar fraction: R_f = 0.45) as a bright yellow oil and the quinone **13** (more polar fraction: R_f = 0.21) as bright yellow crystals (yield: 214 mg, 6%).

12: UV (MeOH): λ = 198, 218 (sh), 241 (sh), 288 nm. IR (neat): ν = 2978, 2941, 1740, 1529, 1486, 1322, 1242, 1097, 1005, 779 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.30 (d, *J* = 6.3 Hz, 3 H), 1.91 (s, 3 H), 2.34 (s, 3 H), 3.08 (dd, *J* = 14.6, 3.9 Hz, 1 H), 3.28 (dd, *J* = 14.6, 9.4 Hz, 1 H), 3.84 (s, 3 H), 3.89 (s, 3 H), 5.06 (m, 1 H), 7.27 (s, 1 H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 12.73 (CH_3), 20.25 (CH_3), 21.07 (CH_3), 33.77 (CH_2), 55.86 (CH_3), 60.30 (CH_3), 70.83 (CH), 106.55 (CH), 124.45 (C), 133.04 (C), 146.70 (C), 150.62 (C), 150.88 (C), 170.28 (C=O). MS (EI): *m/z* = 297 (17) [M^+], 237 (9), 220 (9), 194 (100), 178 (16), 91 (12), 43 (88). HRMS: *m/z* calcd for $C_{14}H_{19}NO_6$ [M^+]: 297.1212; found: 297.1195.

13: ^1H NMR (400 MHz, $CDCl_3$): δ = 1.23 (d, *J* = 6.3 Hz, 3 H), 1.90 (s, 3 H), 2.05 (s, 3 H), 2.65 (dd, *J* = 13.1, 8.6 Hz, 1 H), 2.79 (ddd, *J* = 13.1, 4.5, 0.7 Hz, 1 H), 3.76 (s, 3 H), 4.99 (m, 1 H), 5.85 (s, 1 H). ^{13}C NMR and DEPT (100 MHz, $CDCl_3$): δ = 12.34 (CH_3), 20.46 (CH_3), 21.09 (CH_3), 32.95 (CH_2), 56.09 (CH_3), 70.06 (CH), 107.12 (CH), 140.51 (C), 140.91 (C), 158.26 (C), 170.31 (C=O), 182.36 (C=O), 186.69 (C=O). MS (EI): *m/z* = 252 (1) [M^+], 210 (61), 167 (57), 166 (100), 138 (13), 137 (22), 69 (18), 43

(80). HRMS: *m/z* calcd for $C_{13}H_{16}O_5$ [M^+]: 252.0998; found: 252.1012.

1-(6-Amino-3,4-dimethoxy-2-methylphenyl)propan-2-yl acetate (5)

Palladium on activated carbon (10%, 109 mg) was added to a solution of the nitrobenzene **12** (1.09 g, 3.67 mmol) in MeOH (20 mL). The mixture was vigorously stirred at rt under a hydrogen atmosphere (1.1 atm) for 5 h. Evaporation of the solvent and flash chromatography of the residue (hexane/EtOAc/Et_3N, 5:5:1) on silica gel afforded the arylamine **5** as a light yellow solid, yield: 920 mg (94%). Recrystallization from hexane afforded colorless crystals; mp 80–81 °C. UV (MeOH): λ = 208, 237 (sh), 293 nm. IR (KBr): ν = 3403, 3323 (br), 3226 (br), 2976, 1722, 1604, 1454, 1372, 1258, 1122, 1051, 1007, 951, 818 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.26 (d, *J* = 6.3 Hz, 3 H), 2.05 (s, 3 H), 2.21 (s, 3 H), 2.67 (dd, *J* = 14.3, 8.3 Hz, 1 H), 2.83 (dd, *J* = 14.3, 5.6 Hz, 1 H), 3.69 (s, 3 H), 3.78 (s, 3 H), 4.03 (br s, 2 H), 4.98 (m, 1 H), 6.15 (s, 1H). ^{13}C NMR and DEPT (100 MHz, $CDCl_3$): δ = 12.68 (CH_3), 19.62 (CH_3), 21.39 (CH_3), 33.86 (CH_2), 55.44 (CH_3), 60.45 (CH_3), 71.05 (CH), 98.09 (CH), 112.50 (C), 131.29 (C), 139.77 (C), 141.86 (C), 151.80 (C), 171.26 (C=O). MS (EI): *m/z* = 267 (61) [M^+], 252 (8), 192 (22), 180 (100), 164 (5), 136 (5), 43 (5). HRMS: *m/z* calcd for $C_{14}H_{21}NO_4$ [M^+]: 267.1471; found: 267.1456. Anal. Calcd for $C_{14}H_{21}NO_4$: C 62.90, H 7.92, N 5.24. Found: C 62.96, H 7.91, N 5.49%.

[(1-4-η)-8-(2-Acetoxypropyl)-4a,9a-dihydro-5,6-dimethoxy-7-methyl-9*H*-carbazole]tricarbonyliron (18)

A solution of the iron complex salt **17** (2.72 g, 8.9 mmol) and the arylamine **5** (4.76 g, 17.8 mmol) in MeCN (25 mL) was stirred at rt in the air to the exclusion of light for 7 days. The red brown reaction mixture was poured into a saturated aqueous solution of $NaHCO_3$ (100 mL) and extracted twice with Et_2O (100 mL, 50 mL). The combined organic layers were dried over sodium sulfate and the solvent was removed. Flash chromatography (hexane/EtOAc/Et_3N 8:2:1) of the residue on silica gel provided a 1:1 diasteroisomeric mixture of the iron complex **18** as an orange oil, which on trituration with Et_2O (10 mL) afforded light yellow crystals with no sharp melting point, yield: 3.77 g (88%). UV (MeOH): λ = 214, 298 nm. IR (KBr): ν = 3398, 2939, 2039, 1964, 1930, 1738, 1602, 1453, 1371, 1233, 1129, 1066, 953, 620 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.21 (d, *J* = 6.3 Hz) and 1.26 (d, *J* = 6.3 Hz, Σ 3 H), 2.03 (s) and 2.07 (s, Σ 3 H), 2.13 (s, 3 H), 2.53–2.59 (m) and 2.61–2.66 (m, Σ 2 H), 3.25 (m, 1 H), 3.65–3.68 (m, 1 H), 3.69 (s) and 3.70 (s, Σ 3 H), 3.86–3.90 (m) and 3.98 (dd, *J* = 10.9, 4.1 Hz, Σ 1 H), 3.90 (s, 3 H), 4.18 (br s) and 4.39 (br s, Σ 1 H), 4.31 (dd, *J* = 10.9, 3.0 Hz) and 4.36 (dd, *J* = 11.0, 3.7 Hz, Σ 1 H), 4.79–4.83 (m, 1 H) and 4.84–4.88 (m, Σ 1 H), 5.33 (m) and 5.38–5.41 (m, Σ 2 H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 12.30 (CH_3), 12.36 (CH_3), 19.58 (CH_3), 20.00 (CH_3), 21.46 (CH_3), 21.56 (CH_3), 34.67 (CH_2),

44.56 (CH), 45.17 (CH), 60.19 (CH_3), 60.47 (CH_3), 61.34 (CH), 61.54 (CH), 62.70 (CH), 62.72 (CH), 63.25 (CH), 63.65 (CH), 70.84 (CH), 71.57 (CH), 85.28 (CH), 85.55 (CH), 86.48 (CH), 86.62 (CH), 112.05 (C), 112.71 (C), 121.55 (C), 121.79 (C), 130.47 (C), 130.56 (C), 143.39 (C), 143.46 (C), 145.27 (C), 145.58 (C), 147.85 (C), 171.08 (C=O), 171.19 (C=O), 211.31 (3 CO), 211.43 (3 CO). MS (EI): *m/z* = 483 (57) [M^+], 399 (100), 341 (17), 339 (15), 254 (11), 84 (6). HRMS: *m/z* calcd for $C_{23}H_{25}FeNO_7$ [M^+]: 483.0980; found: 483.0952. Anal. Calcd for $C_{23}H_{25}FeNO_7$: C 57.16, H 5.21, N 2.90. Found: C 57.29, H 5.35, N 3.18%.

1-[3,4-Dimethoxy-2-methyl-(9*H*-carbazol-1-yl)]propan-2-yl acetate (19) and [(5-8-η)-[1-(2-Acetoxy-propyl)-4b,8a-dihydro-4-methoxy-2-methyl-3*H*-carbazol-3-one]-tricarbonyliron (20)

Very active manganese dioxide[24a] (1.01 g) and Alox B "Super I" (ICN) (500 mg) were added to a solution of the iron complex **18** (505 mg, 1.05 mmol) in CH_2Cl_2 (10 mL) and the heterogenous reaction mixture was vigorously stirred for 1.5 h at rt. For completion of the reaction, an additional amount of very active manganese dioxide (500 mg) and Alox B "Super I" (ICN) (250 mg) were added and stirring was continued for 3 h. The reaction mixture was filtered through a short path of Celite, which was subsequently washed with EtOAc. The solvent was removed and the residue was subjected to flash chromatography (hexane/EtAc 2:1) on silica gel to afford the carbazole **19** as the less polar fraction (R_f = 0.48) and the 1:1 diastereoisomeric mixture of the iron complex **20** as the more polar fraction (R_f = 0.42). Both fractions were crystallized from hexane.

19: Light yellow crystals, yield: 179 mg (50%), mp 91–93 °C (hexane). UV (MeOH): λ = 219, 241, 261, 292 (sh), 327, 339 nm. IR (KBr): ν = 3328, 2933, 1711, 1611, 1505, 1456, 1402, 1257, 1108, 1059, 1004, 884, 751 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.29 (d, *J* = 6.3 Hz, 3 H), 2.15 (s, 3 H), 2.41 (s, 3 H), 3.02 (dd, *J* = 13.8, 10.1 Hz, 1 H), 3.25 (dd, *J* = 13.8, 3.0 Hz, 1 H), 3.89 (s, 3 H), 4.12 (s, 3 H), 5.04 (m, 1 H), 7.20 (m, 1 H), 7.38 (m, 1 H), 7.49 (d, *J* = 8.1 Hz, 1 H), 8.23 (d, *J* = 7.8 Hz, 1 H), 9.62 (br s, 1 H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 12.81 (CH_3), 19.33 (CH_3), 21.49 (CH_3), 35.04 (CH_2), 60.42 (CH_3), 60.97 (CH_3), 71.96 (CH), 110.63 (CH), 113.38 (C), 114.60 (C), 119.14 (CH), 122.30 (C), 122.38 (CH), 125.14 (CH), 128.62 (C), 137.18 (C), 139.63 (C), 144.18 (C), 146.90 (C), 172.52 (C=O). MS (EI): *m/z* = 341 (100) [M^+], 326 (17), 281 (6), 266 (31), 254 (63), 210 (6). HRMS: *m/z* calcd for $C_{20}H_{23}NO_4$ [M^+]: 341.1627; found: 341.1615. Anal. Calcd for $C_{20}H_{23}NO_4$: C 70.36, H 6.79, N 4.10. Found: C 70.39, H 6.76, N 4.14%.

20: Orange yellow crystals, yield: 151 mg (31%), mp 116 °C (decomp.) (hexane). UV (MeOH): λ = 197, 220 (sh), 288 nm. IR (KBr): ν = 2950, 2051, 1971, 1736, 1633, 1444, 1377, 1319, 1252, 1138, 1076, 720, 663, 623 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.26 (d, *J* = 6.2 Hz) and 1.27 (d, *J* = 6.2 Hz, Σ 3 H), 1.95

(s) and 1.96 (s, Σ 3 H), 2.046 (s) and 2.050 (s, Σ 3 H), 2.86 (dd, *J* = 13.2, 8.3 Hz, 1 H), 2.91–2.98 (m, 1 H), 3.25–3.30 (m, 1 H), 3.44 (m, 1 H), 3.63–3.67 (m, 1 H), 3.95 (s, 3 H), 4.88 (m, 1 H), 5.07–5.19 (m, 1 H), 5.35–5.42 (m, 2 H). ^{13}C NMR and DEPT (100 MHz, $CDCl_3$): δ = 12.62 (CH_3), 12.80 (CH_3), 20.41 (CH_3), 20.43 (CH_3), 21.26 (CH_3), 21.30 (CH_3), 34.06 (CH_2), 34.19 (CH_2), 44.24 (CH), 44.35 (CH), 57.69 (CH), 57.74 (CH), 59.25 (2 CH), 59.89 (CH_3), 59.91 (CH_3), 70.41 (CH), 70.59 (CH), 78.04 (CH), 78.10 (CH), 85.10 (CH), 85.25 (CH), 86.39 (CH), 86.43 (CH), 136.28 (C), 136.45 (C), 137.59 (C), 137.64 (C), 140.75 (C), 140.92 (C), 147.16 (C), 147.26 (C), 163.53 (C=N), 163.90 (C=N), 170.22 (C=O), 170.34 (C=O), 183.78 (2 C=O), 210.62 (6 CO). MS (EI): *m/z* = 467 (8) [M^+], 439 (54), 383 (97), 368 (16), 323 (100), 296 (10), 236 (10), 43 (12). HRMS: *m/z* calcd for $C_{22}H_{21}FeNO_7$ [M^+]: 467.0667; found: 467.0649. Anal. Calcd for $C_{22}H_{21}FeNO_7$: C 56.55, H 4.53, N 3.00. Found: C 56.84, H 4.64, N 3.05%.

1-[(3,4-Dimethoxy-2-methyl-(9*H*-carbazol-1-yl)]propan-2yl acetate (19) and 1-[1,2,3,4-Tetrahydro-5,6-dimethoxy-7-methyl-(9*H*-carbazol-8-yl)]propan-2-yl acetate (21)

Trimethylamine *N*-oxide dihydrate (5.52 g, 49.7 mmol) was added to a solution of the iron complex **18** (3.0 g, 6.21 mmol) in acetone (60 mL) and the reaction mixture was heated at reflux for 4 h. After cooling, the reaction mixture was filtered through a short path of Celite/silica gel and washed with acetone (3 × 50 mL). The solvent was evaporated in vacuo to afford a brown oil (2.39 g). Without further purification, the crude product was dissolved in dry *o*-xylene (20 mL) followed by addition of palladium on activated carbon (10%, 480 mg). The heterogeneous mixture was heated at reflux under vigorous stirring for 4 h. Removal of the solvent *in vacuo* and flash chromatography (hexane/EtOAc, 2:1) of the residue on silica gel provided the dihydrocarbazole **21** as the less polar fraction (R_f = 0.50) and the carbazole **19** as the more polar fraction (R_f = 0.45). The carbazole **19** was obtained as a light yellow oil which on crystallization from hexane afforded colorless crystals.

19: Colorless crystals, yield: 1.74 g (82%). Spectral data, see above.

21: Colorless oil, yield: 138 mg (6%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.25 (d, *J* = 6.3 Hz, 3 H), 1.82–1.91 (m, 4 H), 2.12 (s, 3 H), 2.31 (s, 3 H), 2.74–2.77 (m, 2 H), 2.90–2.94 (m, 3 H), 3.13 (dd, *J* = 13.6, 2.8 Hz, 1 H), 3.82 (s, 3 H), 3.94 (s, 3 H), 5.00 (m, 1 H), 9.15 (br s, 1 H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 12.39 (CH_3), 19.24 (CH_3), 21.46 (CH_3), 22.59 (CH_2), 23.03 (CH_2), 23.33 (CH_2), 23.67 (CH_2), 34.91 (CH_2), 60.78 (CH_3), 61.54 (CH_3), 72.14 (CH), 108.86 (C), 113.53 (C), 119.30 (C), 123.33 (C), 133.63 (C), 133.71 (C), 144.24 (C), 144.69 (C), 172.44 (C=O). MS (EI): *m/z* = 345 (100) [M^+], 332 (11), 281 (23), 270 (24), 268 (11), 266 (11), 258 (32), 244 (26), 165 (10), 105 (10), 57 (36), 56 (34), 43 (19), 41 (19). HRMS: *m/z* calcd for $C_{20}H_{27}NO_4$ [M^+]: 345.1940; found: 345.1952.

1-[6-Bromo-3,4-dimethoxy-2-methyl-(9*H*-carbazol-1-yl)]propan-2-yl acetate (3)

N-Bromosuccinimide (NBS) (376 mg, 2.11 mmol) was added to a stirred solution of the carbazole **19** (655 mg, 1.92 mmol) in tetrachloromethane (20 mL). The resulting mixture was heated at reflux for 30 min. Removal of the solvent and flash chromatography (hexane/EtOAc, 2:1) of the residue on silica gel provided the bromocarbazole **3** as a light brown solid, 754 mg (93%). Recrystallization from hexane afforded colorless crystals, mp 130–131 °C. UV (MeOH): λ = 224, 246, 268, 298, 336, 348 nm. IR (drift): ν = 3331, 2937, 1712, 1609, 1505, 1453, 1399, 1287, 1251, 1162, 1057, 1008, 803, 618 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.29 (d, *J* = 6.3 Hz, 3 H), 2.16 (s, 3 H), 2.39 (s, 3 H), 3.00 (dd, *J* = 13.7, 10.2 Hz, 1 H), 3.20 (dd, *J* = 13.7, 2.6 Hz, 1 H), 3.86 (s, 3 H), 4.11 (s, 3 H), 4.99 (m, 1 H), 7.35 (d, *J* = 8.6 Hz, 1 H), 7.45 (dd, *J* = 8.6, 2.0 Hz, 1 H), 8.32 (d, *J* = 2.0 Hz, 1 H), 9.77 (br s, 1 H). ^{13}C NMR and DEPT (100 MHz, $CDCl_3$): δ = 12.85 (CH_3), 19.34 (CH_3), 21.50 (CH_3), 35.01 (CH_2), 60.44 (CH_3), 60.88 (CH_3), 71.97 (CH), 111.74 (C), 112.02 (CH), 113.49 (C), 113.73 (C), 124.07 (C), 124.83 (CH), 127.77 (CH), 129.60 (C), 137.49 (C), 138.21 (C), 144.21 (C), 146.85 (C), 172.73 (C=O). MS (EI): *m/z* = 421 (100) [M^++2], 419 (98) [M^+], 406 (11), 404 (11), 346 (30), 344 (31), 334 (50), 332 (52), 288 (5), 91 (40), 43 (15). HRMS: *m/z* calcd for $C_{20}H_{22}BrNO_4$ [M^+]: 419.0732; found: 419.0749. Anal. Calcd for $C_{20}H_{22}BrNO_4$: C 57.15, H 5.28, N 3.33. Found: C 57.20, H 5.39, N 3.48%.

1-[3,4-Dimethoxy-2-methyl-6-(3-methyl-2-butenyl)-(9*H*-carbazol-1-yl)]propan-2-yl acetate (22)

Prenyl bromide (**14**) (0.4 mL, 3.5 mmol) was added to a stirred solution of $Ni(CO)_4$ (1.36 mL, 10.5 mmol) in dry and degassed benzene (20 mL) at 60 °C and stirring was continued for 75 min at the same temperature. After cooling to rt, the solvent was removed from the reaction mixture *in vacuo* to afford the red dimeric π-prenylnickel bromide complex **15**. A solution of the bromocarbazole **3** (730 mg, 1.74 mmol) in dry and degassed DMF (12 mL) was added to the nickel complex **15**. The resulting dark red reaction mixture was stirred at 65 °C for 15 h. After cooling to rt, the black reaction mixture was poured into water (50 mL). The aqueous layer was extracted twice with Et_2O (2 × 30 mL). The combined organic layers were subsequently washed with aqueous HCl (5%, 30 mL) and then with water (30 mL). The organic layer was dried over sodium sulfate and the solvent was removed. Flash chromatography (hexane/EtOAc, 2:1) of the residue on silica gel provided the 6-prenylcarbazole **22** as the less polar fraction (R_f = 0.49) and the carbazole **19** as the more polar fraction (R_f = 0.44).

22: Colorless oil, yield: 575 mg (81%). UV (MeOH): λ = 229 (sh), 244, 253 (sh), 265, 285 (sh), 295, 331, 344 nm. IR (KBr): ν = 3340, 2978, 2931, 1715, 1612, 1501, 1446, 1397, 1373, 1303, 1256, 1136, 1108, 1055, 1009, 805, 617 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.28 (d, *J* = 6.3 Hz, 3 H), 1.77 (s, 3 H), 1.79 (s, 3 H), 2.15 (s, 3 H), 2.40 (s, 3 H), 3.00 (dd, *J* = 13.7, 10.0 Hz, 1 H), 3.24 (dd, *J* = 13.7, 3.0 Hz, 1 H), 3.51 (d, *J* = 7.3 Hz, 2 H), 3.88 (s, 3 H), 4.11 (s, 3 H), 5.03 (m, 1 H), 5.44 (br t, *J* = 7.3 Hz, 1 H), 7.21 (dd,

J = 8.2, 1.6 Hz, 1 H), 7.40 (d, *J* = 8.2 Hz, 1 H), 8.01 (br s, 1 H), 9.49 (br s, 1 H). ^{13}C NMR and DEPT (100 MHz, $CDCl_3$): δ = 12.82 (CH_3), 17.92 (CH_3), 19.35 (CH_3), 21.52 (CH_3), 25.84 (CH_3), 34.51 (CH_2), 35.04 (CH_2), 60.45 (CH_3), 61.00 (CH_3), 71.95 (CH), 110.46 (CH), 113.35 (C), 114.52 (C), 121.61 (CH), 122.46 (C), 124.57 (CH), 125.82 (CH), 128.40 (C), 131.64 (C), 132.60 (C), 137.53 (C), 138.09 (C), 144.04 (C), 146.81 (C), 172.49 (C=O). MS (EI): *m/z* = 409 (100) [M^+], 394 (12), 334 (16), 322 (29). HRMS: *m/z* calcd for $C_{25}H_{31}NO_4$ [M^+]: 409.2253; found: 409.2264.

19: Light yellow crystals, yield: 40 mg (7%). Spectral data, see above.

1-[3,4-Dihydro-2-methyl-6-(3-methyl-2-butenyl)-3,4-dioxo-9*H*-carbazol-1-yl]propan-2-yl acetate [(±)-*O*-Acetylcarquinostatin A] (23)

A solution of ceric ammonium nitrate (395 mg, 0.72 mmol) in H_2O (2 mL) was added dropwise to a solution of the 6-prenylcarbazole **22** (97 mg, 0.237 mmol) in MeCN (4 mL) at 0 °C. The resulting mixture was stirred at 0 °C for 15 min, then water (25 mL) was added and stitrring was continued for an additional 15 min at 0 °C. The resulting precipitate was separated by filtration, washed with EtOH (2 × 0.5 mL), then with Et_2O (3 × 1 mL) and dried in vacuo to afford (±)-*O*-acetylcarquinostatin A (**23**), yield: 56 mg (62%); crystallization afforded a brown solid, mp 210–211 °C (EtOAc, hexane). UV (MeOH): λ = 231, 267, 429 nm. IR (drift): ν = 3217, 1733, 1656, 1639, 1620, 1599, 1588, 1475, 1373, 1251 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.33 (d, *J* = 6.2 Hz, 3 H), 1.71 (s, 6 H), 1.83 (s, 3 H), 1.92 (s, 3 H), 2.88 (dd, *J* = 14.0, 4.7 Hz, 1 H), 2.97 (dd, *J* = 14.0, 9.0 Hz, 1 H), 3.38 (d, *J* = 7.3 Hz, 2 H), 5.09 (m, 1 H), 5.31 (br t, *J* = 7.3 Hz, 1 H), 7.05 (dd, *J* = 8.4, 1.4 Hz, 1 H), 7.41 (d, *J* = 8.4 Hz, 1 H), 7.64 (s, 1 H), 12.25 (br s, 1 H). ^{13}C NMR and DEPT (125 MHz, DMSO-d_6): δ = 12.13 (CH_3), 17.71 (CH_3), 20.08 (CH_3), 20.76 (CH_3), 25.54 (CH_3), 33.86 (CH_2), 34.08 (CH_2), 69.12 (CH), 110.84 (C), 113.13 (CH), 119.32 (CH), 123.73 (CH), 125.11 (CH), 125.99 (C), 131.53 (C), 135.20 (C), 135.53 (C), 137.54 (C), 137.70 (C), 145.68 (C), 169.73 (C=O), 172.52 (C=O), 183.53 (C=O). MS (EI): *m/z* = 381 (100) [M^++2], 380 (8) [M^++1], 379 (14) [M^+], 351 (18), 321 (31), 294 (40), 291 (20), 226 (10), 43 (7). HRMS: *m/z* calcd for $C_{23}H_{25}NO_4$ [M^+]: 379.1784; found: 379.1802. Anal. Calcd for $C_{23}H_{25}NO_4$: C 72.80, H 6.64, N 3.69. Found: C 72.33, H 6.68, N 3.51%.

1-[3,4-Dihydro-2-methyl-6-(3-methyl-2-butenyl)-3,4-dioxo-9*H*-carbazol-1-yl]propan-2-ol [(±)-Carquinostatin A] ((±)-1)

A solution of lithium aluminum hydride in THF (1.0 M, 460 μL, 0.46 mmol) was added dropwise to a solution of (±)-*O*-acetylcarquinostatin A (**23**) (69.2 mg, 0.18 mmol) in THF (5 mL) at rt. After stirring for 22.5 h at rt, the mixture was carefully quenched with aqueous HCl (5%, 10 mL). The organic layer was

separated and the aqueous layer was extracted with EtOAc (5 × 20 mL). The combined organic layers were washed with water (2 × 10 mL), dried over sodium sulfate, and the solvent was removed. Hexane (10 mL) and a few drops of EtOAc were added to the residue, the resulting precipitate was separated by filtration, and dried *in vacuo* to afford (±)-carquinostatin A ((±)-**1**), yield: 37.6 mg (61%) as a brown solid, mp 195–196 °C (hexane/EtOAc) (lit.,[3] **1**: mp 144–145 °C). UV (MeOH): λ (ε) = 231 (28800), 268 (26100), 426 (5300) nm. IR (KBr): ν = 3420 (br), 3222, 2972, 1654 (sh), 1639, 1621, 1600, 1587, 1475 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ = 1.23 (d, *J* = 6.1 Hz, 3 H), 1.70 (s, 6 H), 1.91 (s, 3 H), 2.70–2.77 (m, 2 H), 3.37 (d, *J* = 7.4 Hz, 2 H), 3.90–3.97 (m, 1 H), 4.85 (br s, 1 H), 5.31 (br t, *J* = 7.4 Hz, 1 H), 7.03 (dd, *J* = 8.3, 1.5 Hz, 1 H), 7.40 (d, *J* = 8.3 Hz, 1 H), 7.63 (br s, 1 H), 12.10 (br s, 1 H). ^{13}C NMR and DEPT (125 MHz, DMSO-d_6): δ = 12.18 (CH_3), 17.71 (CH_3), 23.75 (CH_3), 25.53 (CH_3), 33.87 (CH_2), 37.69 (CH_2), 65.88 (CH), 110.67 (C), 113.23 (CH), 119.25 (CH), 123.75 (CH), 124.92 (CH), 126.04 (C), 131.49 (C), 134.50 (C), 135.55 (C), 137.40 (C), 139.85 (C), 146.31 (C), 172.69 (C=O), 183.74 (C=O). MS (EI): *m/z* = 339 (100) [M^++2], 338 (8) [M^++1], 337 (19) [M^+], 335 (29), 320 (12), 319 (15), 295 (25), 294 (93), 278 (13), 226 (22). HRMS: *m/z* calcd for $C_{21}H_{23}NO_3$ [M^+]: 337.1678; found: 337.1647. Anal. Calcd for $C_{21}H_{23}NO_3$: C 74.75, H 6.87, N 4.15. Found: C 74.00, H 7.06, N 4.05%.

1-[3,4-Dimethoxy-2-methyl-6-(3-methyl-2-butenyl)-(9*H*-carbazol-1-yl)]propan-2-ol (24)

A solution of KOH (79 mg, 1.41 mmol) in water (0.5 mL) was added dropwise to a solution of the 6-prenylcarbazole **22** (385 mg, 0.94 mmol) in MeOH (4 mL). The reaction mixture was stirred for 3 h at rt. Removal of the solvent and flash chromatography (hexane/EtOAc, 2:1) of the residue on silica gel afforded compound **24**, yield: 328 mg (95%). Recrystallization from pentane/Et_2O (10:1) provided colorless crystals, mp 107–108 °C. UV (MeOH): λ = 230 (sh), 245, 264, 287 (sh), 295, 331, 344 nm. IR (drift): ν = 3372 (br), 2966, 2929, 1611, 1500, 1477, 1396, 1306, 1118, 1059, 1007, 937, 806 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.34 (d, *J* = 6.2 Hz, 3 H), 1.76 (s, 3 H), 1.78 (s, 3 H), 1.85 (br s, 1 H), 2.37 (s, 3 H), 2.94 (dd, *J* = 14.6, 8.4 Hz, 1 H), 3.03 (dd, *J* = 14.6, 3.5 Hz, 1 H), 3.50 (d, *J* = 7.3 Hz, 2 H), 3.88 (s, 3 H), 4.10 (s, 3 H), 4.17 (m, 1 H), 5.43 (br t, *J* = 7.3 Hz, 1 H), 7.18 (dd, *J* = 8.2, 1.6 Hz, 1 H), 7.29 (d, *J* = 8.2 Hz, 1 H), 8.01 (s, 1 H), 8.47 (br s, 1 H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 12.64 (CH_3), 17.89 (CH_3), 23.46 (CH_3), 25.80 (CH_3), 34.47 (CH_2), 37.99 (CH_2), 60.44 (CH_3), 60.99 (CH_3), 68.92 (CH), 110.41 (CH), 114.95 (C), 115.10 (C), 121.74 (CH), 122.94 (C), 124.48 (CH), 125.80 (CH), 128.87 (C), 131.71 (C), 132.90 (C), 138. 25 (C), 138.28 (C), 144.36 (C), 146.62 (C). MS (EI): *m/z* = 367 (100) [M^+], 352 (30), 323 (17), 322 (78). HRMS: *m/z* calcd for $C_{23}H_{29}NO_3$ [M^+]: 367.2147; found: 367.2133. Anal. Calcd for $C_{23}H_{29}NO_3$: C 75.17, H 7.95, N 3.81. Found: C 75.06, H 7.93, N 3.36%.

1-[3,4-Dihydro-2-methyl-6-(3-methyl-2-butenyl)-3,4-dioxo-9*H*-carbazol-1-yl]propan-2-ol [(±)-Carquinostatin A] ((±)-1)

A solution of ceric ammonium nitrate (444 mg, 0.81 mmol) in water (2 mL) was added dropwise to a stirred solution of the carbazole **24** (99 mg, 0.27 mmol) in MeCN (4 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min, then water (40 mL) was added dropwise and stirring was continued for additional 5 min at 0 °C. The precipitate was isolated by filtration, washed with water and dried *in vacuo* to afford a brown solid (86 mg). The brown solid was dissolved in acetone (40 mL) and then preadsorbed on silica gel (3 g). Purification by flash chromatography (EtOAc/MeOH, 10:1) on silica gel provided (±)-carquinostatin A ((±)-**1**), yield: 58 mg (64%). Recrystallization from EtOH (10 mL) at –30 °C afforded a brown solid, mp 203–204 °C (decomp.) (lit.,[3] **1**: mp 144–145 °C). Spectral data: see above.

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