Synthesis of New Hydroxybenzo[*a*]carbazoles

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Abstract: An investigation of the alkylation sites of 4,7-dihydroxybenzo[*a*]pyrrolo[3,4-*c*]carbazole-1,3(2*H*,8*H*)-dione, as well as the site of reduction in the maleimide upper ring, was carried out which resulted in the synthesis of diversely substituted 4-hydroxybenzo[*a*]pyrrolo[3,4-*c*]carbazoles. Moreover, the synthesis of 5,6-dicyano-1,4-dihydroxy-11*H*-benzo[*a*]carbazole was performed in which the maleimide ring of the above scaffold is missing and is replaced by electron-withdrawing nitrile groups.

Key words: fused-ring systems, Diels–Alder reactions, alkylations, reductions, nitriles

A number of biologically active compounds possess a benzo[*a*]carbazole framework. According to their substituents, these compounds can exhibit antifungal and antitumor activities,[1–4] antiestrogenic properties,[5] or kinase inhibitory activities.[6–8] Various approaches have been reported for the synthesis of benzo[*a*]carbazoles including photocyclization, palladium-catalyzed cross-coupling reactions, Fischer indolization, Diels–Alder reactions, and irradiation of a benzotriazole derivative.[9,10] In the course of studies on benzo[*a*]carbazoles, we were interested in the synthesis of 4,7-dihydroxybenzo[*a*]pyrrolo[3,4-*c*]carbazole and its derivatives (Figure 1).[7,8] In this paper, we report synthetic studies aimed at investigating the alkylation sites of 4,7-dihydroxybenzo[*a*]pyrrolo[3,4-*c*]carbazole-1,3(2*H*,8*H*)-dione, as well as the site of reduction in the maleimide upper ring. For this purpose, two alkyl groups were introduced and the alkylation sites were determined by 2D NMR experiments. Then, the site of reduction in the maleimide upper ring was investigated using several reducing agents. The synthesis of a benzo[*a*]carbazole **9** without the maleimide ring but bearing two nitrile groups instead of the carbonyl groups of the previous scaffold was also carried out (Figure 1).

2-Benzyl-7-(benzyloxy)-4-hydroxybenzo[*a*]pyrrolo[3,4-*c*]carbazole-1,3(2*H*,8*H*)-dione (**1**) and 4-hydroxy-7-methoxy-2-methylbenzo[*a*]pyrrolo[3,4-*c*]carbazole-1,3(2*H*,8*H*)-dione (**2**) were obtained by reaction of diphenol **C** with 4–5 equivalents of benzyl bromide or methyl iodide in the presence of potassium carbonate (Scheme 1). Diphenol **C** was synthesized from indolylmaleimide **A** via a Diels–Alder cycloaddition/oxidation with 1,4-benzoquinone followed by reduction using sodium dithionite.[7] Despite a

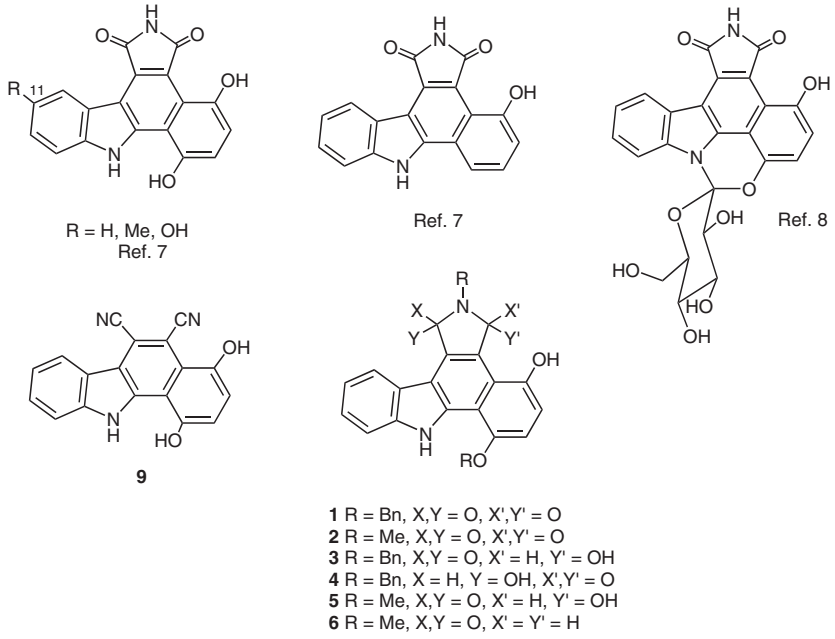

Figure 1

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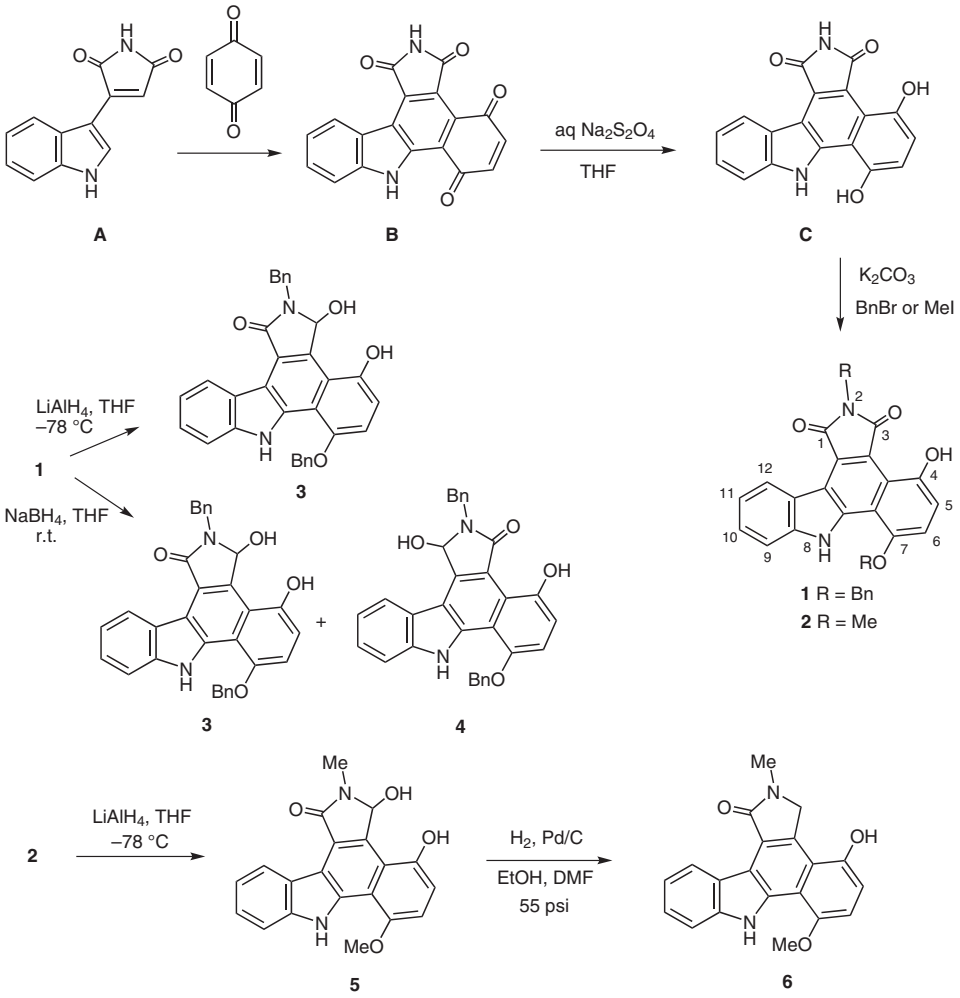


Scheme 1 Synthetic scheme for compounds **1**–**6**

large excess of the base and the alkyl halide, substitution of diphenol **C** with benzyl and methyl groups occurred on the imide nitrogen and on the hydroxy group at the 7-position, but not on the hydroxy group at the 4-position, probably because of a hydrogen bond between the hydroxy group and the oxygen of the carbonyl at the 3-position.

To confirm the hypothesis of a hydrogen bond between the oxygen of the carbonyl at the 3-position and the hydrogen of the hydroxy group at the 4-position, that prevents alkylation of this hydroxy group, conformational analysis was performed using the Monte Carlo Multiple Method with MM3 force field of Macromodel 7.0 program. Indeed, two intramolecular hydrogen bonds were found in compound **C** (Figure 2), one between the indolic NH and the oxygen of the hydroxy group at the 7-position (1.98 Å) and a second between the hydrogen of the hydroxy group at the 4-position and the carbonyl at the 3-position (1.79 Å).

The structure of compound **1** has been confirmed by 2D NMR experiments after the reduction step leading to **3** and/or **4**. Reduction of compound **1** using lithium aluminum hydride at –78 °C provided only compound **3** in a

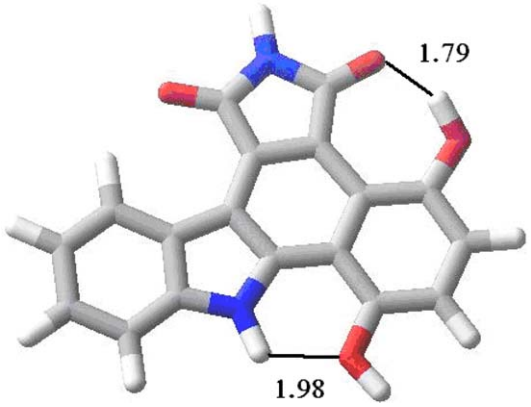


Figure 2 Conformational analysis of compound **C**: hydrogen bonds are shown as thin solid lines

quantitative yield, whereas reduction of **1** with sodium borohydride at room temperature yielded regioisomers **3** and **4** in 60% and 28% yield, respectively (Scheme 1). The structures of compounds **3** and **4** were assigned from NMR experiments (^{1}H,^{1}H-COSY, HSQC, HMBC, 2D-NOESY) (Figure 3). The position of the benzyl group on one of the phenol functions was determined by NOESY

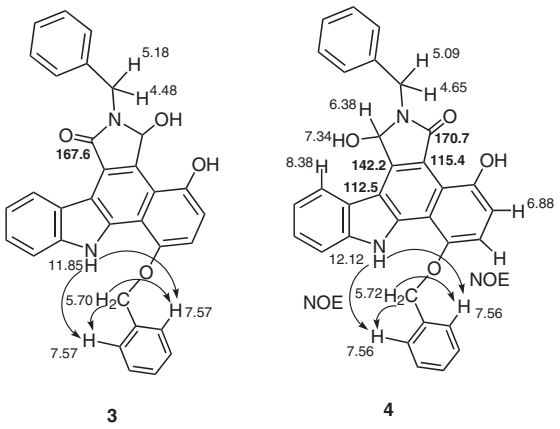
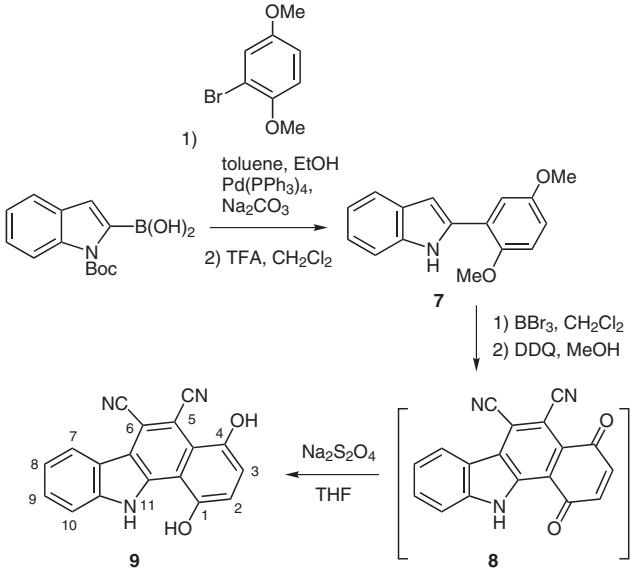


Figure 3 Assignment of the structures of compounds **3** and **4**



Scheme 2 Synthetic scheme for compound **9**

experiments. NOE effects were observed between the indole NH proton at 12.12 ppm in compound **4** and at 11.85 ppm in compound **3** and the aromatic protons in the *ortho* position of the benzyl group at 7.56 ppm in compound **4** and at 7.57 ppm in compound **3**, indicating that the benzyl group was fixed to the oxygen at the 7-position. NOE effects were also observed between these aromatic protons and the methylenic protons of the benzyl group at 5.72 and at 5.70 ppm in compounds **4** and **3**, respectively. ^{1}H,^{13}C-HMBC experiments showed that the second benzyl group was attached to the nitrogen of the hydroxylactam. Indeed, ^{3}J couplings were observed between the methylenic protons of the benzyl group (at 4.48 and 5.18 ppm in compound **3** and at 4.65 and 5.09 ppm in compound **4**) and the carbonyl of the hydroxylactam at 167.6 and at 170.7 ppm in compounds **3** and **4**, respectively. Moreover, the orientation of the hydroxy group of the hydroxylactam was determined by ^{1}H,^{13}C-HMBC experiments on compound **4** based on several couplings:

(i) ^{3}J Couplings were observed between the quaternary carbon at 112.5 ppm and the CH proton of the hydroxylactam at 6.38 ppm and the aromatic proton of the indole moiety at 8.38 ppm.

(ii) The quaternary carbon at 142.2 ppm could be assigned on account of ^{3}J coupling with the proton of the hydroxy at 7.34 ppm, ^{2}J coupling with the proton of the hydroxylactam at 6.38 ppm, and ^{4}J coupling (weak) with the NH indolic proton at 12.12 ppm. It can be noticed that if the structure of compound **4** was that of its regioisomer **3**, coupling between the indolic NH proton and this quaternary carbon would be a ^{5}J coupling that is rarely observed.

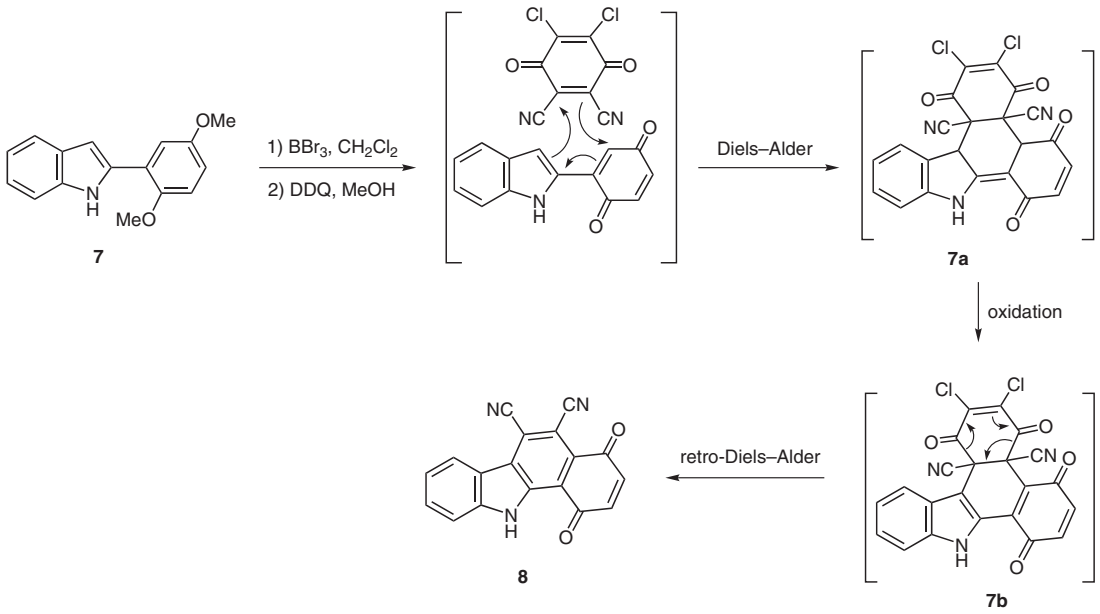
(iii) Two couplings were also found with the quaternary carbon at 115.4 ppm: a ^{3}J coupling with the proton of the hydroxylactam at 6.38 ppm and a ^{4}J coupling (weak) with the aromatic proton of the phenolic moiety at 6.88 ppm.

When lithium aluminum hydride or sodium borohydride is used, a complex could be formed between the carbonyl at the 3-position, the metal, and the oxygen atom at the 4-position, that could guide the approach of the hydride toward the carbon of the carbonyl at the 3-position, leading to hydroxylactam **3** as the unique or the major regioisomer. With sodium borohydride, a weaker complexation leads to the formation of both regioisomers.

Reduction of compound **2** using lithium aluminum hydride in tetrahydrofuran at –78 °C gave hydroxylactam **5** in a quantitative yield. Reduction of **5** by catalytic hydrogenation on Pd/C at 55 psi in an ethanol–*N*,*N*-dimethylformamide mixture yielded lactam **6** (Scheme 1).

For the synthesis of 5,6-dicyano-1,4-dihydroxy-11*H*-benzo[*a*]carbazole (**9**), we first tried a Suzuki coupling reaction between *N*-Boc-1*H*-indol-2-ylboronic acid and 2-bromo-1,4-benzoquinone. The *N*-Boc-1*H*-indol-2-ylboronic acid was prepared by reaction of *N*-Boc-1*H*-indole with lithium diisopropylamide, then quenching with triisopropyl borate, according to the method described by Vazquez and co-workers.[11] The Suzuki coupling with 2-bromo-1,4-benzoquinone failed, probably because of oxidation of the catalyst by the quinone. Therefore, the Suzuki coupling was carried out using commercially available 2-bromo-1,4-dimethoxybenzene, followed by removal of the Boc protecting group with trifluoroacetic acid, which gave the coupling product **7** (Scheme 2). Demethylation was performed using boron tribromide, then reaction with a large excess of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) led to quinone **8** which was further reduced to hydroquinone **9** using aqueous sodium dithionite. The proposed mechanism leading to the formation of compound **8** is outlined in Scheme 3. After demethylation of compound **7** and oxidation to the quinone, a second molecule of DDQ could give rise to a Diels–Alder reaction[12,13] leading to intermediate **7a**. Then, after oxidation to **7b**, a retro-Diels–Alder reaction could lead to compound **8**. The presence of C≡N bonds was confirmed by a large absorption band at 2228 cm^{-1} in the IR spectrum of intermediate **8** and at 2225 cm^{-1} in the IR spectrum of compound **9**.

In conclusion, this work was focused on an examination of the sites of alkylation and reduction of maleimido-4,7-



Scheme 3 Proposed mechanism for the formation of compound **8**

dihydroxybenzo[*a*]carbazoles. The results give an insight into the possible chemical modifications compatible with the interaction with biological targets. 5,6-Dicyano-1,4-dihydroxy-11*H*-benzo[*a*]carbazole, possessing two nitrile groups instead of the two carbonyl groups of the previous framework, was synthesized via a Diels–Alder cycloaddition between DDQ and 2-(2,5-dimethoxyphenyl)-1*H*-indole obtained by a Suzuki coupling reaction.

IR spectra were recorded on a Perkin–Elmer Paragon 500 spectrometer. NMR spectra were recorded on a Bruker Avance 400 and Avance 500 (for the HMBC experiments) instruments (chemical shifts δ in ppm); the following abbreviations are used: singlet (s), broad signal (br s), doublet (d), doublet of doublets (dd), triplet (t), doublet of triplets (dt), multiplet (m), tertiary carbons (C tert), quaternary carbons (C quat). High-resolution mass spectra (ESI+) were determined on a high-resolution Waters Micro Q-Tof apparatus. Chromatographic purifications were performed using silica gel [Geduran SI 60 (Merck), 0.040–0.063 mm] flash column chromatography.

Conformational analysis was performed using the Monte Carlo Multiple Method[14] with MM3 force field[15] of Macromodel 7.0 program (Macromodel 7.0, Schrödinger Inc., 1500 SW First Ave, Suite 1180, Portland, OR 97201, USA).

2-Benzyl-7-(benzyloxy)-4-hydroxybenzo[*a*]pyrrolo[3,4-*c*]carbazole-1,3(2*H*,8*H*)-dione (1)

To a soln of diphenol **C**[7] (70 mg, 0.22 mmol) in acetone (1.5 mL) were added K_2CO_3 (181 mg, 1.32 mmol) and BnBr (124 μL, 1.06 mmol). The mixture was refluxed for 3 h. After cooling, aq 1 N HCl was added until acidic pH. After extraction with EtOAc (3 ×), the organic phase was dried ($MgSO_4$). The solvent was removed and the residue was purified by flash chromatography (cyclohexane–EtOAc, 9:1 →7:3) to give **1** (88 mg, 0.18 mmol, 80% yield) as a red solid; mp >280 °C.

IR (KBr): 1668 and 1752 (C=O), 3300–3600 cm^{-1} (NH, OH).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 4.95 (s, 2 H), 5.73 (s, 2 H), 6.98–7.63 (m, 14 H), 7.97 (d, *J* = 8.0 Hz, 1 H), 9.03 (d, *J* = 8.0 Hz, 1 H), 11.70 (br s, 1 H), 12.33 (s, 1 H).

Due to the insolubility of **1**, its ^{13}C NMR spectrum could not be recorded.

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $C_{32}H_{23}N_2O_4$: 499.1658; found: 499.1635.

4-Hydroxy-7-methoxy-2-methylbenzo[*a*]pyrrolo[3,4-*c*]carbazole-1,3(2*H*,8*H*)-dione (2)

To a soln of diphenol **C**[7] (200 mg, 0.63 mmol) in acetone (6 mL) were added K_2CO_3 (348 mg, 2.52 mmol) and MeI (150 μL, 2.52 mmol). The mixture was refluxed for 3 h. After cooling, aq 1 N HCl was added until acidic pH. After extraction with EtOAc (3 ×), the organic phase was dried ($MgSO_4$). The solvent was removed and the residue was purified by flash chromatography (cyclohexane–EtOAc, 8:2 →1:1) to give **2** (193 mg, 0.56 mmol, 89% yield) as a red solid; mp >280 °C.

IR (KBr): 1610 (C=C), 1669 and 1751 (C=O), 3300–3600 cm^{-1} (NH, OH).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.08 (s, 3 H), 4.07 (s, 3 H), 6.93 (d, *J* = 8.5 Hz, 1 H), 7.10 (d, *J* = 8.5 Hz, 1 H), 7.37 (t, *J* = 7.5 Hz, 1 H), 7.57 (t, *J* = 7.5 Hz, 1 H), 7.89 (d, *J* = 8.0 Hz, 1 H), 8.88 (d, *J* = 8.0 Hz, 1 H), 11.58 (s, 1 H), 11.93 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 24.0 and 55.9 (CH_3), 108.7, 112.5, 112.9, 120.7, 123.7, and 126.4 (C tert), 112.0, 114.2, 116.4, 117.7, 119.7, 127.2, 139.6, 139.7, 146.9, and 148.6 (C quat), 168.3 and 173.7 (C=O).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{15}N_2O_4$: 347.1032; found: 347.1031.

2-Benzyl-7-(benzyloxy)-3,8-dihydro-3,4-dihydroxybenzo[*a*]pyrrolo[3,4-*c*]carbazol-1(2*H*)-one (3)

To a soln of compound **1** (100 mg, 0.20 mmol) in THF (9 mL) at –78 °C was added 2 M $LiAlH_4$ in THF (500 μL). The mixture was stirred at –78 °C for 3 h, then aq 1 N HCl was added until acidic pH. After extraction with EtOAc (3 ×), the organic phase was washed with brine, then dried ($MgSO_4$). The solvent was removed to give **3** (100 mg, 0.20 mmol, 100% yield) as a beige solid; mp >280 °C.

IR (KBr): 1670 (C=O), 3400–3600 cm^{-1} (NH, OH).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 4.48 (d, *J* = 15.5 Hz, 1 H), 5.18 (d, *J* = 15.5 Hz, 1 H), 5.70 (s, 2 H), 6.36 (d, *J* = 7.0 Hz, 1 H, C*H*OH),

6.40 (d, *J* = 7.0 Hz, 1 H, CHO*H*), 6.88 (d, *J* = 8.5 Hz, 2 H), 7.07 (t, *J* = 8.5 Hz, 1 H), 7.29–7.45 (m, 8 H), 7.49 (dt, J_1 = 7.0 Hz, J_2 = 1.0 Hz, 1 H), 7.57 (d, *J* = 7.0 Hz, 2 H), 7.88 (d, *J* = 8.0 Hz, 1 H), 9.29 (d, *J* = 8.0 Hz, 1 H), 9.98 (s, 1 H), 11.85 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 42.2 and 69.1 (CH_2), 81.6, 109.7, 110.1, 111.8, 119.3, 124.7, 125.0, 127.1, 127.2 (2 C), 127.6 (3 C), 128.4 (2 C), and 128.5 (2 C) (C tert), 112.2, 115.6, 118.6, 120.9, 124.9, 133.8, 135.4, 137.5, 138.2, 138.8, 146.8, and 147.8 (C quat), 167.6 (C=O).

HRMS (ESI+): *m*/*z* [M + H – H_2O]$^+$ calcd for $C_{32}H_{23}N_2O_3$: 483.1709; found: 483.1703.

2-Benzyl-7-(benzyloxy)-1,8-dihydro-1,4-dihydroxybenzo[*a*]pyrrolo[3,4-*c*]carbazol-3(2*H*)-one (4)

To a soln of compound **1** (50 mg, 0.10 mmol) in THF (2 mL) at 0 °C was added $NaBH_4$ (4 mg, 0.10 mmol). The mixture was stirred at r.t. for 4 h. Aq 1 N HCl was added until acidic pH. After extraction with EtOAc (3 ×), the organic phase was washed with brine, then dried ($MgSO_4$). The solvent was removed and the residue was purified by flash chromatography (cyclohexane–EtOAc, 9:1 → 1:1). Both regioisomers were isolated as beige solids: compound **3** (30 mg, 0.060 mmol, 60% yield) and compound **4** (14 mg, 0.028 mmol, 28% yield); mp >280 °C.

IR (KBr): 1670 (C=O), 3300–3600 cm^{-1} (NH, OH).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 4.65 (d, *J* = 15.5 Hz, 1 H), 5.09 (d, *J* = 15.5 Hz, 1 H), 5.72 (s, 2 H), 6.38 (d, *J* = 10.0 Hz, 1 H, C*H*OH), 6.88 (d, *J* = 8.5 Hz, 1 H), 7.15 (d, *J* = 8.5 Hz, 1 H), 7.28–7.43 (m, 8 H), 7.47 (d, *J* = 7.5 Hz, 2 H), 7.53–7.57 (m, 3 H), 7.93 (d, *J* = 8.0 Hz, 1 H), 8.38 (d, *J* = 8.0 Hz, 1 H), 12.12 (s, 1 H), 13.22 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 43.0 and 69.2 (CH_2), 81.1, 109.9, 112.2, 112.4, 120.3, 122.5, 125.3, 127.1 (2 C), 127.3, 127.6, 127.7 (2 C), 128.5 (2 C), and 128.6 (2 C) (C tert), 112.5, 114.4, 115.4, 118.5, 120.3, 137.3, 137.5, 137.9, 139.0, 142.2, 146.5, and 148.8 (C quat), 170.7 (C=O).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $C_{32}H_{25}N_2O_4$: 501.1814; found: 501.1805.

3,8-Dihydro-3,4-dihydroxy-7-methoxy-2-methylbenzo[*a*]pyrrolo[3,4-*c*]carbazol-1(2*H*)-one (5)

To a soln of compound **2** (70 mg, 0.20 mmol) in THF (9 mL) at –78 °C was added 2 M $LiAlH_4$ in THF (500 μL). The mixture was stirred at –78 °C for 20 min, then aq 1 N HCl was added until acidic pH. After extraction with EtOAc (3 ×), the organic phase was washed with brine, then dried ($MgSO_4$). The solvent was removed to give **5** (70 mg, 0.20 mmol, 100% yield) as a beige solid; mp >280 °C.

IR (KBr): 1619, 1637, 1679, and 1697 (C=C, C=O), 3300–3600 cm^{-1} (NH, OH).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.14 (s, 3 H), 4.16 (s, 3 H), 6.43 (d, *J* = 7.5 Hz, 1 H), 6.48 (d, *J* = 7.5 Hz, 1 H), 7.05 (d, *J* = 8.5 Hz, 1 H), 7.16 (d, *J* = 8.5 Hz, 1 H), 7.28 (dt, J_1 = 6.5 Hz, J_2 = 1.0 Hz, 1 H), 7.47 (dt, J_1 = 8.0 Hz, J_2 = 1.0 Hz, 1 H), 7.87 (d, *J* = 8.0 Hz, 1 H), 9.25 (d, *J* = 8.0 Hz, 1 H), 10.06 (s, 1 H), 11.74 (s, 1 H).

Due to the insolubility of **5**, its ^{13}C NMR spectrum could not be recorded.

HRMS (ESI+): *m*/*z* [M + H – H_2O]$^+$ calcd for $C_{20}H_{15}N_2O_3$: 331.1083; found: 331.1089.

3,8-Dihydro-4-hydroxy-7-methoxy-2-methylbenzo[*a*]pyrrolo[3,4-*c*]carbazol-1(2*H*)-one (6)

A soln of hydroxylactam **5** (63 mg, 0.18 mmol) in EtOH–DMF (50 mL:5 mL) was hydrogenated for 24 h (55 psi) in the presence of 10% Pd/C (19 mg). The mixture was filtered over Celite®, then the solvent was removed. The residue was purified by flash chromatography (cyclohexane–EtOAc, 1:1) to give compound **6** (30 mg, 0.09 mmol, 50% yield) as a brown solid; mp >280 °C.

IR (KBr): 1619, 1640, and 1697 (C=C, C=O), 3300–3600 cm^{-1} (NH, OH).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.39 (s, 3 H), 4.15 (s, 3 H), 5.09 (s, 2 H), 7.01 (d, *J* = 8.5 Hz, 1 H), 7.13 (d, *J* = 8.5 Hz, 1 H), 7.26 (t, *J* = 7.5 Hz, 1 H), 7.44 (t, *J* = 8.0 Hz, 1 H), 7.85 (d, *J* = 8.0 Hz, 1 H), 9.32 (d, *J* = 8.0 Hz, 1 H), 10.07 (s, 1 H), 11.65 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 29.0 and 55.8 (CH_3), 54.9 (CH_2), 107.1, 109.0, 111.7, 118.9, 124.5, and 124.8 (C tert), 112.6, 114.7, 118.4, 121.1, 125.6, 131.5, 134.0, 138.5, 148.5, and 148.7 (C quat), 168.5 (C=O).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{17}N_2O_3$: 333.1233; found: 333.1233.

2-(2,5-Dimethoxyphenyl)-1*H*-indole (7)

To a mixture of 2-bromo-1,4-dimethoxybenzene (1.00 g, 4.62 mmol) and $Pd(PPh_3)_4$ (432 mg, 0.37 mmol) in toluene (27 mL) was added *N*-Boc-1*H*-indol-2-ylboronic acid (2.35 g, 9.24 mmol) in EtOH (13 mL). Then, a soln of Na_2CO_3 (3.61 g) in H_2O (6.7 mL) was added and the mixture was refluxed for 3 h. After cooling, H_2O was added. After extraction with EtOAc (3 ×), the organic phase was dried ($MgSO_4$). The solvent was removed and the residue was purified by flash chromatography (cyclohexane → cyclohexane–EtOAc, 9:1). The coupling product mixed with 2-bromo-1,4-dimethoxybenzene (850 mg) was dissolved in CH_2Cl_2 (9 mL) and stirred at r.t. for 18 h in the presence of TFA (8 mL). H_2O was added. After extraction with CH_2Cl_2 (3 ×), the organic phase was dried ($MgSO_4$). The solvent was removed and the residue was purified by flash chromatography (cyclohexane–EtOAc, 9:1) to give compound **7** (407 mg, 1.61 mmol, 35% yield) as a beige solid; mp 85 °C.

IR (KBr): 1617 and 1638 (C=C), 3300–3600 cm^{-1} (NH).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.86 (s, 3 H), 3.98 (s, 3 H), 6.85 (dd, J_1 = 9.0 Hz, J_2 = 3.0 Hz, 1 H), 6.91 (dd, J_1 = 1.0 Hz, J_2 = 0.5 Hz, 1 H), 6.97 (d, *J* = 9.0 Hz, 1 H), 7.12 (dt, J_1 = 7.0 Hz, J_2 = 1.0 Hz, 1 H), 7.20 (dt, J_1 = 7.0 Hz, J_2 = 1.0 Hz, 1 H), 7.40 (d, *J* = 3.0 Hz, 1 H), 7.43 (dd, J_1 = 8.5 Hz, J_2 = 0.5 Hz, 1 H), 7.65 (d, *J* = 8.0 Hz, 1 H), 9.75 (br s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.8 and 56.6 (CH_3), 99.9, 111.0, 113.3, 113.4, 113.7, 119.8, 120.3, and 122.0 (C tert), 121.4, 128.0, 135.8, and 136.2 (C quat), 150.3 and 154.2 (C–O).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{16}NO_2$: 254.1181; found: 254.1190.

5,6-Dicyano-1,4-dihydroxy-11*H*-benzo[*a*]carbazole (9)

A 1 M soln of BBr_3 in CH_2Cl_2 (800 μL) was added dropwise to a soln of compound **7** (50 mg, 0.20 mmol) in CH_2Cl_2 (5 mL) at –78 °C. The mixture was stirred at r.t. for 12 h. The mixture was cooled to 0 °C and H_2O was added. After extraction with EtOAc (3 ×), the organic phase was dried ($MgSO_4$). The solvents were removed, the residue was dissolved in MeOH (5 mL), and the solution was refluxed for 30 min in the presence of DDQ (816 mg, 3.6 mmol). The solvent was removed and EtOAc was added to the residue. The mixture was filtered and the solid was washed with EtOAc to yield intermediate **8**. A soln of $Na_2S_2O_4$ (70 mg, 0.40 mmol) in H_2O (500 μL) was added to a soln of quinone **8** in THF (2 mL). The mixture was stirred at r.t. for 4 h. The solvent was removed and the residue was purified by flash chromatography (EtOAc–cyclohexane, 7:3) to give **9** (31 mg, 0.10 mmol, 52% yield) as a beige solid; mp >280 °C.

IR (KBr): 1618, 1638, and 1657 (C=C), 2225 (C≡N), 3000–3600 cm^{-1} (NH, OH).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.08 (d, J = 8.0 Hz, 1 H), 7.20 (d, J = 8.0 Hz, 1 H), 7.46 (dt, J_1 = 7.0 Hz, J_2 = 1.0 Hz, 1 H), 7.61 (dt, J_1 = 8.0 Hz, J_2 = 1.0 Hz, 1 H), 8.03 (d, J = 8.0 Hz, 1 H), 8.47 (d, J = 8.0 Hz, 1 H), 10.49 (s, 1 H), 10.84 (s, 1 H), 12.31 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 101.3, 110.2, 113.5, 114.6, 116.7, 118.2, 119.4, 120.4, 136.9, 139.4, 145.6, and 146.6 (C quat), 112.5, 113.4, 113.5, 119.0, 121.1, and 126.4 (C tert).

HRMS (ESI+): m/z [M + H]$^+$ calcd for $C_{18}H_{10}N_3O_2$: 300.0773; found: 300.0775.

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