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Indoloquinones - 3.[1] Palladium-Promoted Synthesis of Hydroxy-Substituted 5-Cyano-5*H*-benzo[*b*]carbazole-6,11-diones

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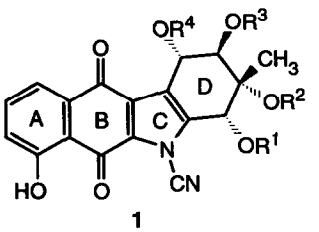
Abstract: A short synthesis of hydroxy-substituted benzo[*b*]carbazoloquinone cyanamides based on a palladium-promoted oxidative coupling as the key step is described. Pyridine hydrochloride has been used for chemoselective cleavage of a methyl ether in the presence of an *N*-cyano group.

Introduction

The kinamycin antibiotics, first reported in 1970, were isolated from *Streptomyces murayamaensis*[2,3] and more recently, from other actinomycetes.[4] These antibiotics are strongly active against Gram-positive and less active against Gram-negative bacteria. They also exhibit modest antitumour properties.[2,3] Omura and coworkers proposed the structure **1** for the kinamycin family, based on chemical and spectroscopic data,[2] and an X-ray analysis[2d] of the *p*-bromobenzoate of kinamycin C. The unusual structural features associated with the supposed alkaloids **1**, such as the cyanamide and the benzo[*b*]carbazole ring system have stimulated considerable interest in the biosynthesis[5] and the chemical synthesis[1,6-10] of the kinamycins.

	R^1	R^2	R^3	R^4
1 A	Ac	Ac	Ac	H
1 B	H	Ac	H	H
1 C	Ac	H	Ac	Ac
1 D	Ac	H	Ac	H
1 E	Ac	H	H	H
1 F	H	H	H	H



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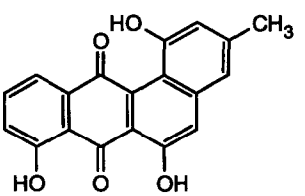

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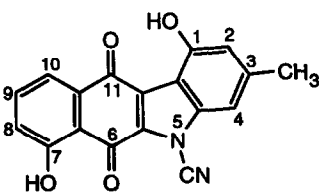
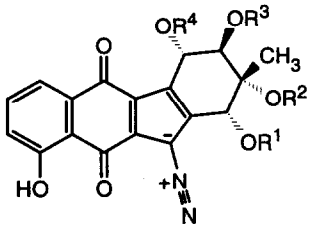
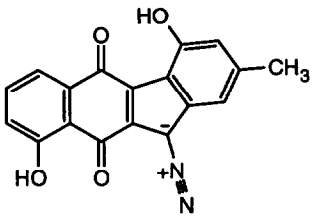


3

Extensive studies by Gould on the biosynthesis of these antibiotics established that they are derived from a single chain decaketide precursor and that dehydrorabelomycin **2**, is a crucial intermediate.[5] Gould and co-workers isolated and characterized a number of intermediates including the biogenetic precursor prekinamycin which was assigned structure **3**.[3] In 1993, Echavarren reported the first synthesis of compound **3**.[6] However, the spectral data of the synthetic compound were not in agreement with those described by Gould for the corresponding natural product (prekinamycin).[3] The ^{13}C-NMR signals of the *N*-cyano groups reported by Echavarren were in the range of 115-123 ppm,[6] whereas for kinamycin D[5e] the resonance for this carbon was observed at 78.5 ppm. From a number of *N*-cyanoindoloquinones synthesized by Dmitrienko, it was clear that the IR bands due to the *N*-cyano group appear in the range of 2237-2259 cm^{-1} and that the ^{13}C-NMR resonances for the *N*-cyano carbons show up at δ 104-109 ppm.[7] We recently described the palladium-promoted synthesis of a 7-deoxyprekinamycin isomer.[1] The IR stretching band of the *N*-cyano group of our derivative[1] appeared at 2252 cm^{-1}, which is in agreement with the data reported for related compounds[7] by Dmitrienko. We found the signal for the *N*-cyano carbon at 106 ppm and therefore, our data are more in agreement with Dmitrienko's rather than those of Echavarren. However, the IR bands assigned to the *N*-cyano moiety of the kinamycins were found in the region of 2119-2170 cm^{-1}.[2-4] More recently, Gould[11] and Dmitrienko[7c] both have reexamined the structures of the kinamycins and of prekinamycin. Gould has unequivocally confirmed the structure of the kinamycins by an X-ray crystal structure determination of the (+)-α-methylbutyrate of kinamycin D with refinements, which demonstrate that the kinamycins and prekinamycin are not benzo[*b*]carbazole cyanamides but 5-diazobenzo[*b*]fluorenes.[11a] The revised structures of the kinamycins and of prekinamycin (**4**), which are shown below, fit well with the observed spectroscopic data. The ^{13}C-NMR signals of the diazo carbon atoms show up in the range of δ 63-93 ppm and the IR values for the diazo bands of diazo model compounds fall in the range of 2065-2200 cm^{-1}. The kinamycins differ from each other only in the oxygen substituents, and the substitution pattern of the D-ring is the same as originally reported for compound **1** (see above).



kinamycin

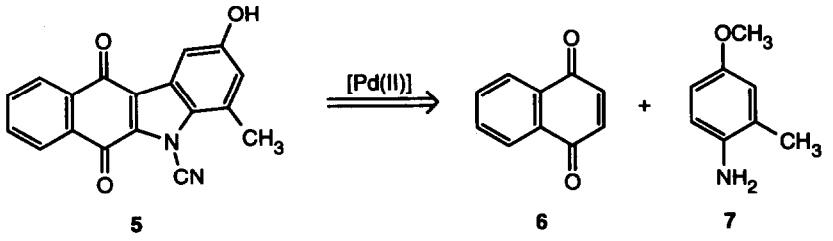


prekinamycin (4)

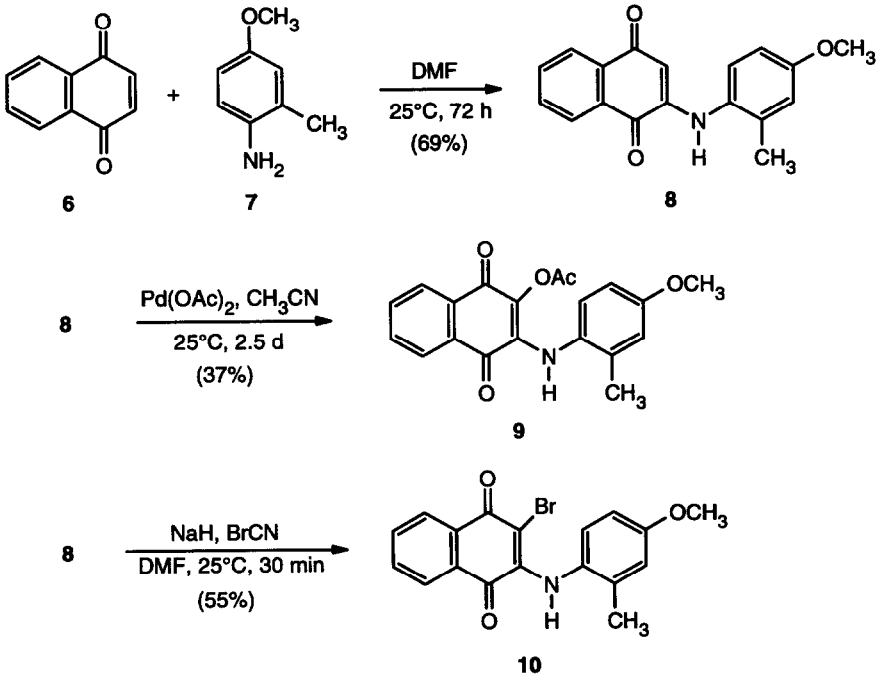
Several syntheses of 5*H*-benzo[*b*]carbazole-6,11-diones have been reported previously.[6-9,10b,12] In this paper we describe a short synthesis of hydroxy-substituted 5-cyano-5*H*-benzo[*b*]carbazole-6,11-diones using a palladium-promoted oxidative coupling as the key step. Pyridine hydrochloride has been used as a chemoselective reagent for the cleavage of aryl methyl ethers of alkaloid quinones in the presence of a cyanamide moiety.

Results and Discussion

Recently, palladium-promoted oxidative couplings have attracted considerable attention because they open up the way to convergent syntheses of carbazole alkaloids. The cyclizations of diarylamines to carbazoles[13] and of 2-anilino-1,4-benzoquinones to carbazoloquinones[12b,14] have been described. Therefore, we decided to elaborate a short synthesis of benzo[*b*]carbazoloquinones based on a palladium-promoted C-C bond formation as the key step. We envisaged that the *N*-cyanobenzo[*b*]carbazoloquinone **5**, which is a regioisomer of the 7-deoxy derivative of **3**, could be prepared by the methodology indicated in the retrosynthesis (Scheme 1). Nucleophilic addition of **7** to **6** followed by the palladium-promoted oxidative coupling should provide the benzo[*b*]carbazoloquinone framework.



Scheme 1



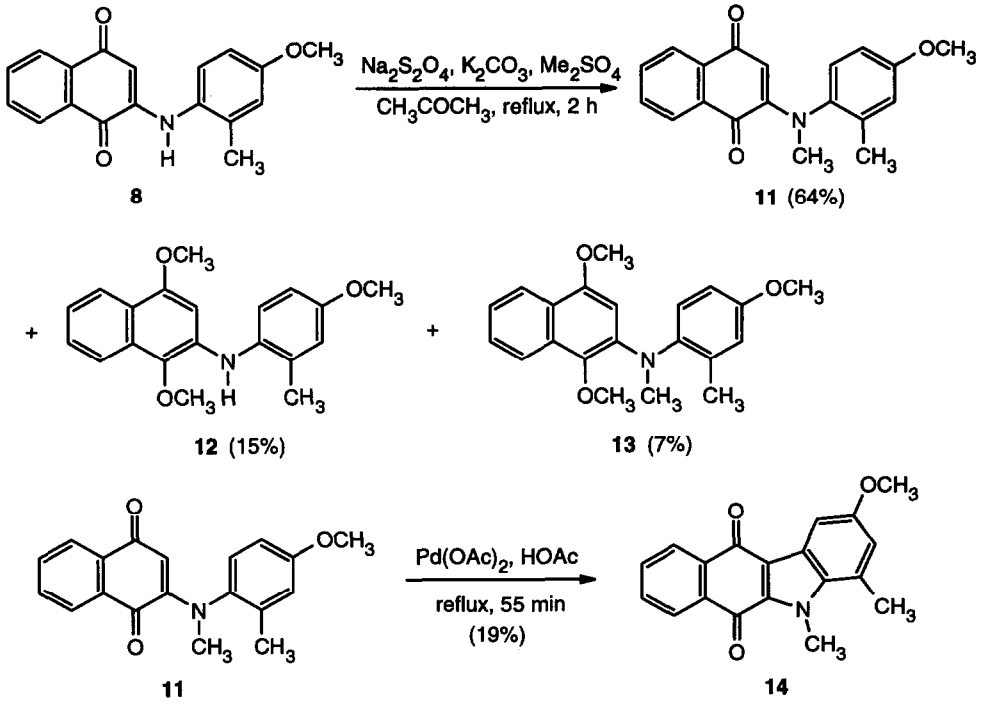
Scheme 2

Reaction of 1,4-naphthoquinone **6** with the commercially available arylamine **7** in DMF at room temperature provided the 2-anilino-1,4-naphthoquinone **8** in 69% yield (Scheme 2). However, the palladium-promoted

cyclization of **8** to the benzo[*b*]carbazoloquinone could not be achieved. A wide variety of reaction conditions either resulted in the formation of decomposition products or gave recovered starting material. The attempt to modify the reaction conditions by performing the palladium-promoted cyclization in acetonitrile at room temperature gave the 2-acetoxy-1,4-naphthoquinone **9** in 37% yield. Compound **9** decomposed on the column and therefore must be chromatographed rapidly. The failed cyclization of **8** was surprising, since Furukawa and coworkers, in contrast to our results, have recently cyclized 2-(*para*-methoxyanilino)-1,4-benzoquinones to the carbazoloquinones.[14b]

We thought that cyanation of **8** at the amino position would possibly enable the palladium-promoted cyclization to the desired *N*-cyanobenzo[*b*]carbazoloquinone framework of **5**. However, it was found that treatment of the 2-anilino-1,4-naphthoquinone **8** with sodium hydride followed by reaction with an excess of cyanogen bromide in DMF[6b] led to the 2-bromo-1,4-naphthoquinone **10** in 55% yield (Scheme 2).

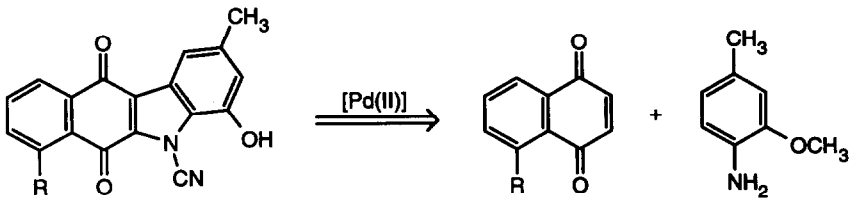
The palladium-promoted cyclization of the 2-arylamino-1,4-dimethoxynaphthalene **12** and subsequent treatment with ceric ammonium nitrate would also provide the 5*H*-benzo[*b*]carbazoloquinone framework. However, reduction of the 2-anilino-1,4-naphthoquinone **8** with sodium dithionite followed by *in situ* methylation with dimethyl sulfate and potassium carbonate in acetone at reflux for 2 h[15] gave **12** only in low yield (15%) along with the quinone **11** (64% yield) and 7% of the trimethylated derivative **13** (Scheme 3). Prolongation of the reaction time to 15 h led to a different product distribution (31% of quinone **11**, 18% of **12**, and 51% of **13**). The quinone **11** could be cyclized to the *N*-methylbenzo[*b*]carbazoloquinone **14** in only 19% yield by reaction with palladium(II) acetate in glacial acetic acid at reflux for 55 min.



8 **11** (64%) **12** (15%) **13** (7%) **11** **14**

Scheme 3

Next we turned our attention towards the synthesis of the *N*-cyanobenzo[*b*]carbazoloquinone **16**, which is a regioisomer of **3**. As a more simple model compound, 5-cyano-4-hydroxy-2-methyl-5*H*-benzo[*b*]carbazole-6,11-dione **15** was selected as the initial target.[1] Formal disconnection suggested that **15** could be derived from 1,4-naphthoquinone **6** and the arylamine **18** (Scheme 4).

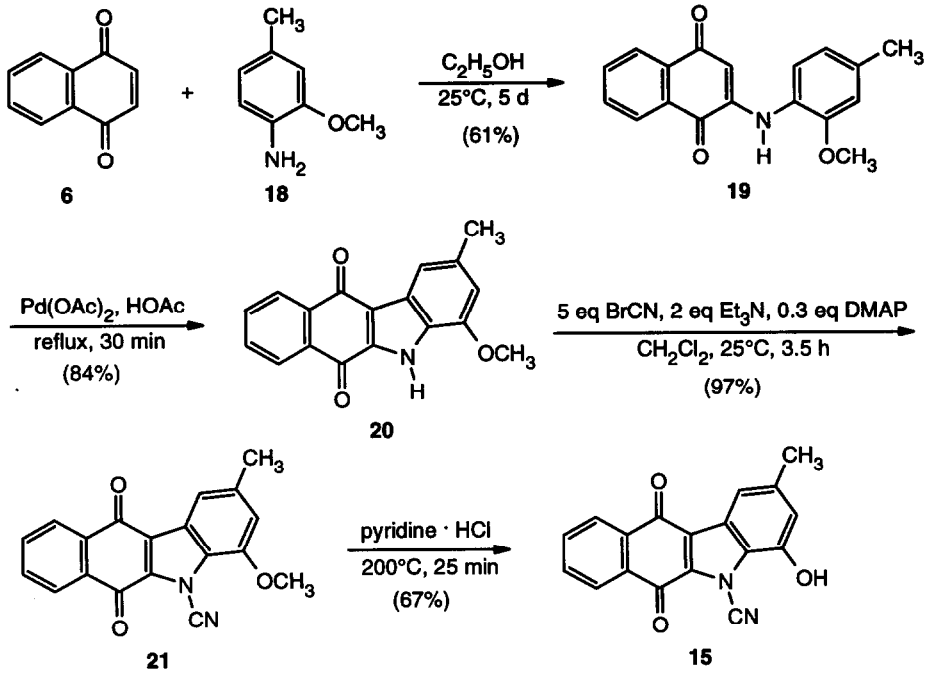


15 R = H
16 R = OH

6 R = H
17 R = OH

18

Scheme 4



6 **18** **19**

20

21 **15**

Scheme 5

The arylamine **18** served already as starting material for the iron-mediated total synthesis of the cytotoxic carbazole alkaloid koenoline.[16] Addition of **18** to the naphthoquinone **6** led to the 2-anilino-1,4-naphthoquinone **19** in 61% yield (Scheme 5). Compound **19** was smoothly converted to the corresponding benzo[*b*]carbazoloquinone **20** by treatment with stoichiometric amounts of palladium(II) acetate in refluxing glacial acetic acid for 30 min (84% yield).[1]

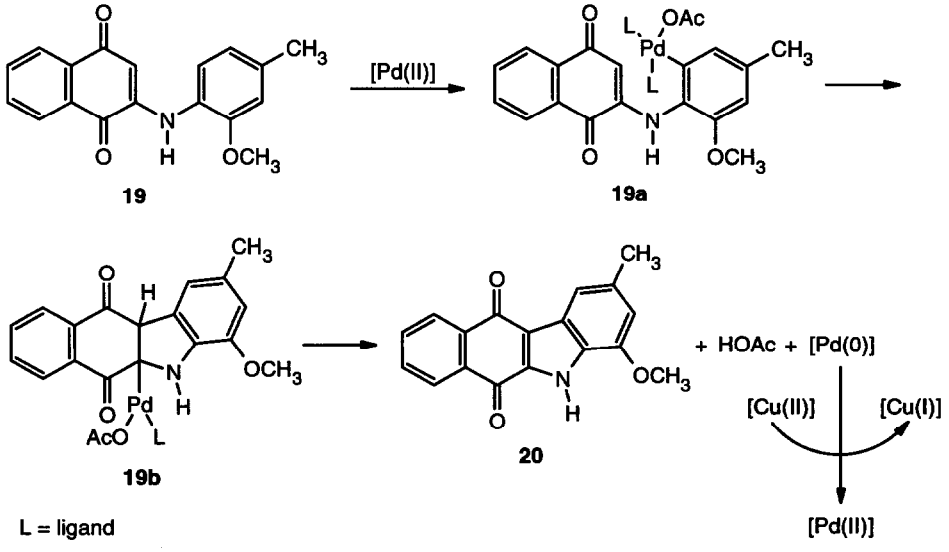
So far, no extensive investigation of the palladium-promoted aryl-quinone coupling process of 2-anilino-1,4-benzoquinones to the corresponding carbazoloquinones has been reported. Our studies confirm that this oxidative coupling is a palladium(II)-promoted reaction (see experiments summarized in Table 1).

Table 1. Cyclization of the 2-Anilino-1,4-naphthoquinone **19** to the Benzo[*b*]carbazoloquinone **20**

Reaction Conditions	Recovered **19** [%]	**20**, Yield [%]
1 eq $Pd(OAc)_2$, HOAc, reflux, 30 min	-	84
1 eq $Pd(OAc)_2$, Et_3N (large excess), 25°C, 10 min; subsequently followed by addition of HOAc, reflux, 1.75 h	90	6
0.12 eq $Pd(OAc)_2$, HOAc, reflux, 1 h	80	11
0.12 eq $Pd(OAc)_2$, 1.1 eq $Cu(OAc)_2$, HOAc, reflux, 17 h	56	34

The oxidative coupling described above would be of much greater synthetic utility by using only catalytic amounts of palladium. Since the reaction is a palladium(II)-promoted process which generates one equivalent of palladium(0), a catalytic cyclization should be feasible by reoxidation of palladium(0) to palladium(II), *e.g.* with oxidizing agents such as copper(II) acetate.[17,18]

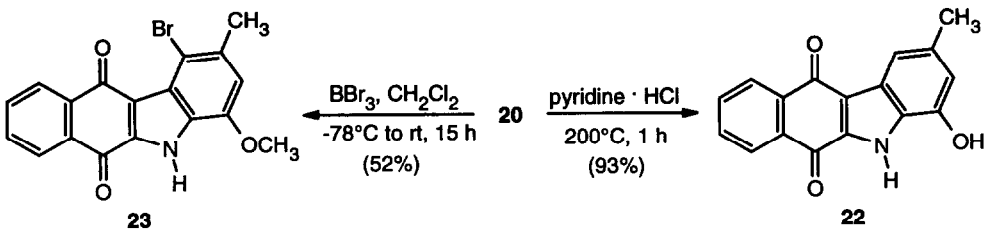
For a blank experiment, the 2-anilino-1,4-naphthoquinone **19** was heated under reflux as described above with 0.12 equivalents of palladium(II) acetate in glacial acetic acid to give the corresponding benzo[*b*]carbazole **20** in only 11% yield along with 80% of reisolated starting material **19** (Table 1). However, when the reaction was carried out with the same substrate using catalytic amounts of palladium(II) acetate and equimolar copper(II) acetate under argon, the desired cyclized product **20** was obtained in 34% yield. This result indicates the potential for a palladium-catalyzed oxidative cyclization to benzo[*b*]carbazoloquinones.



Scheme 6

By analogy with known palladium(II)-promoted aryl-olefin coupling processes, we propose the following mechanism for the cyclization to the 5*H*-benzo[*b*]carbazoloquinones (Scheme 6).[18,19] Initial electrophilic attack of the palladium(II) species at the aromatic ring of **19** generates the σ-arylpalladium(II) complex **19a**. Subsequent insertion of the quinone double bond affords the σ-alkylpalladium(II) complex **19b**, which on reductive β-elimination provides the benzo[*b*]carbazoloquinone **20**.

The next problem was to achieve a chemoselective cleavage of the aryl methyl ether in the presence of the labile *N*-cyano group. Chemoselective cleavage of the methyl ether of the cyanamide **21** while keeping the *N*-cyano group intact proved to be extremely difficult and use of a variety of conditions simply resulted in reisolation of the starting material or cleavage of the *N*-cyano group. The cleavage of aryl methyl ethers of *N*-cyanobenzo[*b*]carbazoloquinones to the corresponding hydroxy-substituted *N*-cyanobenzo[*b*]carbazoloquinones has been reported by Echavarren.[6] However, when the cyanamide **21** was subjected to the same reaction conditions as described in the literature (BBr_3, CH_2Cl_2, at -78°C)[6b] only starting material was reisolated. In our investigation we found that pyridine hydrochloride[20] is the reagent of choice in order to overcome this selectivity problem.

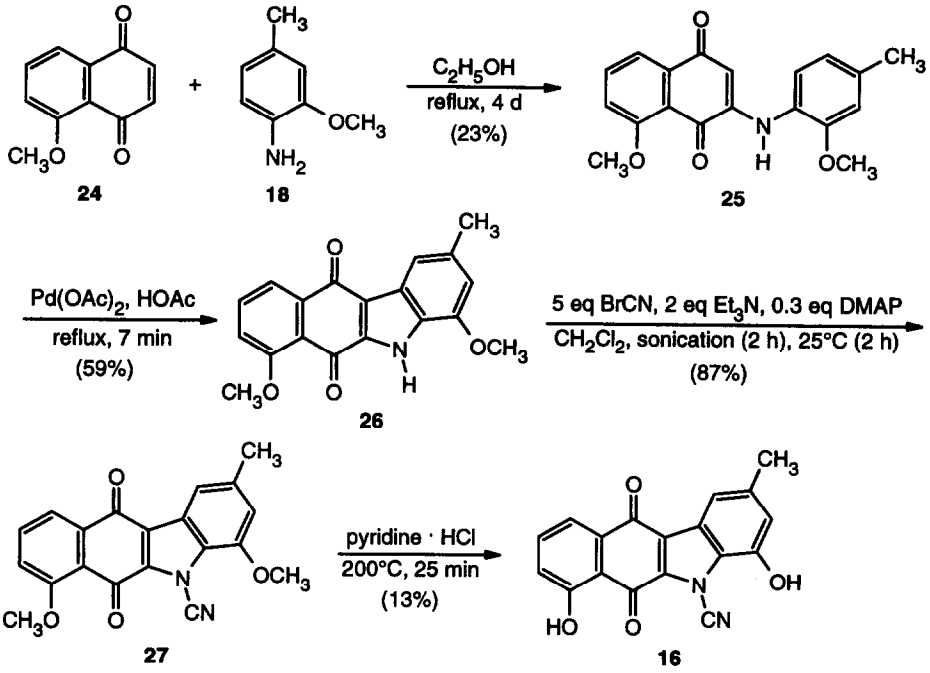


23 **22**

Scheme 7

In a model study we first investigated the ether cleavage at the stage of compound **20** (Scheme 7). When compound **20** was subjected to the conditions described in the literature (BBr_3, CH_2Cl_2, at -78°C)[6b] and then allowed to attain room temperature overnight,[21] the desired product **22** was not obtained, but electrophilic bromination at the C-1 position occurred to give the 1-bromobenzo[*b*]carbazole **23** in 52% yield. On the other hand treatment of the benzo[*b*]carbazole **20** with an excess of pyridine hydrochloride[20] without solvent at approximately 200°C for 1 hour under argon provided the 4-hydroxy derivative **22** in excellent yield (93%).

Reaction of **20** with NaH and phenyl cyanate[22] in DMF failed to afford the desired cyanamide **21**.[7a] However, the cyano group was smoothly introduced by treatment of **20** with an excess of cyanogen bromide and Et_3N in the presence of *p*-dimethylaminopyridine in CH_2Cl_2[6b] to give the desired cyanamide **21** in 97% yield (Scheme 5).[1] When the cyanamide **21** was treated with 5 equivalents of BBr_3 in CH_2Cl_2 and then allowed to attain room temperature overnight,[21] mainly starting material was recovered along with only traces of the desired product **15**. We also investigated other reagents for the cleavage of the aryl methyl ethers. Hydrobromic acid, particularly with HOAc as a co-solvent, has been extensively used to cleave methyl ethers of alkaloids. In our case, it resulted in an initial cleavage of the *N*-cyano group followed by cleavage of the methyl ether. When the cyanamide **21** was treated with either TMSI in $CHCl_3$[23] or NaCN in DMSO[24] only **20** was isolated in both cases. The selective cleavage of the methyl ether again was achieved simply by carrying out the reaction in the presence of an excess of pyridine hydrochloride[20] at 200°C with no additional solvent to afford **15** in 67% yield, along with minor amounts recovered starting material **21** (6%), and **22** (7%).



24 **18** **25** **26** **27** **16**

Scheme 8

Finally, we extended the methodology described above to the synthesis of **16**. Juglone (5-hydroxy-1,4-naphthoquinone) **17** was used as the starting material and converted to *O*-methyljuglone **24** according to a literature procedure (treatment with methyl iodide in chloroform in the presence of silver oxide, 92% yield).[25] A solution of **24** and the arylamine **18** in ethanol was heated at reflux to give regioselectively the 2-anilino-1,4-naphthoquinone **25** in a low yield (23%) along with reisolated **24** (Scheme 8). This reaction required higher temperatures and proceeded in lower yields than the corresponding reaction with 1,4-naphthoquinone **6** probably as a result of the reduced electrophilicity of the methoxy-substituted derivative **24**. The regioselectivity of the addition (attack at C-3) is supported by literature precedence.[26] Compound **25** was cyclized to the benzo[*b*]carbazoloquinone **26** by treatment with stoichiometric amounts of palladium(II) acetate in glacial acetic acid at reflux (59% yield). Cyanation of the benzo[*b*]carbazoloquinone **26** with an excess of cyanogen bromide and triethylamine in the presence of *p*-dimethylaminopyridine in dichloromethane furnished the desired cyanamide **27** in 87% yield. The ether cleavage was carried out by reaction with an excess of pyridine hydrochloride[20] at approximately 200°C under argon for 25 min to afford 42% of recovered cyanamide **27**, 12% of monomethyl ether, and the desired product **16** in 13% yield. The benzo[*b*]carbazoloquinones **27** and **16** are extremely difficult to purify, since they are very polar and virtually insoluble in most organic solvents.

In conclusion, a simple straightforward route to hydroxy-substituted 5-cyano-5*H*-benzo[*b*]carbazole-6,11-diones was established by the following four-step sequence: addition of an arylamine to a naphthoquinone, palladium(II)-promoted oxidative cyclization, *N*-cyanation with cyanogen bromide, and chemoselective ether cleavage using pyridine hydrochloride.

EXPERIMENTAL SECTION

All reactions were carried out using anhydrous and degassed solvents under an inert gas atmosphere. Flash chromatography: Baker silica gel (0.03-0.06 mm). Melting points: Büchi 535. UV: Perkin Elmer Lambda 2. IR: Bruker IFS-88. ^{1}H-NMR and ^{13}C-NMR spectra: Bruker AM-400; internal standard: tetramethylsilane or chloroform; coupling constants in Hz. Mass spectra: Finnigan MAT-90; ionization potential: 70 eV. Elemental analyses: Heraeus CHN-Rapid.

_N_-(4-Methoxy-2-methylphenyl)-2-amino-1,4-naphthoquinone (8)

4-Methoxy-2-methylaniline **7** (1.88 ml, 14.58 mmol) was added dropwise to a stirred solution of 1,4-naphthoquinone **6** (4.61 g, 29.15 mmol) in DMF (40 ml), and stirred at room temperature for further 72 h. After this time, water was added (150 ml), and extracted with dichloromethane. The organic extracts were washed with water, 20% sulphuric acid, water, brine, dried over magnesium sulfate, and evaporated to dryness. Purification of the residue by flash chromatography on silica gel (preadsorbtion on silica gel, gradient elution with hexane to hexane/ether, 1:1) and subsequent recrystallization from methanol gave 2.95 g (69%) of **8** as orange red crystals, m.p. 157-158°C. UV (MeOH): λ 269, 329, 460 nm; IR (KBr): ν 3359, 3334, 3281, 1669, 1597, 1572, 1565, 1516, 1493, 1352, 1303, 1247, 1121, 1039, 783, 728 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.23 (s, 3 H), 3.82 (s, 3 H), 5.78 (s, 1 H), 6.79 (dd, J = 8.6, 2.8, 1 H), 6.82 (d, J = 2.8, 1 H), 7.15 (d, J = 8.6, 1 H), 7.19 (br s, 1 H), 7.65 (dt, J = 1.3, 7.6, 1 H), 7.74 (dt, J = 1.3, 7.6, 1 H), 8.08-8.12 (m, 2 H); ^{13}C-NMR and DEPT (100 MHz, $CDCl_3$): δ 18.00 (CH_3), 55.45 (CH_3), 102.63 (CH), 112.26 (CH), 116.49 (CH), 126.13 (CH), 126.30 (CH), 126.95 (CH), 128.03 (C), 130.51 (C), 132.12 (CH), 133.48 (C), 134.80 (CH), 135.52 (C), 146.75 (C), 158.45 (C), 182.18 (C), 183.54 (C); MS (105°C): *m/z* 293 (M^+, 100), 278 (22), 147 (14); HRMS calcd for $C_{18}H_{15}NO_3$ (M^+): 293.1052, found: 293.1042.

_N_-(4-Methoxy-2-methylphenyl)-2-acetoxy-3-amino-1,4-naphthoquinone (9)

A mixture of compound **8** (100 mg, 0.34 mmol) and palladium(II) acetate (77 mg, 0.34 mmol) in acetonitrile (9 ml) was stirred at room temperature for 2.5 days. The reaction mixture was then filtered through Celite, which was subsequently washed with dichloromethane. Removal of the solvent and flash chromatography (ether/hexane, 3:7) of the residue on silica gel gave 44 mg (37%) of the acetoxy-1,4-naphthoquinone **9** as an orange red solid, m.p. 149-150°C. UV (MeOH): λ 271, 465 nm; IR (KBr): ν 3269, 2928, 1769, 1682, 1642, 1615, 1507, 1350, 1283, 1238, 1194, 970, 730, 632 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.57 (s, 3 H), 2.24 (s, 3 H), 3.80 (s, 3 H), 6.72 (dd, J = 8.6, 2.7, 1 H), 6.77 (d, J = 2.7, 1 H), 7.04 (m, 2 H), 7.66 (t, J = 7.6, 1 H), 7.74 (t, J = 7.6, 1 H), 8.10 (d, J = 7.6, 2 H); ^{13}C-NMR and DEPT (100 MHz, $CDCl_3$): δ 18.28 (CH_3), 19.41 (CH_3), 55.49 (CH_3), 111.11 (CH), 115.40 (CH), 126.52 (2 CH), 127.61 (C), 128.31 (CH), 129.12 (C), 129.98 (C), 132.00 (C), 132.55 (CH), 135.01 (CH), 136.77 (C), 136.91 (C), 158.51 (C), 167.79 (C), 176.91 (C), 182.15 (C); MS (100°C): *m/z* 351 (M^+, 10), 309 (100), 292 (18), 122 (7); HRMS calcd for $C_{20}H_{17}NO_5$ (M^+): 351.1107, found: 351.1116.

_N_-(4-Methoxy-2-methylphenyl)-3-amino-2-bromo-1,4-naphthoquinone (10)

To a flask charged with sodium hydride (80%, 4 mg, 0.13 mmol) was added dry hexane (3 ml). The mixture was stirred for 10 min, the hexane removed by a syringe, and the NaH dried under argon. A solution of

compound **8** (30 mg, 0.10 mmol) in DMF (4 ml) was added dropwise and the mixture was stirred at room temperature for 10 min. Subsequently, cyanogen bromide (54 mg, 0.51 mmol) was added in one portion and the mixture was stirred at room temperature for an additional 30 min. Water (30 ml) was then cautiously added and the mixture was extracted with dichloromethane. The combined extracts were washed with water and brine, dried over magnesium sulfate, and evaporated. Purification of the residue by flash chromatography (ether/hexane, 3:7) on silica gel afforded a purple solid. Recrystallization from dichloromethane/hexane provided 21 mg (55%) of the bromo-1,4-naphthoquinone **10** as a purple solid, m.p. 193-194°C. UV (MeOH): λ 229, 275, 332, 477 nm; IR (KBr): ν 3256, 2924, 1672, 1595, 1568, 1511, 1492, 1296, 1226, 1136, 1034, 847, 823, 718 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.23 (s, 3 H), 3.82 (s, 3 H), 6.72 (dd, *J* = 8.6, 2.9, 1 H), 6.76 (d, *J* = 2.9, 1 H), 7.01 (d, *J* = 8.6, 1 H), 7.53 (br s, 1 H), 7.67 (dt, *J* = 1.4, 7.6, 1 H), 7.75 (dt, *J* = 1.4, 7.6, 1 H), 8.09-8.12 (m, 1 H), 8.17-8.19 (m, 1 H); ^{13}C-NMR and DEPT (100 MHz, $CDCl_3$): δ 18.68 (CH_3), 55.38 (CH_3), 104.33 (C), 111.06 (CH), 115.39 (CH), 126.97 (CH), 127.37 (CH), 128.46 (CH), 129.05 (C), 129.66 (C), 132.57 (C), 132.66 (CH), 135.01 (CH), 136.54 (C), 144.72 (C), 158.62 (C), 177.21 (C), 180.01 (C); MS (115°C): *m/z* 373 (M^+, 99.8), 371 (M^+, 100), 358 (10), 356 (11), 327 (13), 292 (47), 277 (12), 248 (15); HRMS calcd for $C_{18}H_{14}NO_3{}^{79}Br$ (M^+): 371.0157, found: 371.0122.

***N*-(4-Methoxy-2-methylphenyl)-*N*-methyl-2-amino-1,4-naphthoquinone (11)** and
***N*-(4-Methoxy-2-methylphenyl)-2-amino-1,4-dimethoxynaphthalene (12)** and
***N*-(4-Methoxy-2-methylphenyl)-*N*-methyl-2-amino-1,4-dimethoxynaphthalene (13)**

To a solution of **8** (200 mg, 0.68 mmol) in acetone (40 ml) was added $Na_2S_2O_4$ (214 mg, 1.23 mmol) in one portion. After stirring at room temperature for 45 min, K_2CO_3 (2.83 g, 20.48 mmol) and dimethyl sulfate (2.26 ml, 23.89 mmol) were added. The suspension was stirred for an additional 30 min at room temperature and then heated under reflux for 2 h. After cooling, aqueous ammonia (15 ml) was added. The solution was concentrated and extracted with dichloromethane. The organic extracts were washed with water and brine, dried over $MgSO_4$, and evaporated. Flash chromatography of the residue (gradient elution: hexane to hexane/ethyl acetate, 4:1 to elute the first two non-polar spots, and finally hexane/ethyl acetate, 1:1 to elute **11**) gave 17 mg (7%) of **13** as a pale yellow oil, 34 mg (15%) of **12** as a colorless oil (stored under argon, otherwise it turns red), and 133 mg (64%) of the quinone **11** as an orange oil.

13: IR (film): ν 2929, 1623, 1595, 1500, 1462, 1370, 1237, 1094, 1048, 766 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.10 (s, 3 H), 3.42 (s, 3 H), 3.76 (s, 3 H), 3.79 (s, 3 H), 3.81 (s, 3 H), 6.27 (s, 1 H), 6.78 (m, 2 H), 7.13 (d, *J* = 8.3, 1 H), 7.30 (br t, *J* = 7.6, 1 H), 7.45 (br t, *J* = 7.6, 1 H), 7.99 (d, *J* = 8.4, 1 H), 8.09 (d, *J* = 8.4, 1 H); ^{13}C-NMR and DEPT (100 MHz, $CDCl_3$): δ 19.06 (CH_3), 40.92 (CH_3), 55.34 (CH_3), 55.53 (CH_3), 59.63 (CH_3), 99.97 (CH), 111.73 (CH), 116.54 (CH), 120.88 (CH), 121.93 (C, CH), 123.00 (CH), 124.71 (CH), 126.68 (CH), 129.99 (C), 134.98 (C), 138.27 (C), 138.87 (C), 141.95 (C), 151.97 (C), 156.03 (C); MS (72°C): *m/z* 337 (M^+, 58), 322 (100), 153 (16), 135 (41); HRMS calcd for $C_{21}H_{23}NO_3$ (M^+): 337.1678, found: 337.1702.

12: IR (KBr): ν 3394, 2935, 1627, 1601, 1502, 1451, 1387, 1287, 1221, 1160, 1092, 765 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.30 (s, 3 H), 3.80 (s, 3 H), 3.82 (s, 3 H), 3.89 (s, 3 H), 5.83 (br s, 1 H), 6.41 (s, 1 H), 6.76 (dd, *J* = 8.6, 3.0, 1 H), 6.85 (d, *J* = 3.0, 1 H), 7.19 (d, *J* = 8.6, 1 H), 7.25 (br t, *J* = 7.6, 1 H), 7.47 (br t, *J* = 7.6, 1 H), 7.89 (br d, *J* = 8.4, 1 H), 8.10 (br d, *J* = 8.4, 1 H); ^{13}C-NMR and DEPT (100 MHz, $CDCl_3$): δ 18.34 (CH_3), 55.47 (CH_3), 55.63 (CH_3), 60.51 (CH_3), 95.78 (CH), 111.79 (CH), 116.44 (CH), 119.72 (CH),

120.43 (C), 121.90 (CH), 122.39 (CH), 124.23 (CH), 126.91 (CH), 128.80 (C), 133.54 (C), 133.87 (C), 133.99 (C), 134.97 (C), 152.62 (C), 156.18 (C); MS (68°C): *m/z* 323 (M^+, 44), 308 (100), 201 (36), 151 (58), 135 (69); HRMS calcd for $C_{20}H_{21}NO_3$ (M^+): 323.1521, found: 323.1536.

11: UV (MeOH): λ 237, 275, 461 nm; IR (KBr): ν 3066, 1678, 1630, 1593, 1556, 1501, 1290, 1266, 779, 723 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.20 (s, 3 H), 3.33 (br s, 3 H), 3.79 (s, 3 H), 5.93 (br s, 1 H), 6.72 (br d, *J* = 8, 1 H), 6.81 (d, *J* = 2.7, 1 H), 6.91 (br d, *J* = 8, 1 H), 7.56 (t, *J* = 7.6, 1 H), 7.66 (dt, *J* = 1.2, 7.6, 1 H), 7.88 (br d, *J* = 5.3, 1 H), 8.02 (d, *J* = 7.6, 1 H); ^{13}C-NMR and DEPT (100 MHz, $CDCl_3$): δ 17.91 (CH_3), 42.56 (CH_3), 55.42 (CH_3), 108.55 (CH), 112.40 (CH), 116.59 (CH), 125.46 (CH), 126.54 (CH), 126.95 (CH), 132.21 (CH), 132.29 (C), 132.75 (C), 133.92 (CH), 135.78 (C), 139.13 (C), 151.72 (C), 158.59 (C), 182.63 (C), 183.44 (C); MS (77°C): *m/z* 307 (M^+, 100), 292 (56), 174 (10), 135 (16); HRMS calcd for $C_{19}H_{17}NO_3$ (M^+): 307.1208, found: 307.1193.

2-Methoxy-4,5-dimethyl-5*H*-benzo[*b*]carbazole-6,11-dione (14)

A mixture of compound **11** (130 mg, 0.42 mmol) and $Pd(OAc)_2$ (95 mg, 0.42 mmol) in glacial acetic acid (5 ml) was heated under reflux for 55 min. After cooling, the reaction mixture was filtered through Celite, which was subsequently washed with acetone. Removal of the solvent and flash chromatography of the residue on silica gel (gradient elution: hexane/CH_2Cl_2, 1:4 eluted the desired product, and then ether/hexane/CH_2Cl_2, 2:8:90 to reisolate starting material **11**) gave 24 mg (19%) of the benzo[*b*]carbazoloquinone **14** as an orange solid, m.p. 258-259°C. UV (CH_2Cl_2): λ 275, 429 nm; IR (KBr): ν 2961, 2925, 2853, 1657, 1644, 1589, 1486, 1262, 1240, 1106, 957, 843, 715 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6, at 60°C): δ 2.76 (s, 3 H), 3.84 (s, 3 H), 4.48 (s, 3 H), 6.88 (s, 1 H), 7.62 (s, 1 H), 7.79-7.84 (m, 2 H), 8.07-8.10 (m, 2 H); ^{13}C-NMR and DEPT (100 MHz, DMSO-d_6, at 60°C): δ 19.28 (CH_3), 34.38 (CH_3), 55.07 (CH_3), 100.02 (CH), 117.03 (C), 120.52 (CH), 125.10 (C), 125.18 (C, CH), 125.95 (CH), 132.79 (CH), 133.28 (2 C), 133.56 (CH), 134.08 (C), 134.53 (C), 156.76 (C), 177.74 (C), 179.72 (C); MS (105°C): *m/z* 305 (M^+, 100), 290 (12), 262 (9); HRMS calcd for $C_{19}H_{15}NO_3$ (M^+): 305.1052, found: 305.1037.

***N*-(2-Methoxy-4-methylphenyl)-2-amino-1,4-naphthoquinone (19)**

A solution of 2-methoxy-4-methylaniline **18** (2.00 g, 14.58 mmol)[16] in ethanol (25 ml) was added dropwise to a stirred, ice cooled solution of 1,4-naphthoquinone **6** (4.61 g, 29.15 mmol) in ethanol (250 ml). The ice bath was removed, and the reaction mixture was then stirred at room temperature for an additional 5 d. After this time, the solvent was removed, water was added, and extracted with dichloromethane. The organic extracts were washed with water, 20% sulphuric acid (to remove the arylamine **18**), water, brine, dried over magnesium sulfate, and evaporated. The residue was purified by flash chromatography (gradient elution: hexane to ether/hexane, 1:4) to give a purple residue. Recrystallization of the residue from dichloromethane/ hexane gave 2.62 g (61%) of the 2-amino-1,4-naphthoquinone **19** as a purple solid, m.p. 159-161°C. UV (MeOH): λ 244, 275, 382, 482 nm; IR (KBr): ν 3297, 3002, 1676, 1624, 1577, 1546, 1331, 1295, 1268, 1037, 991, 787, 734 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.32 (s, 3 H), 3.86 (s, 3 H), 6.38 (s, 1 H), 6.73 (br s, 1 H), 6.77 (br d, *J* = 8.2, 1 H), 7.25 (d, *J* = 8.0, 1 H), 7.61 (dt, *J* = 1.0, 7.6, 1 H), 7.71 (dt, *J* = 1.0, 7.6, 1 H), 7.87 (br s, 1 H), 8.07 (dd, *J* = 1.0, 7.6, 2 H); ^{13}C-NMR and DEPT (100 MHz, $CDCl_3$): δ 21.49 (CH_3), 55.66 (CH_3), 103.10 (CH), 112.03 (CH), 120.99 (CH), 121.18 (CH), 124.18 (C), 126.01 (CH), 126.43 (CH), 130.47 (C), 132.14 (CH), 133.32 (C), 134.69 (CH), 135.75 (C), 144.00 (C), 151.02 (C), 182.05 (C), 183.77 (C); MS

(90°C): *m/z* 293 (M^+, 100), 278 (34), 262 (6); HRMS calcd for $C_{18}H_{15}NO_3$ (M^+): 293.1052, found: 293.1043. Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78. Found: C, 73.51; H, 5.14; N, 4.90.

4-Methoxy-2-methyl-5*H*-benzo[*b*]carbazole-6,11-dione (20)

A mixture of the 2-amino-1,4-naphthoquinone **19** (500 mg, 1.71 mmol) and palladium(II) acetate (383 mg, 1.71 mmol) in glacial acetic acid (30 ml) was heated under reflux for 30 min. After cooling, the reaction mixture was filtered through Celite, which was subsequently washed with acetone. Removal of the solvent gave a brown residue, which was recrystallized from CH_2Cl_2/hexane. The residue was washed with CH_2Cl_2, to give 399 mg (80%) of the cyclized benzo[*b*]carbazole **20**. The filtrate was then evaporated to dryness and flash chromatography of the brown residue (hexane/ethyl acetate, 4:1) gave a total of 419 mg (84%) of the cyclized benzo[*b*]carbazole **20** as a brick-red solid, m.p. > 278°C. UV (MeOH): λ 245, 269, 402 nm; IR (KBr): ν 3281, 1661, 1595, 1536, 1366, 1288, 1272, 958, 715 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.51 (s, 3 H), 3.99 (s, 3 H), 6.68 (s, 1 H), 7.69 (dt, *J* = 1.4, 7.6, 1 H), 7.75 (dt, *J* = 1.4, 7.6, 1 H), 7.75 (m, 1 H), 8.17 (dd, *J* = 7.6, 1.4, 1 H), 8.25 (dd, *J* = 7.6, 1.4, 1 H), 9.38 (br s, 1 H); ^{13}C-NMR and DEPT (100 MHz, DMSO-d_6): δ 21.76 (CH_3), 55.52 (CH_3), 108.64 (CH), 113.52 (CH), 117.38 (C), 125.61 (C), 125.94 (CH), 125.99 (CH), 127.61 (C), 132.79 (C), 133.11 (CH), 134.01 (C, CH), 134.70 (C), 136.78 (C), 147.09 (C), 177.06 (C), 180.41 (C); MS (125°C): *m/z* 291 (M^+, 100), 276 (18), 248 (17); HRMS calcd for $C_{18}H_{13}NO_3$ (M^+): 291.0895, found: 291.0905.

Pd(II)-Catalyzed Cyclization of *N*-(2-Methoxy-4-methylphenyl)-2-amino-1,4-naphthoquinone (19)

A mixture of compound **19** (100 mg, 0.34 mmol), copper(II) acetate (70 mg, 0.385 mmol), and palladium(II) acetate (9 mg, 0.04 mmol) in glacial acetic acid (5 ml) was heated under reflux and stirred for 17 h. After cooling, the reaction mixture was filtered through Celite, which was washed with large amounts of acetone. Removal of the solvent from the filtrates and purification of the brown residue by flash chromatography (hexane/ethyl acetate, 4:1) on silica gel gave 56 mg (56%) of recovered starting material **19** and 34 mg (34%) of benzo[*b*]carbazoloquinone **20**.

5-Cyano-4-methoxy-2-methyl-5*H*-benzo[*b*]carbazole-6,11-dione (21)

Et_3N (0.23 ml, 1.65 mmol) was added dropwise to a stirred suspension of the benzo[*b*]carbazole **20** (240 mg, 0.82 mmol), cyanogen bromide (437 mg, 4.12 mmol) and 4-dimethylaminopyridine (30 mg, 0.25 mmol) in CH_2Cl_2 (40 ml). The reaction mixture was stirred at room temperature for 3.5 h. After this time, water was cautiously added and the resulting mixture was extracted with CH_2Cl_2. The organic extracts were washed with water, brine, dried over $MgSO_4$, and evaporated. Recrystallization of the orange residue from CH_2Cl_2/hexane gave 253 mg (97%) of the cyanamide **21** as an orange solid, m.p. 288-290°C. UV (CH_2Cl_2): λ 253, 261, 282, 321, 387 nm; IR (KBr): ν 2257, 1670, 1595, 1558, 1488, 1290, 1267, 1245, 1213, 964, 944, 708 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.50 (s, 3 H), 4.03 (s, 3 H), 6.85 (s, 1 H), 7.78-7.83 (m, 3 H), 8.21-8.25 (m, 2 H); ^{13}C-NMR and DEPT (100 MHz, $CDCl_3$): δ 22.04 (CH_3), 56.15 (CH_3), 105.66 (C≡N), 112.21 (CH), 115.69 (CH), 122.60 (C), 125.21 (C), 126.29 (C), 126.90 (CH), 126.93 (CH), 132.42 (C), 133.29 (C), 133.98 (CH), 134.51 (CH), 135.93 (C), 138.77 (C), 147.43 (C), 175.83 (C), 180.75 (C); MS (145°C): *m/z* 316 (M^+, 100), 301 (5), 273 (10), 248 (11), 190 (10); HRMS calcd for $C_{19}H_{12}N_2O_3$ (M^+): 316.0848, found: 316.0862. Anal. Calcd for $C_{19}H_{12}N_2O_3$: C, 72.15; H, 3.82; N, 8.86. Found: C, 72.01; H, 4.00; N, 9.05.

5-Cyano-4-hydroxy-2-methyl-5*H*-benzo[*b*]carbazole-6,11-dione (15)

The cyanamide **21** (50 mg, 0.16 mmol) was heated with anhydrous pyridine hydrochloride (914 mg, 7.91 mmol) at 200°C for 25 min under argon. After cooling, the fused mass was filtered and subsequently washed with water (1 l). The brown residue was preadsorbed on silica gel in acetone and purified by flash chromatography with gradient elution (first using dichloromethane in order to elute the starting material **21**, then with dichloromethane/ether, 95:5) to afford 3 mg (6%) of recovered starting material **21**, 3 mg (7%) of **22** (data given below), and 32 mg (67%) of the cyanamide **15** as an orange crystalline solid, m.p. 260-262°C. UV (CH_2Cl_2): λ 224, 261, 280, 382 nm; IR (KBr): ν 2921, 2259, 1669, 1596, 1557, 1486, 1417, 1286, 1267, 1229, 1000, 983, 845, 706 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6, at 50°C): δ 2.39 (s, 3 H), 6.86 (s, 1 H), 7.54 (s, 1 H), 7.89-7.93 (m, 2 H), 8.11-8.14 (m, 2 H), 10.90 (br s, 1 H); ^{13}C-NMR and DEPT (100 MHz, DMSO-d_6, at 50°C): δ 21.08 (CH_3), 105.58 (C≡N), 113.23 (CH), 115.91 (CH), 121.54 (C), 124.88 (C), 125.09 (C), 126.05 (2 CH), 132.12 (C), 132.72 (C), 133.92 (CH), 134.39 (CH), 136.34 (C), 137.81 (C), 145.10 (C), 175.42 (C), 180.31 (C); MS (160°C): *m/z* 302 (M^+, 100), 277 (4), 259 (15), 231 (3); HRMS calcd for $C_{18}H_{10}N_2O_3$ (M^+): 302.0691, found: 302.0672.

4-Hydroxy-2-methyl-5*H*-benzo[*b*]carbazole-6,11-dione (22)

The benzo[*b*]carbazole **20** (100 mg, 0.34 mmol) was heated with anhydrous pyridine hydrochloride (1.99 g, 17.22 mmol) at 200°C for 1 h under argon. After cooling, the fused mass was filtered, washed with 10% HCl (50 ml) and water (1 l). Recrystallization of the crude black product from CH_2Cl_2/hexane and subsequent washing with CH_2Cl_2 and hexane gave 88 mg (93%) of **22** as a brown solid, m.p. > 290°C. UV (MeOH): λ 246, 271, 403 nm; IR (KBr): ν 3600-3200, 3346, 1667, 1593, 1533, 1470, 1375, 1295, 1259, 713 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.36 (s, 3 H), 6.63 (s, 1 H), 7.46 (s, 1 H), 7.78-7.86 (m, 2 H), 8.06-8.10 (m, 2 H), 10.02 (br s, 1 H), 12.83 (br s, 1 H); ^{13}C-NMR and DEPT (100 MHz, DMSO-d_6): δ 21.46 (CH_3), 112.30 (2 CH), 117.27 (C), 125.87 (2 CH), 126.03 (C), 127.31 (C), 132.68 (C), 132.96 (CH), 133.96 (CH), 134.08 (C), 134.73 (C), 136.49 (C), 144.64 (C), 177.08 (C), 180.24 (C); MS (160°C): *m/z* 277 (M^+, 100), 248 (4); HRMS calcd for $C_{17}H_{11}NO_3$ (M^+): 277.0739, found: 277.0722.

1-Bromo-4-methoxy-2-methyl-5*H*-benzo[*b*]carbazole-6,11-dione (23)

A solution of benzo[*b*]carbazole **20** (100 mg, 0.34 mmol) in CH_2Cl_2 (60 ml) was kept at -78°C during the dropwise addition of a 1 M solution of BBr_3 in CH_2Cl_2 (1.37 ml, 1.37 mmol). The reaction mixture was warmed slowly to room temperature over a period of 15 h, subsequently poured onto ice-water (5 ml) and extracted with CH_2Cl_2. The organic extracts were washed with water, brine, and dried over $MgSO_4$. Removal of the solvent and purification of the red residue by flash chromatography (hexane/EtOAc) on silica gel gave 66 mg (52%) of the bromobenzo[*b*]carbazole **23** as an orange solid, m.p. > 290°C. UV (CH_2Cl_2): λ 249, 270, 296, 340, 387 nm; IR (KBr): ν 3276, 1667, 1519, 1389, 1356, 1271, 1163, 951, 720 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.49 (s, 3 H), 3.94 (s, 3 H), 7.00 (s, 1 H), 7.78 (t, J = 7.5, 1 H), 7.85 (t, J = 7.5, 1 H), 8.05 (d, J = 7.5, 1 H), 8.09 (d, J = 7.5, 1 H), 13.36 (br s, 1 H); ^{13}C-NMR and DEPT (100 MHz, DMSO-d_6): δ 24.24 (CH_3), 55.92 (CH_3), 106.19 (C), 109.88 (CH), 117.34 (C), 125.38 (CH), 125.97 (C), 126.64 (CH), 129.17 (C), 131.65 (C), 132.74 (CH), 134.21 (C), 134.31 (CH), 135.19 (C), 138.33 (C), 146.32 (C), 177.21 (C), 177.99 (C); MS (155°C): *m/z* 371 (M^+, 100), 369 (M^+, 99), 356 (26), 354 (26), 328 (6), 326 (6), 291 (8), 190 (11); HRMS calcd for $C_{18}H_{12}NO_3{}^{81}Br$ (M^+): 370.9981, found: 370.9961.

5-Methoxy-1,4-naphthoquinone (24)

Juglone methyl ether **24**,[25] orange needles, m.p. 185-186°C (lit.[25] 187°C). UV (MeOH): λ 205, 245, 395 nm; IR (KBr): ν 3015, 1657, 1616, 1585, 1472, 1301, 1276, 1170, 1023, 856, 831, 779 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 3.98 (s, 3 H), 6.82, 6.85 (AB system, J = 10.5, 2 H), 7.29 (dd, J = 7.9, 1.7, 1 H), 7.64-7.70 (m, 2 H); ^{13}C-NMR and DEPT (100 MHz, $CDCl_3$): 56.44 (CH_3), 117.88 (CH), 119.10 (CH), 119.58 (C), 133.95 (C), 134.98 (CH), 136.16 (CH), 140.84 (CH), 159.55 (C), 184.33 (C), 185.16 (C); MS (86°C): *m/z* 188 (M^+, 100), 159 (11), 130 (13), 104 (18); HRMS calcd for $C_{11}H_8O_3$ (M^+): 188.0473, found: 188.0467.

***N*-(2-Methoxy-4-methylphenyl)-3-amino-5-methoxy-1,4-naphthoquinone (25)**

A solution of 2-methoxy-4-methylaniline **18** (995 mg, 7.25 mmol)[16] in ethanol (15 ml) was added dropwise to a stirred solution of 1,4-naphthoquinone **24** (2.73 g, 14.52 mmol) in ethanol (250 ml). The reaction mixture was subsequently heated under reflux for 4 d. After cooling, the solvent was evaporated, water was added, and the mixture was extracted with CH_2Cl_2. The organic extracts were washed with 20% H_2SO_4 (to remove the arylamine **18**), water, brine, dried over $MgSO_4$, and evaporated to dryness. The residue was purified by flash chromatography (slow gradient elution: hexane to hexane/EtOAc, 7:3) to give a purple residue. Recrystallization of the residue from CH_2Cl_2/hexane provided 530 mg (23%) of the 1,4 naphthoquinone **25** as purple needles, m.p. 195-196°C. UV (MeOH): λ 275, 394, 481 nm; IR (KBr): ν 3308, 2951, 2843, 1664, 1619, 1605, 1585, 1536, 1494, 1355, 1273, 1190, 1133, 1054, 1034, 983, 813, 788 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.35 (s, 3 H), 3.86 (s, 3 H), 4.03 (s, 3 H), 6.38 (s, 1 H), 6.76 (br s, 1 H), 6.79 (br d, J = 8, 1 H), 7.21 (dd, J = 8, 1, 1 H), 7.28 (d, J = 8, 1 H), 7.68 (t, J = 8, 1 H), 7.78 (dd, J = 8, 1, 1 H), 8.12 (br s, 1 H); ^{13}C-NMR and DEPT (100 MHz, $CDCl_3$): δ 21.51 (CH_3), 55.67 (CH_3), 56.43 (CH_3), 101.58 (CH), 112.02 (CH), 116.02 (CH), 118.22 (C), 118.90 (CH), 120.85 (CH), 121.14 (CH), 124.49 (C), 135.59 (C), 135.74 (C), 136.05 (CH), 144.89 (C), 151.07 (C), 160.16 (C), 180.45 (C), 183.44 (C); MS (105°C): *m/z* 323 (M^+, 100), 308 (16), 292 (7); HRMS calcd for $C_{19}H_{17}NO_4$ (M^+): 323.1158, found: 323.1170.

4,7-Dimethoxy-2-methyl-5*H*-benzo[*b*]carbazole-6,11-dione (26)

A mixture of compound **25** (500 mg, 1.55 mmol) and palladium(II) acetate (348 mg, 1.55 mmol) in glacial acetic acid (30 ml) was heated under reflux for 7 min. After cooling, the reaction mixture was filtered through Celite, which was subsequently washed with large amounts of acetone. Removal of the solvent gave a brown residue, which was recrystallized from dichloromethane/hexane and washed with dichloromethane to give 205 mg (41%) of the product. The filtrate was then evaporated to dryness and flash chromatography (hexane/ethyl acetate) of the black residue gave a total of 291 mg (59%) of the cyclized product **26** as an orange solid, m.p. > 278°C. UV (CH_2Cl_2): λ 238, 268, 405 nm; IR (KBr): ν 3414, 2975, 1653, 1586, 1545, 1467, 1362, 1288, 1276, 1187, 973, 835, 739 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.49 (s, 3 H), 3.98 (s, 3 H), 4.05 (s, 3 H), 6.66 (s, 1 H), 7.28 (s, 1 H), 7.66-7.70 (m, 2 H), 7.95 (br d, J = 7.6 Hz, 1 H), 9.35 (br s, 1 H); ^{13}C-NMR and DEPT (100 MHz, DMSO-d_6): δ 21.81 (CH_3), 55.54 (CH_3), 56.41 (CH_3), 108.29 (CH), 113.56 (CH), 115.61 (C), 118.37 (CH), 118.66 (CH), 119.89 (C), 125.47 (C), 127.35 (C), 134.35 (C), 135.24 (CH), 136.61 (C), 138.75 (C), 147.18 (C), 160.13 (C), 176.60 (C), 179.76 (C); MS (150°C): *m/z* 321 (M^+, 100), 306 (4), 302 (25), 274 (12), 260 (5); HRMS calcd for $C_{19}H_{15}NO_4$ (M^+): 321.1001, found: 321.0992.

5-Cyano-4,7-dimethoxy-2-methyl-5*H*-benzo[b]carbazole-6,11-dione (27)

Triethylamine (0.21 ml, 1.51 mmol) was added dropwise to a stirred suspension of benzo[*b*]carbazole **26** (245 mg, 0.76 mmol), cyanogen bromide (404 mg, 3.81 mmol) and 4-dimethylaminopyridine (28 mg, 0.23 mmol) in CH_2Cl_2 (40 ml). The reaction mixture was sonicated for 2 h, and then stirred at room temperature for an additional 2 h. After this time, water was cautiously added and the mixture was extracted with warm CH_2Cl_2. The organic extracts were washed with water, brine, and dried over $MgSO_4$. Removal of the solvent *in vacuo* gave an orange residue, which was recrystallized from CH_2Cl_2/hexane to provide 299 mg (87%) of the cyanamide **27** as a bright orange solid, m.p. > 290°C. UV (CH_2Cl_2): λ 231, 263, 281, 414 nm; IR (KBr): ν 3105, 2994, 2949, 2255, 1668, 1586, 1577, 1473, 1378, 1307, 1283, 1222, 1202, 981, 969, 948, 830, 784, 730 cm^{-1}; ^{1}H-NMR (400 MHz, CD_2Cl_2): δ 2.50 (s, 3 H), 4.02 (s, 3 H), 4.04 (s, 3 H), 6.90 (s, 1 H), 7.37 (dd, *J* = 8, 1, 1 H), 7.74 (t, *J* = 8, 1 H), 7.76 (s, 1 H), 7.87 (dd, *J* = 8, 1, 1 H); MS: *m/z* 346 (M^+, 100), 318 (47), 290 (20), 276 (9), 248 (8), 190 (5); HRMS calcd for $C_{20}H_{14}N_2O_4$ (M^+): 346.0954, found: 346.0964.

5-Cyano-4,7-dihydroxy-2-methyl-5*H*-benzo[*b*]carbazole-6,11-dione (16)

The cyanamide **27** (165 mg, 0.48 mmol) was heated with anhydrous pyridine hydrochloride (2.76 g, 23.88 mmol) at 200°C for 25 min under argon. After cooling, the fused mass was filtered and subsequently washed with water (1 l). The dark brown residue was purified by flash chromatography (preadsorbtion on silica gel in acetone, slow gradient elution with dichloromethane to dichloromethane/ether, 98:2) to give 70 mg (42%) of recovered starting material **27**, 19 mg (12%) of monomethyl ether, and 19 mg (13%) of the cyanamide **16** as a red crystalline solid, m.p. 260°C (dec.). UV (CH_2Cl_2): λ 259 (sh), 283, 323 (sh), 435 nm; IR (KBr): ν 3260, 2276, 1663, 1633, 1597, 1558, 1449, 1393, 1292, 1207, 1151, 1070, 1039, 833, 730 cm^{-1}; ^{1}H-NMR (400 MHz, acetone-d_6): δ 2.45 (s, 3 H), 7.01 (s, 1 H), 7.36 (dd, *J* = 8, 1, 1 H), 7.70 (s, 1 H), 7.76 (dd, *J* = 8, 1, 1 H), 7.82 (t, *J* = 8, 1 H), 9.85 (br s, 1 H), 11.80 (br s, 1 H); MS (165°C): *m/z* 318 (M^+, 100), 293 (7), 274 (22), 190 (8); HRMS calcd for $C_{18}H_{10}N_2O_4$ (M^+): 318.0641, found: 318.0615.

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