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A New Synthetic Entry to Fused Azaquinones by a Cycloaddition/Ring Transformation Sequence starting from Pyrido[1,2-a]pyrazines

Thomas Billert [a], Rainer Beckert * [a], Peer Fehling [b], Manfred Döring* [b] and Helmar Görls [b]

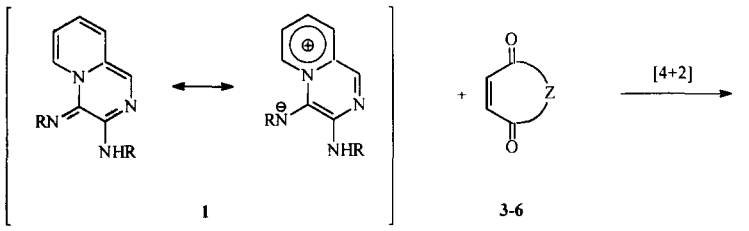
[a] Institut für Organische und Makromolekulare Chemie der Friedrich -Schiller-Universität, Humboldtstr.10, D-07743 Jena, Deutschland

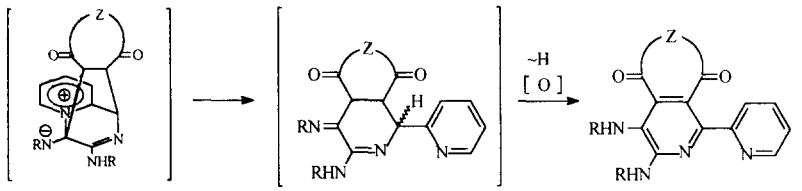
[b] Institut für Anorganische und Analytische Chemie der Friedrich-Schiller-Universität, August-Bebel-Str.2, D-07743 Jena, Deutschland

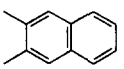
Abstract: An expedient one-pot synthesis via a novel cycloaddition/ring transformation sequence allows the introduction of two arylamino groups and a pyridine substructure on azaquinones. Using 1,4-benzoquinone a twofold regioselective reaction yields the deeply blue colored 2,7-diaza-anthraquinones **8**, which could be determinated by NMR spectroscopy. In addition, an X-ray structural analysis of the juglone derivative **11** reveals the regioselective arrangement of the bipyridine subunit into the quinone moiety. © 1997 Elsevier Science Ltd.

Quinones, including heterocyclic ring systems, especially azanaphthoquinones and azaanthraquinones are involved in numerous biochemical processes because of their facile reduction-oxidation and play an important role in electron transfer processes as well as in oxidative phosphorylations. Furthermore, their biological activity includes enzyme inhibition and some have chemotherapeutic value as antibacterial, antifungal and cancerostatic agents [1,2]. Moreover, by relatively simple substitution with electron donors in several positions of quinones, compounds can be produced that absorb in any desired region of the visible spectrum. Thus, substituted anthraquinone derivatives, the well known carbonyl dyes, have also become important as anionic, cationic, disperse and functional dyes or as pigments.

There are a few direct methods for the synthesis of azaanthraquinones [3-7] but short routes to highly substituted derivatives remain unexplored. We now report a novel route to aza- and diazaanthraquinones and related fused systems by a cycloaddition/ring transformation sequence starting from pyrido[1,2-a]pyrazines **1** and quinones **2-5** or 2,3-dihydro-1,4-benzoquinones **6** and **7**. The bicyclic oxalic amidines **1** prepared as previously described [8] from 2-picolylamine and bis-imidoylchlorides of oxalic acid exhibit a new heterocyclic system containing a reactive endocyclic 2-aza-1,3-diene subunit [9]. For the conversion of **1** to fused azaquinones a three-step pathway was exemplified in Scheme 1: (i) Considering the well demonstrated dienophilic ability of the quinone double bond, we reasoned that a [4+2] cycloaddition with the heterodiene **1** took place. (ii) A ring opening process led to the reconversion of the pyridine ring, substituted in 2-position. This pathway is also essentially based on the isolation and characterization of an intermediate **14** starting from maleinimide and **1**, previously published by us [8]. (iii) The tautomeric structure **14** underwent a 1,5-hydrogen shift and was finally oxidized to aromatic bipyridine derivatives **9-12**. [8] Using the unsymmetrical 5-hydroxy-1,4-naphthoquinone (juglone) **5** one transformation product **11** was isolated. The X-ray structure determination of **11** could be carried out (Figure 1) [12]. We have evidence for the regioselectivity of that cycloaddition. As expected the azaquinone substructure shows planarity. The exocyclic part of the 2,2'-bipyridine is twisted out of plane.





Z	3: 	4: 	5: 	6: 
R	**9**: m-CF_3Ph	**10**: p-CH_3Ph	**11**: p-CH_3Ph	**12**: p-CH_3Ph

Scheme 1

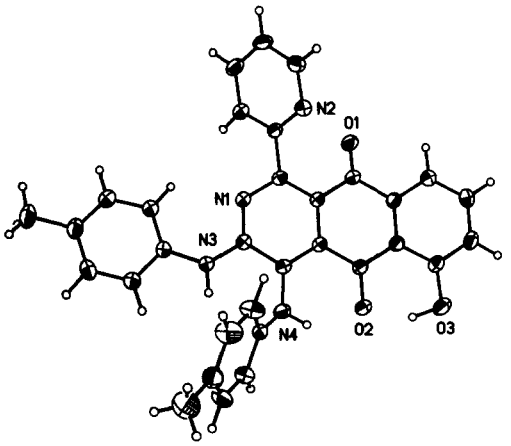
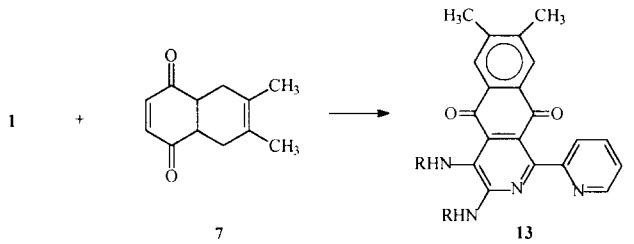


Figure 1. Molecular structure of **11**.[12]

According to the reaction course (Scheme 1) treatment of **1** with the monofunctional 1,4-naphthoquinone **3** as well as 1,4-anthraquinone **4** afforded the derivatives **9** and **10** in generally good yield. The spectroscopic data are in agreement with those of the proposed structures. Starting with 2,3-dihydro-1,4-benzoquinones **6** [10]

and 7 [11] as dienophiles an other behavior was observed. During 5 days in boiling toluene compound 7 produced the oxidized dimethyl substituted 2-azaanthraquinone **13** as the only product (Scheme 2).

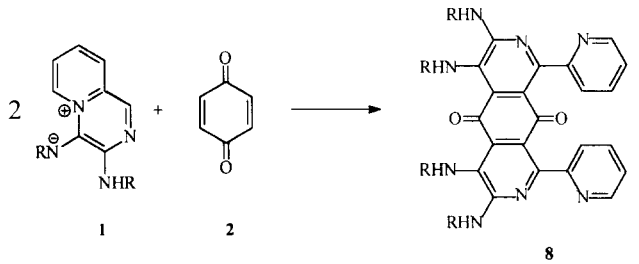


Scheme 2

Because of the high tendency to form the aromatic ring system the isolation of an intermediate dihydroderivative **14** failed. A distinguishing feature of that oxidation process is the absence of methylene signals and the deshielding of the CH_3 protons (2.32 ppm and 2.35 ppm) as a consequence of the aromatic substituents in the proton NMR spectrum of **13**. In contrast, partial hydrogenated cycloadduct **12'** could be isolated as a mixture of diastereoisomers. An oxidative aromatization (slowly at room temperature, rapidly in boiling toluene) furnished the quinone **12**. Because of the presence of a methylene bridge in **12**, an aromatization comparing to **13** can not be effected. However, caused by a retro Diels-Alder reaction compound **8a** was isolated as the main product on treatment of **1a** with **6** .

Starting with bifunctional 1,4-benzoquinone **2** a twofold cycloaddition/ring transformation was observed. The reaction of **2** with the pyridopyrazines **1a-e** in boiling methylene chloride resulted in selective formation of the 2,7-diazaanthraquinones **8a-e** as dark blue crystals in high state of purity (Scheme 3). Spectral investigation was preferably carried out with the trifluoromethyl derivative **8b** because of relatively low solubility of related compounds in most solvents. ^{1}H-, ^{13}C NMR, and mass spectral data confirmed the structural assignments; e.g. in the proton NMR spectrum of **8b** the characteristic splitting pattern of the 2-substituted pyridine ring was found. The ^{13}C NMR spectrum revealed two resonance signals for the quinone carbonyls at 188.39 and 183.01 ppm. The ^{15}N NMR spectrum of the ^{15}N-enriched probe **8e** (starting from **1e**) in both exocyclic amino positions revealed two signals at -265.12 (d, $^1J(^{15}N,H)$ = 90,4 Hz) and -299.28 (d, $^1J(^{15}N,H)$ = 87.18 Hz).

The detection of only one isomer **8** demonstrates again the regioselectivity of the cycloaddition.



1, 8	R
a	p-CH_3Ph
b	m-CF_3Ph
c	p-EtOOCPh
d	Ph
e	^{15}N-Aza-Ph

Scheme 3

The [4+2]-cycloaddition/ring transformation sequence described herein will be applicable to the synthesis of diverse substituted 2,2'-bipyridines by changing the dienophilic compound. The extension of this chemistry

to other pyrido-bicycles should open further synthetic vistas. Our current work is aimed at defining and expending the scope of this new and useful cycloaddition/ring transformation methodology and at obtaining further information concerning questions of mechanism.

Acknowledgment: This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

EXPERIMENTAL

All reagents were of commercial quality (Aldrich, Fluka, Merck). 1,4-benzoquinone was freshly sublimed before used. Solvents were dried and purified using standard techniques. Reactions were monitored by thin layer chromatography (TLC), on plastic plates coated with silica gel and flourescent indicator (Polygram SIL G/UV_{254} from Macherey-Nagel) or plastic plates coated with neutral alumina with flourescence indicator (Polygram ALOX N/UV_{254} from Macherey-Nagel). Flash chromatography was carried out on silica gel (Merck, Silica gel 60, particle size 0.063mm-0.2mm, 70-230 mesh ASTM) or neutral alumina (Merck, aluminium oxide 90 active neutral, activity I, particle size 0.063mm-0.2mm, 70-230 mesh ASTM). Melting points were measured with a Galen III (Boetius system) from Cambridge Instruments, and are uncorrected. UV-VIS spectra were obtained using a Perkin Elmer Lambda 19 spectrophotometer . Infrared spectra were recorded on a Nicolet Impact 400 spectrometer (KBr). The ^{1}H- and ^{13}C NMR spectra were obtained on Bruker DRX 400 (400 MHz) and Bruker AC 250 (250 MHz) spectrometers. Mass spectra were taken from measurements on a Finnigan MAT SAQ 710 mass spectrometer. Elemental analyses were carried out in-house with an automatic analyzer LECO CHNS 932. Elemental analyses were taken from all compounds except of those derivatives with a high content of flourine.

Synthesis of Azaquinones 9-11, General Procedure

A solution of the pyrido[1,2-a]pyrazine **1** (1 mmol) and the appropriate quinone (1 mmol) were heated at reflux in 30 ml of methylene chloride, and the progress of the reaction was controlled by TLC. Usually, reaction times were between 3 h and 10 h. The solvent was removed in vacuo and the residue was separated by chromatography on silica gel with 3:1 of $CHCl_3$ and ethyl acetate. The solution was concentrated (ca. 5 ml) and cooled (-78°C) overnight, yielding dark colored crystalline solid of the azaquinones.

3,4-Bis[(3-trifluoromethylphenyl)amino]-1-(2-pyridinyl)-benzo[g]isoquinoline-5,10-dione (**9**)

Yield, 82 %. Mp, 184 - 186 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 10.14 (s, 1H, N*H*); 8.59 (d, J = 4 Hz, 1H); 8.10 (t, J = 7 Hz, 2H); 8.00 (s, 1H, N*H*); 7.91 (t, J = 7 Hz, 1H); 7.66-7.74 (m, 8H); 7.01 (d, J = 7 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 101 MHz) δ: 186.85, 181.40 (2 *C*=O); 158.78; 154.09; 149.93; 148.79; 141.28; 138.72; 136.76; 134.89; 134.47; 133.50; 133.45; 131.97 (^{2}J(F,C) = 33 Hz); 131.11 (^{2}J(F,C) = 32 Hz) (2 ipso-*C*F_3); 129.98; 129.22; 127.49; 127.08; 126.79; 125.40; 123.21; 123.02; 122.94; 123.84 (^{1}J(F,C) = 268 Hz); 123.64 (^{1}J(F,C) = 270 Hz) (2 *C*F_3); 121.47; 118.41; 120.10 (^{3}J(F,C) = 4 Hz); 119.62 (^{3}J(F,C) = 4 Hz); 116.92 (^{3}J(F,C) = 4 Hz); 115.66 (^{3}J(F,C) = 4 Hz) (4 ortho-*C*F_3) ppm.

MS (CI with H_2O) *m/e*: 605 (95 %, $(M+1)^+$); 585 (26 %, $(M-F)^+$); 449 (57 %); 429 (28 %); 159 (100 %); 102 (77 %). IR (KBr) cm^{-1}: 3426 (s); 3072 (w); 1662 (m); 1568 (m); 1452 (m); 1333 (s); 1262 (s); 1126 (m). UV-VIS ($CHCl_3$) λ: 254.6(lgε = 4.5979); 356.2(lgε = 3.9483); 499.4(lgε = 4.0413) nm.

3,4-Bis[(4-methylphenyl)amino]-1-(2-pyridinyl)-naphtho[2,3-g]isoquinoline-5,12-dione (**10**)

Yield, 69 %. Mp, 267 - 271 °C. ^1H NMR (CD_2Cl_2, 250 MHz) δ: 10.48 (s, 1H); 8.69 (s, 1H); 8.61 (d, J = 5 Hz, 1H); 8.61 (d, J = 5 Hz, 1H); 8.55 (s, 1H); 7.92-8.07 (m, 2H); 7.14 (d, J = 8 Hz, 1H); 6.95-7.03 (m, 5H); 2.32, 2.24 (2s, 6H) ppm. ^{13}C NMR (CD_2Cl_2, 63 MHz) δ: 187.15, 181.64 (2 *C*=O); 160.49; 150.43; 149.00; 138.56; 136.70; 136.42; 135.77; 135.05; 134.03; 133.73; 131.20; 130.81; 130.35; 130.16; 129.80; 129.57; 129.37; 129.33; 128.68; 128.23; 123.29; 122.85; 120.77; 120.58; 20.88 (CH_3Ar) ppm. MS (CI with H_2O) *m/e*: 547 (100 %, $(M+1)^+$). IR (KBr) cm^{-1}: 3419 (s); 3031 (w); 2920 (w); 1663 (m); 1616 (m); 1562 (m); 1520 (s); 1451 (s); 1274 (s); 1052 (m). UV-VIS (CH_2Cl_2) λ: 301.6 (lgε = 4.5877); 321.6; 400.8 (lgε = 3.9789); 520.8 (lgε = 4.1349) nm. Anal. Calcd. for $C_{36}H_{26}N_4O_2$: C 79.12 %, H 4.76 %, N 10.26 %; Found: C: 78.77 %, H: 5.06 %; N: 9.99%.

3,4-Bis[(4-methylphenyl)amino]-1-(2-pyridinyl)-9-hydroxy-benzo[g]isoquinoline-5,10-dione (**11**)

Yield, 89 %. Mp, 239 - 241 °C. ^1H NMR (CD_2Cl_2, 250 MHz) δ: 12.49 (s, 1H, O*H*); 10.47 (s, 1H, N*H*); 8.62 (d, J = 6 Hz, 1H); 8.07 (t, J = 9 Hz, 1H); 7.56-7.74 (m, 4H); 7.17-7.25 (m, 5H); 6.97-7.04 (m, 5H); 2.24 (2s, 6H, 2 CH_3) ppm. ^{13}C NMR (CD_2Cl_2, 63 MHz) δ: 191.38, 180.29 (2 *C*=O); 162.06; 159.58; 152.92; 149.93; 148.44; 137.68; 136.87; 136.20; 135.71; 134.87; 134.04; 133.43; 129.32; 129.04; 128.36; 124.05; 123.76; 122.70; 122.37; 120.60; 120.32; 118.45; 116.89; 116.39; 20.31 (CH_3Ar) ppm. MS (CI with H_2O) *m/e*: 513 (100 %, $(M+1)^+$); 256 (22 %); 154 (18 %); 108 (18 %). IR (KBr) cm^{-1}: 3409 (m); 3269 (w); 3025 (m); 1656 (m); 1594 (m); 1556 (m); 1520 (s); 1447 (s); 1376 (m); 1279 (s); 1221 (m). UV-VIS (CH_2Cl_2) λ: 255.2 (lgε = 4.4785); 291.2; 388.0 (lgε = 3.8980); 552.0 (lgε = 4.1036) nm. Anal. Calcd. for $C_{32}H_{24}N_4O_3$: C 75.00 %, H 4.69 %, N 10.94 %; Found: C 75.27 %, H 4.87 %, N 10.84 %.

Synthesis of Diazaquinones 8

These compounds were prepared in an analogous manner to that for compounds **9** - **11**, but 2 equivalents of **1** were used. After purification by flash chromatography over silica gel with ethyl acetate the solution was concentrated (ca. 5 ml) and cooled at -78°C overnight, yielding the diazaquinones as dark blue solids.

1,8-Bis(2-pyridyl)-3,4,5,6-tetrakis[(4-methylphenyl)amino]-2,7-diazaanthracene-9,10-dione (**8a**)

Yield, 92 %. Mp, 264 - 267 °C. ^1H NMR (CD_2Cl_2, 400 MHz) δ: 10.02 (s, 1H, N*H*); 8.61 (d, J = 4 Hz, 1H); 7.79 (t, J = 8 Hz, 1H); 7.73 (d, J = 8 Hz, 1H); 7.29 (t, J = 6 Hz, 1H); 7.26 (d, J = 8 Hz, 2H); 7.17 (d, J = 8 Hz, 2H); 7.02 (d, J = 8 Hz, 2H); 6.92 (d, J = 8 Hz; 2H); 6.77 (s, 1H, N*H*); 2.30 (s, 3H, CH_3); 2.25 (s, 3H, CH_3) ppm. ^{13}C NMR (CD_2Cl_2, 101 MHz) δ: 190.08, 183.20 (2 *C*=O); 159.04; 150.97, 149.94; 149.75; 148.65; 136.48; 134.07; 133.47; 130.31; 129.55; 126.78; 124.20; 122.96; 120.70; 120.55; 120.00; 116.36; 20.60, 20.51 (2 CH_3Ar) ppm. MS (CI with H_2O) *m/e*: 785 (12 %, $(M+1)^+$); 392 (7 %); 111 (100 %). Anal. Calcd. for $C_{50}H_{40}N_8O_2$: C 76.53 %, H 5.10 %; N 14.29 %; Found: C 76.48 %, H 5.18 %, N 14.27 %.

1,8-Bis(2-pyridyl)-3,4,5,6-tetrakis[(3-trifluoromethylphenyl)amino]-2,7-diazaanthracene-9,10-dione (**8b**)
Yield, 84 %. Mp, 297 - 302 °C. ^{1}H NMR (THF-d_8, 250 MHz) δ: 9.13 (s, 1H, N*H*); 8.59 (d, J = 5 Hz, 1H); 8.41 (s, 1H, N*H*); 8.09 (s, 1H); 7.76-7.85 (m, 2H); 7.58 (d, J = 8 Hz, 1H); 7.13-7.31 (m, 5H); 7.04 (d, J = 8 Hz, 1H); 6.82 (d, J = 8 Hz, 1H) ppm. ^{13}C NMR (THF-d_8, 63 MHz) δ: 188.39, 183.01 (2 *C*=O); 159.00; 153.48; 151.73; 149.27; 143.99; 141.28; 137.24; 136.53; 131.75 (^2J(F,C) = 30 Hz); 131.36 (^2J(F,C) = 43 Hz) (2 ipso-*C*F$_3$); 130.28; 129.77; 125.34 (^1J(F,C) = 251 Hz); 125.24 (^1J(F,C) = 263 Hz) (2 *C*F$_3$); 124.87; 124.07; 123.54; 121.97; 120.86; 119.58 (^3J(F,C) = 4 Hz); 118.12 (^3J(F,C) = 4 Hz) ; 117.57 (^3J(F,C) = 4 Hz); 115.50 (^3J(F,C) = 4 Hz) (4 ortho-*C*F$_3$); 116.34 ppm. MS (CI with H_2O) *m/e*: 1001 (6 %, $(M+1)^+$); 555 (16 %); 500 (30 %); 301 (48 %); 279 (23 %); 205 (41 %); 154 (45 %); 111 (100 %). IR (KBr) cm^{-1}: 3428 (s); 3061 (m); 1660 (m); 1603 (m); 1559 (s); 1490 (m); 1452 (s); 1334 (s); 1124 (s) cm^{-1}. UV-VIS (CH_2Cl_2) λ: 287.2 (lgε = 4.6572); 366.4 (lgε = 4.2280); 557.6 (lgε = 4.1792) nm.

1,8-Bis(2-pyridyl)-3,4,5,6-tetrakis[(4-carbonylethoxyphenyl)amino]-2,7-diazaanthracene-9,10-dione (**8c**)
Yield, 90 %. Mp, 295 - 298 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 9.45 (s, 1H, N*H*); 8.59 (d, J = 5 Hz, 1H); 7.68-7.85 (m, 6H); 7.29-7.37 (m, 4H); 6.73 (d, J = 9 Hz, 2H); 4.21-4.32 (m, 4H, 2 C*H*$_2$); 1.23-1.35 (m, 6H, 2 C*H*$_3$) ppm. ^{13}C NMR ($CDCl_3$, 101 MHz) δ: 187.90, 181.57 (2 *C*=O); 166.00, 165.98 (2 *C*=O); 157.68; 149.74; 148.16; 144.79; 142.46; 139.37; 136.67; 131.10; 130.47; 129.22; 124.68; 124.37; 123.89; 123.80; 123.22; 120.17; 118.56; 117.34; 60.81, 60.64 (2 *C*H$_2$); 14.32, 14.29 (2 *C*H$_3$) ppm. MS (CI with H_2O) *m/e*: 1017 (100%, $(M+1)^+$); 989 (17 %); 971 (13 %); 508 (13 %); 205 (12 %); 166 (90 %); 108 (35 %). Anal. Calcd. for $C_{58}H_{48}N_8O_{10}$: C 68.50 %, H 4.72 %, N 11.02 %; Found: C 68.30%, H 4.70 %, N 10.94 %.

1,8-Bis(2-pyridyl)-3,4,5,6-tetrakis(phenylamino)-2,7-diazaanthracene-9,10-dione (**8d**)
Yield, 88 %. Mp, 270 - 273 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 10.04 (d, 1H, N*H*); 8.66 (d, J = 4 Hz, 1H); 7.78 (m, 2H); 7.15-7.35 (m, 8H); 7.06 (t, J = 7 Hz, 1H); 6.97 (d, J = 7 Hz, 2H); 6.95 (s, 1H); 6.78 (d, 1H, N*H*) ppm. ^{13}C NMR ($CDCl_3$, 101 MHz) δ: 189.87, 183.11 (2 *C*=O); 158.27; 151.38; 149.12; 148.52; 140.35; 138.75; 136.16; 129.56; 128.76; 127.08; 125.78; 123.83; 123.75; 123.22; 122.75; 120.12; 115.96 ppm. MS (CI with H_2O) *m/e*: 729 (65 %, $(M+1)^+$); 279 (15 %); 257 (26 %); 167 (50 %); 151 (58 %); 120 (45 %). Anal. Calcd. for $C_{46}H_{32}N_8O_2$: C 75.82 %, H 4.40 %, N 15.38 %; Found: C 75.39 %, H 4.33 %, N 15.46 %.

1,8-Bis(2-pyridyl)-3,4,5,6-tetrakis(phenyl-[^{15}N-aza]amino)-2,7-diazaanthracene-9,10-dione (**8e**)
Yield, 85 %. Mp, 274 - 276 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 10.04 (d, ^1J(^{15}N, H) = 87 Hz, 1H, ^{15}N*H*); 8.66 (d, J = 4 Hz, 1H); 7.78 (m, 2H); 7.15-7.35 (m, 8H); 7.06 (t, J = 7 Hz, 1H); 6.97 (d, J = 7 Hz, 2H); 6.95 (s, 1H); 6.78 (d, ^1J(^{15}N, H) = 90 Hz, 1H, ^{15}N*H*) ppm. ^{13}C NMR ($CDCl_3$, 101 MHz) δ: 189.81, 182.87 (2 *C*=O); 158.16; 151.00; 149.09; 148.24; 140.26; 138.68; 136.43; 129.57; 128.78; 126.90; 126.04; 123.84; 123.80; 123.28; 122.84; 119.95; 119.90; 116.08 ppm. ^{15}N NMR ($CDCl_3$, 41 MHz) δ: -265.12 (d, ^1J(^{15}N, H) = 90 Hz); -299.28 (d, ^1J(^{15}N, H) = 87 Hz) ppm. MS (CI with H_2O) *m/e*: 733 (12 %, $(M+1)^+$); 366 (46 %); 279 (12 %); 205 (15 %); 111 (35 %). Anal. Calcd. for $C_{46}H_{32}N_4{}^{15}N_4O_2$: C 75.41 %, H 4.37 %, N 15.85 %; Found: C 75.28 %, H 4.39 %, N 15.59 %.

Synthesis of the Partially Hydrogenated Cycloadduct 12'

1 mmol of the pyrido[1,2-a]pyrazine **1** and the dihydrobenzoquinone derivative **6** (1 mmol) were dissolved in 50 ml of methylene chloride, and a constant stream of air was allowed to bubble through the reaction mixture for 10 h, while stirring it vigorously. After concentration of the reaction mixture, a yellowish solid was separated.

4a,5a,6,9,9a,10a-Hexahydro-3,4-bis[(4-methylphenyl)amino]-1-(2-pyridinyl)-6,9-methanobenzo[g]-isoquinoline-5,10-dione (**12'**)

Yield, 65 %. Mp, 167 °C (dec.). ^{1}H NMR (CD_2Cl_2, 250 MHz) δ: 8.43 (d, J = 5 Hz, 1H) 8.37 (s, 1H); 7.67-7.78 (m, 3H); 7.56 (d, J = 8 Hz, 1H); 7.08-7.23 (m, 5H); 6.72 (d, J=8 Hz, 2H); 6.09-6.13 (m, 1H); 5.49-5.53 (m, 1H); 5.23 (s, 0.5H); 5.18 (s, 0.5H); 3.78 (d, J = 4 Hz, 0.5H); 3.73 (d, J = 4 Hz, 0.5H); 3.51-3.58 (m, 3H); 3.32 (s, 1H); 2.84 (d, J = 4 Hz, 0.5H); 2.78 (d, J = 4Hz, 0.5H); 2.30, 2.35 (2s, 6H); 1.46 (s, 2H) ppm. ^{13}C NMR (CD_2Cl_2, 63 MHz) δ: 207.16, 204.88 (2 *C*=O); 162.15; 151.92; 148.50; 145.43; 140.06; 137.72; 137.38; 135.80; 133.80; 132.09; 129.92; 129.60; 122.79; 121.18; 119.16; 119.20; 61.17; 59.35; 52.70; 51.73; 50.54; 49.90; 49.68; 47.08; 30.06; 21.00; 20.86 (2 *C*H$_3$Ar) ppm. MS(CI with H_2O) *m/e*: 515(23 %, $(M+1)^+$). IR (KBr) cm^{-1}: 3353 (m); 3305 (m); 2994 (w); 2868 (w); 1707 (s); 1664 (m); 1627 (m); 1590 (m); 1529 (s); 1435 (w); 1312 (w); 1244 (m). UV-VIS (CH_2Cl_2) λ: 289.6 (lgε = 3.9603); 342.4 (lgε = 3.9177) nm. Anal. Calcd. for $C_{33}H_{30}N_4O_2$: C 77.04 %, H 5.84 %, N 10.89 %; Found: C 76.85 %, H 5.85 %, N 10.77 %.

Oxydation of 12' to 12

1 mmol of **12'** was suspended in 40 ml of toluene and heated at reflux for 10 h. The solvent was removed *in vacuo* and the mixture was chromatographed over neutral alumina with toluene/acetone (5:1). **12** crystallized from a concentrated solution (ca. 10 ml) at -78°C.

5a,6,9,9a-Tetrahydro-3,4-bis[(4-methylphenyl)amino]-1-(2-pyridinyl)-6,9-methanobenzo[g]-isoquinoline-5,10-dione (**12**)

Yield, 57 %. Mp, 97 - 100 °C. ^{1}H NMR (CD_2Cl_2, 250 MHz) δ: 9.19 (s, 1H); 8.52 (d, J = 5 Hz, 1H); 7.74-7.88 (m, 2H); 7.25-7.29 (m, 3H); 7.08 (t, J = 8 Hz, 4H); 6.82 (d, J = 8 Hz, 2H); 6.73 (s, 1H); 6.24 (m, 1H); 5.99 (m, 1H); 3.59 (s, 2H); 3.47 (s, 2H); 1.50-1.54 (m, 2H) ppm. ^{13}C NMR (CD_2Cl_2, 63 MHz) δ: 202.36, 197.71 (2 *C*=O); 158.52; 150.34; 148.88; 139.15; 137.77; 136.85; 136.75; 135.28; 133.29; 133.01; 130.28; 129.55; 123.81; 123.36; 123.18; 120.67; 119.21; 53.90; 52.11; 48.90; 48.29; 47.33; 20.86; 20.79 (2 *C*H$_3$Ar) ppm. MS(CI with H_2O) *m/e*: 513 (10 %, $(M+1)^+$). IR (KBr): cm^{-1}: 3678 (w); 3405 (w); 3289 (m); 3025 (m); 2924 (m); 2855 (m); 1652 (m); 1594 (s); 1520 (s); 1444 (m); 1363 (m); 1293 (m); 1269 (m). UV-VIS (CH_2Cl_2) λ: 358.4 (lgε = 3.8950); 564.8 (lgε = 3.9142) nm. Anal. Calcd. for $C_{33}H_{28}N_4O_2$: C 77.34 %, H 5.47 %, N 10.94 %; Found: C 77.00 %, H 5.31 %, N 10.78 %.

Synthesis of the Azaquinone 13

A mixture of the pyrido[1,2-a]pyrazine **1** (1 mmol) and **7** (1 mmol) in 30 ml of toluene were heated at 110°C for 5 days. Toluene was removed *in vacuo*, and the residue was chromatographed on silica gel (toluene/acetone, 5 : 1). The azaquinone **13** crystallized from a concentrated solution (5 ml) at 0°C.

7,8-Dimethyl-3,4-bis(phenylamino)-1-(2-pyridinyl)-benzo[g]isoquinoline-5,10-dione (**13**)

Yield, 79 %. Mp, 224 - 226 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 10.41 (s, 1H, N*H*); 8.65 (d, J = 4 Hz, 1H); 7.83-7.90 (m, 3H); 7.62 (d, J = 8 Hz, 1H); 7.35-7.38 (3H); 7.29 (t, J = 8 Hz, 2H); 7.18 (t, J = 8 Hz, 2H); 7.07 (t, J = 7 Hz, 1H); 6.95-7.02 (4H); 2.35 (s, 3H, CH_3); 2.32 (s, 3H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 101 MHz) δ: 187.14, 181.67 (2 *C*=O); 159.79; 153.21; 150.12; 148.78; 144.68; 143.13; 140.77; 138.55; 136.58; 132.60; 131.78; 129.57; 128.78; 127.94; 127.54; 127.24; 125.87; 123.62; 123.44; 122.89; 122.71; 119.99; 119.79; 117.31; 20.27 (*C*H_3Ar); 20.18 (*C*H_3Ar) ppm. MS (CI with H_2O) *m/e*: 497 (100 %, $(M+1)^+$); 248 (17 %); 213 (7 %); 120 (15 %); 94 (15 %). IR (KBr) cm^{-1}: 3412 (w); 3269 (m); 3056 (m); 2923 (m); 1661 (m); 1597 (s); 1562 (s); 1524 (m); 1496 (m); 1446 (m); 1359 (s); 1291 (s). UV-VIS($CHCl_3$) λ: 268.8 (lgε = 4.5361); 517.6 (lgε = 3.9960) nm. Anal. Calcd. for $C_{32}H_{24}N_4O_2$: C 77.42 %, H: 4.84 % N 11.29 %; Found: C 77.22 %, H: 4.90 %, N 11.19 %.

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12. Crystal Data for **11**: $C_{39}H_{32}N_4O_3$, Mr = 604.7 gmol^{-1}, dark red prisms, size 0.41 x 0.38 x 0.38 mm^3, triclinic, space group $P\bar{1}$, a = 10.056(1), b = 11.486(1), c = 14.776(3) Å, α = 72.80(1), β = 82.21(1), χ = 67.27(1)°, V = 1503.3 (4) Å^3, Z = 2, $\rho_{calcd.}$ = 1.336 gcm^{-3}, μ (Mo-K$_\alpha$) = 0.86 cm^{-1}, F(000) = 636, 7165 reflections in ±h, -k, ±l, measured in the range 2.20° ≤ Θ ≤ 27.40°, 6823 independent reflections, R_{int} = 0.015, 5359 reflections with $F_o > 4\sigma(F_o)$, 531 parameters, R = 0.045, wR^2 = 0.126, GOOF = 1.04, largest difference peak: 0.31 e Å^{-3}.
    Further details of the crystal structure investigations are available on requests from the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-76344 Eggenstein-Leopoldshafen, on quoting the depository number CSD-405882, the names of the authors, and the journal citation.

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