[^{3}H]gallopmil as above in a 1-mL total assay volume. The remaining procedures were as described above. Each data point shown represents the mean of triplicate determinations. Each experiment was repeated at least 3 times.

Acknowledgment. We acknowledge support of this work by the National Heart, Lung, and Blood Institute through research Grant HL-34052 to W. L. Nelson and by the Veterans Administration through a merit review grant to J. C. Giacomini.

Registry No. (±)-1·HCl, 23313-68-0; (±)-2, 102852-52-8; (±)-3, 102852-53-9; (±)3·HCl, 102852-54-0; Ca, 7440-70-2.

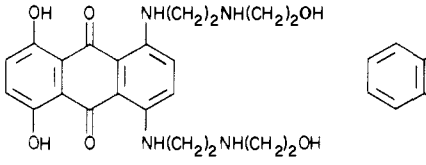
Amino-Substituted *p*-Benzoquinones

Abraham E. Mathew, Robert K.-Y. Zee-Cheng, and C. C. Cheng*

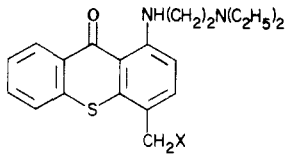
Department of Pharmacology, Toxicology, and Therapeutics and Drug Development Laboratory, The University of Kansas Medical Center, Kansas City, Kansas 66103. *Received August 8, 1985*

Based on the observation of outstanding antineoplastic activity of a number of amino-substituted anthraquinones, thioxanthones, and *N*-(aminoethyl)-substituted naphthalimides, four types of amino-substituted *p*-benzoquinones were designed, synthesized, and their biological activity evaluated. Although none of these compounds exhibited inhibitory activity against P388 leukemia, 2,5-bis[[4-[(dimethylamino)methyl]phenyl]amino]-3,6-dibromo-1,4-benzoquinone and the corresponding dichloro compound demonstrated good inhibitory activity against the proliferating human colon adenocarcinoma in vitro. The dichloro compound was also found to be active against the leukemia L1210 screening in vitro. 2,5-Bis[[2-(dimethylamino)ethyl]amino]-1,4-benzoquinone possessed inhibitory activity against *Neisseria catarrhali*.

A common *o*-aminoquinoid unit was reported[1] among several antitumor antibiotics including streptonigrin, actinomycin D, the mitomycins, and porfiromycin. On the basis of this concept, the AB ring units of streptonigrin[2,3] and amino-containing benzoquinones[4] and naphthoquinones[5] were synthesized and evaluated for their biological activity. Knowledge gained through these studies led to the proposition of a N–O–O working hypothesis.[6] Adamson[7] subsequently postulated a structural modification approach for the anthracyclines including adriamycin and daunomycin. Repeated structural designs and syntheses, together with a structural lead from the National Cancer Institute,[8] culminated in the synthesis of a dihydroxylated amino-containing anthraquinone DHAQ,[9] 1,4-dihydroxy-5,8-bis[[2-[(2-hydroxyethyl)amino]ethyl]-amino]anthraquinone (1), which displayed outstanding anticancer activity and is being evaluated in cancer patients.[10–12]



1



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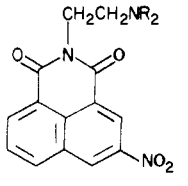

3

The DHAQ side chain contains an (aminoethyl)amino unit in common with two other types of antineoplastic agents **2** (e.g., hycanthone,[13,14] X = OH) and **3** (e.g., mitonafide,[15–17] R = CH_3). The presence of the distal nitrogen atom among the three structurally different ring systems,[8–14] together with the report that DNA binding or intercalation may not be the true mechanism of action for the anticancer activity of DHAQ,[18] suggested that incorporation of the substituted (aminoethyl)amino group and related side chains into other simpler ring systems should be studied. Consequently, synthesis of compounds containing the following amino-substituted side chains attached to the opposite sides of *p*-benzoquinone was conducted.

Type I (Compounds 4a–c). *p*-Benzoquinones containing the 2-[(dimethylamino)ethyl]amino side chains with or without substituents at other positions.

Type II (Compounds 5a,b). The ethylene linkage of

* Address correspondence to Drug Development Laboratory, University of Kansas Cancer Center, Kansas City, KS 66103.

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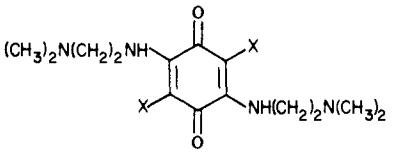
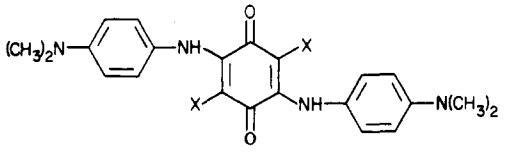
type I compounds is replaced by a *p*-phenylene unit, i.e., compounds containing the *p*-(dimethylamino)anilino functions.

Type III (Compounds 6a–d). To increase the basicity of the distal amino function of compounds of type II, a methylene linkage is inserted between the distal amino and the phenyl linkage, i.e., compounds containing the *p*-[(dimethylamino)methyl]anilino functions.

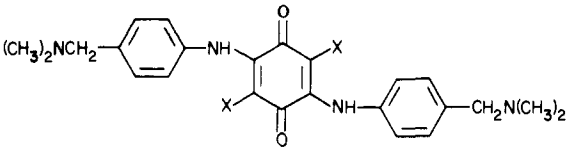
In addition, several amino-containing *p*-benzoquinone derivatives having bis(substituted-phenyl) functions attached to the opposite positions (**7**) were also prepared. These compounds are analogues of polyporic acid that have shown inhibitory activity against Walker 256 carcinosarcoma in rats.[4]



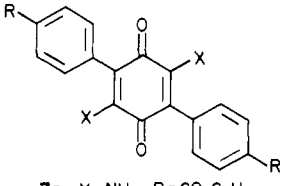
4a, X = H
b, X = Cl
c, X = OCH_3



5a, X = H
b, X = Cl



6a, X = H
b, X = Br
c, X = Cl
d, X = OCH_3



7a, X = NH_2, R = $CO_2C_2H_5$
b, X = Cl, R = $N(CH_3)_2$
c, X = OH, R = $N(CH_3)_2$
d, X = OH, R = $CH_2N(CH_3)_2$

Chemistry. Compounds **4a**, **5a**, and **6a** were prepared by treating the appropriate amine with excess 1,4-benzoquinone. Excess quinone rather than the amine was used because the reaction of this type involves the 1,4-addition of the amine to the quinone, followed by rearrangement to the substituted hydroquinone and oxidation by a second molecule of quinone;[19,20] hence, the unsubstituted 1,4-hydroquinone is produced as a byproduct. The use of excess quinone could be avoided by passing O_2 into the reaction mixture.[21] Depending on the availability of the appropriate quinones or the amines, reaction conditions could be selected based on the aforementioned information; for better results, the reaction temperature should be kept at room temperature or below. Compounds **4b**, **5b**, and **6c** were obtained from chloranil and 2 equiv of the amine. In general, for the aliphatic amines, room temperature and the use of nonpolar solvents are preferred, but more polar solvents, higher reaction temperature, and excess amines are desirable for the aromatic amines. The corresonding dibromo derivative **6b** was prepared in a similar manner. The dimethoxy derivatives **4c** and **6d** were prepared from 2,3,5,6-tetramethoxy-1,4-benzoquinone and excess amine at elevated reaction temperature.

Treatment of 2,5-dichloro-1,4-benzoquinone with the diazonium salt of ethyl *p*-aminobenzoate yielded 2,5-bis-[4-(ethoxycarbonyl)phenyl]-3,6-dichloro-1,4-benzoquinone, which was converted to the corresponding diamino derivative **7a** by using ethanolic NH_3. Compound **7b** was prepared from the diazonium salt of 4-(dimethylamino)-aniline. In this experiment, the pH of the reaction mixture is very critical. Optimum pH was found to be 4.7, since at higher pH a polymeric material resulted and at lower pH the reaction proceeded very slowly and led to the formation of undesired compounds. The pH of the reaction mixture, therefore, should be checked occasionally and adjusted to 4.7 with NaOAc solution.

Base hydrolysis of compound **7b** readily yielded **7c**, the polyporic acid[4] analogue. Compound **7d** was obtained by the base hydrolysis of 2,5-bis(dimethylamino)-3,6-bis[4-[(dimethylamino)methyl]phenyl]-1,4-benzoquinone. The latter was prepared by the bromination of 2,5-dichloro-3,6-bis(4-tolyl)-1,4-benzoquinone[4] with *N*-bromosuccinimide followed by the treatment with dimethylamine.

Biological Activity. Among the benzoquinones synthesized, 2,5-bis[[4-[(dimethylamino)methyl]phenyl]-amino]-3,6-dibromo-1,4-benzoquinone (**6b**) showed significant inhibitory activity against human colon adenocarcinoma in vitro (proliferating) at an average ID_{50} of 1.4×10^{-7} M. The corresponding dichloro compound **6c** had an average ID_{50} value of 1.0×10^{-7} M. In addition, **6c** demonstrated outstanding inhibitory activity against the leukemia L1210 in vitro[22] with an average ID_{50} value of 3.7×10^{-8} M, which is comparable to the activity of mithramycin ($ID_{50} = 8.0 \times 10^{-8}$ M). Borderline activity against the human colon adenocarcinoma was noted with compound **6a** and against in vitro L1210 with compound **6d**. In the antibacterial/antifungal screen, 2,5-bis[[2-(dimethylamino)ethyl]amino]-1,4-benzoquinone (**4a**) was found to have inhibitory activity against *Neisseria catarrhali*. None of the benzoquinones possess inhibitory activity against the NCI leukemia L1210 screening.

Experimental Section

All melting points were taken on a Thomas-Hoover melting point apparatus. Where analyses are indicated only by symbols of the elements, analytical results obtained for these elements were within ±0.4% of the theoretical values.

2,5-Bis[[2-(dimethylamino)ethyl]amino]-1,4-benzoquinone (4a). To a stirred solution of 10.8 g (100 mmol) of 1,4-benzoquinone in 300 mL of EtOH was added dropwise 4.4 g (50 mmol) of [2-(dimethylamino)ethyl]amine in 10 mL of EtOH. The mixture was stirred at room temperature for 7 h and allowed to stand overnight. It was then concentrated to 100 mL. To the solution was added 100 mL of Et_2O. A small amount of polar impurity deposited was removed by filtration. The filtrate was diluted with 200 mL of Et_2O and evaporated slowly under reduced pressure. The solid that formed was collected by filtration and dried to give 9.1 g (59% yield) of crude **4a**, mp 138–141 °C. It was recrystallized from a mixture of EtOH and petroleum ether (bp 35–40 °C) to give 6.2 g (44% yield) of **4a**: mp 157–159 °C; UV λ_{max} (MeOH) 210 nm (log ϵ 4.27), 245 (3.51), 340 (4.22); NMR

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($CDCl_3$) δ 2.2 (s, 12 H, CH_3), 2.8 (t, 4 H, CH_2), 3.2 (t, 4 H, CH_2), 5.25 (s, 2 H, vinyl H), 6.9 (br s, 2 H, NH). Anal. ($C_{14}H_{24}N_4O_2$) C, H, N.

2,5-Bis[[2-(dimethylamino)ethyl]amino]-3,6-dichloro-1,4-benzoquinone Dihydrochloride (4b). To a stirred solution of 5 g (20 mmol) of chloranil in 100 mL of C_6H_6 was added dropwise at room temperature a solution of 3.6 g (40 mmol) of [2-(dimethylamino)ethyl]amine in 50 mL of C_6H_6 in 1 h. The color of the reaction mixture gradually changed to dark brown. Stirring was continued overnight. The resulting brown solid was collected by filtration and washed with Et_2O (2 × 20 mL) to give 7 g (95% yield). An analytical sample was obtained by recrystallization from MeOH: mp 250–252 °C; UV λ_{max} (MeOH) 226 nm (log ε 4.30), 354 (4.39); NMR ($CDCl_3$) δ 2.3 (s, 12 H, NCH_3), 3.5 (q, 2 H, CH_2), 3.9 (q, 2 H, CH_2), 7.6 (br s, 2 H, NH). Anal. ($C_{14}H_{22}Cl_2N_4O_2 \cdot 2HCl$) C, H, N.

2,5-Bis[[2-(dimethylamino)ethyl]amino]-3,6-dimethoxy-1,4-benzoquinone Dihydrochloride (4c). To a warm (45–50 °C) solution of 1.2 g (5 mmol) of 2,3,5,6-tetramethoxy-1,4-benzoquinone in a mixture of 40 mL of MeOH and 2 mL of H_2O was added, with stirring, a solution of 1.2 g (14 mmol) of [2-(dimethylamino)ethyl]amine in 5 mL of MeOH. The mixture was refluxed for 5 min, then allowed to stir at room temperature overnight. The resulting solution was evaporated to dryness under reduced pressure. The residue was triturated with 50 mL of petroleum ether (bp 35–40 °C) and the solid collected by filtration to give 1.7 g (95% yield) of the free base of **4c** as a dark-purple solid, mp 134–136 °C. One-half gram of the product was dissolved in a mixture of 40 mL of MeOH and 30 mL of petroleum ether (bp 35–40 °C). To this was added 2 mL of HCl in MeOH (3.5 mmol of HCl/mL of MeOH). The mixture was diluted with 20 mL of Et_2O. The precipitated solid was collected by filtration and washed with Et_2O (2 × 10 mL) to give 0.52 g of **4c**, mp 230–232 °C. Recrystallization from a mixture of MeOH and Et_2O yielded 0.4 g of analytically pure product, mp 232–234 °C. Compound **4c** was found to be readily soluble in H_2O or MeOH: UV λ_{max} (MeOH) 228 nm (log ε 4.39), 360 (4.34). Anal. ($C_{16}H_{28}N_4O_4 \cdot 2HCl \cdot H_2O$) C, H, N.

2,5-Bis[[4-(dimethylamino)phenyl]amino]-1,4-benzoquinone (5a). This product was reported previously[19] without much detailed information on procedure, product characterization, and analyses. To a stirred solution of 9.7 g (90 mmol) of 1,4-benzoquinone in 100 mL of EtOH was added 10.5 g (50 mmol) of 4-(dimethylamino)aniline hydrochloride followed by 12.5 g of AcONa. The mixture was stirred at room temperature for 2 days. The resulting precipitate was collected by filtration, washed with EtOH and H_2O, and dried to give 9.6 g (51% yield) of **5a**, mp >300 °C. It was recrystallized from AcOH to afford 6 g of analytically pure **5a**: mp >300 °C; UV λ_{max} ($CHCl_3$) 270 nm (log ε 4.49), 318 (4.40) 485 (4.15); mass spectrum, m/e 376 (M^+). Anal. ($C_{22}H_{24}N_4O_2 \cdot 0.25H_2O$) C, H, N.

2,5-Bis[[(4-dimethylamino)phenyl]amino]-3,6-dichloro-1,4-benzoquinone (5b). To a stirred solution of 6.1 g (25 mmol) of chloranil in 350 mL of EtOH was added 8.4 g (62 mmol) of 4-(dimethylamino)aniline. The mixture was refluxed for 90 min, then was allowed to stir at room temperature overnight. The reaction mixture was concentrated to one-third of its original volume, and the resulting precipitate was collected by filtration. It was then washed with Et_2O and dried to give 10.1 g of light-green product. The solid was suspended in NH_4OH, stirred for 30 min, and filtered. It was washed with H_2O and dried to give 7.7 g (70% yield) of **5b**: mp >300 °C; UV λ_{max} ($CHCl_3$) 270 nm (log ε 4.50), 340 (4.27), 530 (4.03). Anal. ($C_{22}H_{22}Cl_2N_4O_2$) C, H, N.

2,5-Bis[[4-[(dimethylamino)methyl]phenyl]amino]-1,4-benzoquinone (6a). A mixture of 5.61 g (37 mmol) of 1,4-benzoquinone, 3.8 g (18 mmol) of 4-[(dimethylamino)methyl]-aniline, and 200 mL of EtOH was refluxed for 5.5 h, then allowed to stir overnight. The solid product was collected by filtration (1.69 g). The mother liquor was evaporated under reduced pressure, and the residue was triturated with 100 mL of EtOH to yield another 0.65 g of **6a** (total yield 2.34 g, 31%), mp >300 °C. The product was recrystallized from a mixture of EtOH and $CHCl_3$: UV λ_{max} (MeOH) 273 nm (log ε 4.26), 388 (4.28); NMR ($CDCl_3$) δ 2.30 (12 H, N-CH_3), 3.40 (s, 4 H, CH_2), 6.10 (2 H, vinyl-H), 7.10–7.50 (m, 8 H, Ar-H), 8.15 (2 H, NH); mass spectrum, m/e 404 (M^+). The free base **6a** was dissolved in $CHCl_3$, and methanolic HCl was added until pH 1 was reached. The solid formed was collected by filtration and purified by recrystallization from MeOH to give the dihydrochloride salt of **6a**: mp >330 °C. Anal. ($C_{24}H_{28}N_4O_2 \cdot 2HCl \cdot 0.5H_2O$) C, H, N.

2,5-Bis[[4-[(dimethylamino)methyl]phenyl]amino]-3,6-dibromo-1,4-benzoquinone (6b). To a stirred and boiling solution of 5.9 g (14 mmol) of 2,3,5,6-tetrabromo-1,4-benzoquinone in 500 mL of EtOH was added 4.5 g (30 mmol) of 4-[(dimethylamino)methyl]aniline. The resulting mixture was refluxed for 45 min and allowed to cool overnight. The solid product was collected by filtration, washed with EtOH, and dried to give 8.1 g of the hydrobromide salt of **6b**, mp >300 °C. It was dissolved in 500 mL of H_2O. A small amount of insoluble material was separated by filtration. The filtrate was basified with 10% $NaHCO_3$ and extracted with $CHCl_3$ (4 × 100 mL). After removal of the solvent, 4.5 g (57% yield) of **6b** was obtained: mp >300 °C; UV λ_{max} (MeOH) 252 nm (log ε 4.26), 395 (4.17); NMR ($CDCl_3$) δ 2.3 (s, 12 H, CH_3), 3.4 (s, 4 H, CH_2), 7.0–7.5 (m, 8 H, Ar-H), 8.2–8.8 (br s, 2 H, NH); mass spectrum m/e 560 (M^+), 561, 563. Anal. ($C_{24}H_{26}Br_2N_4O_2 \cdot H_2O$) C, H, N.

The free base (2.8 g) was dissolved in 250 mL of $CHCl_3$. To the solution was added methanolic HCl until pH 1 was reached. The resulting precipitate was collected by filtration, washed with $CHCl_3$ and EtOH, and dried to give 3.4 g of the dihydrochloride salt of **6b**: mp >3000 °C. Anal. ($C_{24}H_{26}Br_2N_4O_2 \cdot 2HCl \cdot 1.5H_2O$) C, H, N.

2,5-Bis[[4-[(dimethylamino)methyl]phenyl]amino]-3,6-dichloro-1,4-benzoquinone (6c). To a boiling solution of 2.0 g (8.1 mmol) of chloranil in 150 mL of EtOH was added, with stirring, 2.65 g (18 mmol) of 4-[(dimethylamino)methyl]aniline. The resulting solution was refluxed for 40 min and chilled overnight. The solid product was collected by filtration, washed with EtOH, and dried to yield 4.4 g of the dihydrochloride salt of **6c**, mp >300 °C. The salt was dissolved in 1% dilute HCl solution; a minute amount of insoluble material was removed by filtration, and the filtrate was made basic with $NaHCO_3$. It was extracted immediately with $CHCl_3$ (3 × 50 mL). After drying over anhydrous Na_2SO_4 and removing solvent, the residue was recrystallized from a mixture of $CHCl_3$ and EtOH to give 2.75 g (69% yield) of **6c**: mp >300 °C; UV λ_{max} (MeOH) 270 nm (log ε 4.32), 395 (4.23); NMR ($CDCl_3$) δ 2.3 (s, 12 H, NCH_3), 3.5 (s, 4 H, CH_2), 7.2–7.6 (m, 8 H, Ar-H); mass spectrum m/e 472 ($M^+ - 1$), 474 ($M^+ + 1$). Anal. ($C_{24}H_{26}Cl_2N_4O_2 \cdot H_2O$) C, H, N.

2,5-Bis[[4-[(dimethylamino)methyl]phenyl]amino]-3,6-dimethoxy-1,4-benzoquinone (6d). A mixture of 3.41 g (15 mmol) of 2,3,5,6-tetramethoxy-1,4-benzoquinone and 5.50 g (37 mmol) of 4-[(dimethylamino)methyl]aniline in 275 mL of MeOH was refluxed for 24 h. Solvent was removed and the residue triturated with Et_2O. The resulting solid was collected by filtration to give 3.25 g of dark-green product **6d**. It was dissolved in 200 mL of $CHCl_3$, and the volume of the solution was reduced to 30 mL. To the solution was added 50 mL of petroleum ether (bp 35–40 °C). A small amount of solid was removed by filtration. To the filtrate was added an additional 100 mL of petroleum ether, and the mixture was allowed to stand overnight. The resulting solid was collected by filtration and dried to give 2.6 g (55% yield) of **6d**: mp 165–168 °C; UV λ_{max} (MeOH) 276 nm (log ε 4.51), 408 (4.24); NMR ($CDCl_3$) δ 2.3 (s, 12 H, CH_3), 3.3 (s, 6 H, OCH_3), 3.5 (s, 4 H, CH_2), 7.0–7.4 (m, 8 H, Ar-H), 7.7 (br s, 2 H, NH). Anal. ($C_{26}H_{32}N_4O_4$) C, H, N.

2,5-Bis[4-(ethoxycarbonyl)phenyl]-3,6-dichloro-1,4-benzoquinone. The diazonium salt of ethyl *p*-aminobenzoate was prepared by adding a solution of 13.2 g of $NaNO_2$ in 15 mL of H_2O to a cooled solution (−5 to 0 °C) of 29.7 g (180 mmol) of the amine in 36 mL of HCl and 30 mL of H_2O. The diazonium chloride thus prepared was added dropwise, with stirring, to 10.5 g (60 mmol) of 2,5-dichloro-1,4-benzoquinone in a mixture of 400 mL of MeOH and 130 mL of Et_2O at 5–10 °C. During the addition, a solution of 36 g (440 mmol) of NaOAc in 100 mL of H_2O was simultaneously added dropwise so that the reaction mixture remained neutral throughout the addition. After addition, the mixture was stirred at room temperature for 20 h, concentrated under reduced pressure to ca. 150 mL, and poured into 1.5 L of H_2O. The resulting solid was collected by filtration, washed with H_2O, dried, and then washed with petroleum ether (bp 35–40 °C)

to give 28 g of crude product. It was recrystallized from a mixture of $CHCl_3$ and petroleum ether to give 9.8 g (35% yield) of the chloroester: mp 248–250 °C; NMR (CF_3CO_2H) δ 1.5 (t, 6 H, CH_3), 4.6 (q, 4 H, CH_2), 7.8 (ABq, 8 H, J = 7 cps, Ar-H); mass spectrum m/e 472 ($M^+ - 1$), 474 ($M^+ + 1$). Anal. ($C_{24}H_{18}Cl_2O_6 \cdot 0.5H_2O$) C, H.

2,5-Bis[4-(ethoxycarbonyl)phenyl]-3,6-diamino-1,4-benzoquinone (7a). A solution of 5 g (10 mmol) of the aforementioned chloroester in 150 mL of 18% ethanolic NH_3 and 175 mL of EtOH was stirred at 0 °C for 2 h, then at room temperature for 30 h. The resulting solid was collected by filtration, washed with H_2O, and dried to give 4.0 g of crude **7a**, mp 294–297 °C. Recrystallization from 150 mL of $HCON(CH_3)_2$ afforded 3.5 g (83% yield) of **7a** mp 303–305 °C; UV λ_{max} (MeOH) 228 nm (log ε 4.48), 335 (4.44). Anal. ($C_{24}H_{22}N_2O_6$) C, H, N.

2,5-Bis[4-(dimethylamino)phenyl]-3,6-dichloro-1,4-benzoquinone (7b). To a solution of 23 g (110 mmol) of 4-(dimethylamino)aniline hydrochloride in 10 mL of H_2O and 15 mL of concentrated HCl cooled to −5 to 0 °C was added dropwise, in 3 h, a solution of 7.8 g (110 mmol) of $NaNO_2$ in 20 mL of H_2O. The diazonium chloride thus prepared was added simultaneously with 15 g (180 mmol) of NaOAc in 35 mL of H_2O to a solution of 5.5 g (31 mmol) of 2,5-dichloro-1,4-benzoquinone in 200 mL of MeOH and 120 mL of Et_2O at 12–15 °C. The pH of the reaction mixture was kept at 4.6. After the addition, the pH of the mixture was carefully adjusted to 4.7, and the reaction mixture was stirred at room temperature for 16 h, then at 60–65 °C for 5 h. It was concentrated under reduced pressure to almost dryness, then added into 1.5 L of 1% aqueous NaOAc. The resulting solid was collected by filtration, washed with H_2O, and dried to give 11.4 g of crude product. It was recrystallized from 250 mL of $CHCl_3$ to give 0.96 g of crystallized **7b**. The mother liquor was concentrated and chromatographed over SiO_2 column (22 cm, 100 g) and eluted successively with 1:1 C_6H_6–$CHCl_3$ and $CHCl_3$. From the $CHCl_3$ fraction, an additional 1.60 g of the same product was collected. The total yield of **7b** was therefore 20%: mp >300 °C; UV λ_{max} (MeOH) 265 nm (log ε 4.18), 295 (4.22), 570 (3.61); mass spectrum, m/e 414 ($M^+ - 1$), 416 ($M^+ + 1$). Anal. ($C_{22}H_{20}Cl_2N_2O_2 \cdot 1.5H_2O$) C, H, N.

From the initial C_6H_6–$CHCl_3$ elution there was obtained 0.7 g of the mono-aryl-substituted 2,4-dichloro-3-(4-dimethylamino)phenyl-1,4-benzoquinone: mp 188–190 °C; NMR ($CDCl_3$) δ 3.1 (s, 6 H, NCH_3), 6.7–7.5 (m, 5 H, Ar- & vinyl-H). Anal. ($C_{14}H_{11}Cl_2NO_2$) C, H. N.

2,5-Bis[4-(dimethylamino)phenyl]-3,6-dihydroxy-1,4-benzoquinone (7c). To a hot (55 °C) solution of 200 mL of 10% NaOH was added, with stirring, a slurry of 2.2 g (5 mmol) of **7b** in 150 mL of MeOH. The mixture was stirred and refluxed for 75 min and filtered while hot. The filtrate was cooled and acidified with 10% HCl to pH 2, then made basic (to pH 8) with saturated NaOAc solution. The resulting solid was collected by filtration, washed with a small amount of H_2O, and dried. The product was purified by recrystallization from $CHCl_3$, mp >300 °C. The yield was 1.38 g (69%): UV λ_{max} (MeOH) 292 nm (log ε 4.55), 460 (3.35); mass spectrum, m/e 378 (M^+). Anal. ($C_{22}H_{22}N_2O_4$) C, H, N.

2,5-Bis(dimethylamino)-3,6-bis[4-[(dimethylamino)-methyl]phenyl]-1,4-benzoquinone. A mixture of 6 g (17 mmol) of 2,5-dichloro-3,6-bis(4-tolyl)-1,4-benzoquinone[4] and 6 g (34 mmol) of *N*-bromosuccinimide in 650 mL of CCl_4 containing 200 mg of benzoyl peroxide was refluxed for 16 h. Solvent was removed under reduced pressure, and the residue was dissolved in 200 mL of CH_3CN. The solution was cooled to 0–5 °C, and dry Me_2NH was bubbled into the mixture for 90 min (ca. 1–2 bubbles/s). The reaction mixture was stirred at room temperature for 24 h and evaporated under reduced pressure. The resulting viscous residue was dissolved in 200 mL of Et_2O and extracted with 10% HCl (5 × 50 mL). The acid extract was made basic with saturated $NaHCO_3$ solution, then extracted with $CHCl_3$ (3 × 100 mL). The $CHCl_3$ extract was dried (Na_2SO_4), and solvent was removed to yield 5.0 g of the crude product (mp 187–190 °C), which was recrystallized from a mixture of EtOH and $CHCl_3$ to give 3.7 g (48% yield) of pure product: mp 207–209 °C dec; UV λ_{max} (MeOH) 305 nm (log ε 4.10), 370 (4.24); NMR ($CDCl_3$) δ 2.20 (br s, 12 H, benzylic NCH_3), 2.85 (br s, 12 H, NCH_3), 3.40 (br s, 4 H, CH_2), 7.0–7.8 (m, 8 H, Ar-H). The product was used in the following experiment.

2,5-Bis[4-[(dimethylamino)methyl]phenyl]-3,6-dihydroxy-1,4-benzoquinone (7d). A mixture of 2.3 g (5 mmol) of the preceding product and 80 mL of 25% NaOH was refluxed for 2.5 h. The mixture was cooled, and the solid was collected by filtration. It was dissolved in 30 mL of H_2O, and the insoluble material was removed by filtration. The filtrate was carefully neutralized to pH 7.2 with dilute HCl, and the precipitate formed was collected by filtration and dried to give 1.34 g (66% yield) of **7d**: mp >300 °C; UV λ_{max} (MeOH) 308 nm (log ε 3.32), 530 (3.18). The dihydrochloride salt of **7d** was prepared by dissolving **7d** in $CHCl_3$, and to the solution was added methanolic HCl to pH 1. The mixture was allowed to stand overnight, and the precipitated solid was collected by filtration. It was recrystallized from a mixture of MeOH and $CHCl_3$ to give 1.32 g of the dihydrochloride salt of **7d**: mp >300 °C. Anal. ($C_{24}H_{26}N_2O_4 \cdot 2HCl \cdot 1.25H_2O$) C, H, N.

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Registry No. **4a**, 102780-56-3; **4b**, 102780-57-4; **4c**, 102780-59-6; **4c**·2HCl, 102780-58-5; **5a**, 102780-60-9; **5b**, 95887-85-7; **6a**, 102780-61-0; **6a**·2HCl, 102780-62-1; **6b**, 102780-63-2; **6b**·HBr, 102780-64-3; **6b**·2HCl, 102780-65-4; **6c**, 102780-66-5; **6c**·2HCl, 102780-67-6; **6d**, 102780-68-7; **7a**, 102780-70-1; **7b**, 102780-71-2; **7b** (monosubstituted), 102780-72-3; **7c**, 102780-73-4; **7d**, 102780-75-6; **7d**·2HCl, 102780-76-7; $H_2N(CH_2)_2NMe_2$, 108-00-9; 4-$H_2NC_6H_4NMe_2$, 99-98-9; 4-$H_2NC_6H_4NMe_2 \cdot HCl$, 2052-46-2; 4-$H_2NC_6H_4CH_2NMe_2$, 6406-74-2; 4-$MeCH_2O_2CC_6H_4N_2^+Cl^-$, 2028-79-7; 4-$Me_2NC_6H_4N_2^+Cl^-$, 100-04-9; 1,4-benzoquinone, 106-51-4; chloranil, 118-75-2; 2,3,5,6-tetrabromo-1,4-benzoquinone, 488-48-2; 2,5-bis[4-(ethoxycarbonyl)phenyl]-3,6-dichloro-1,4-benzoquinone, 102780-69-8; 2,5-dichloro-1,4-benzoquinone, 615-93-0; 2,5-bis-[dimethylamino]-3,6-bis[4-[(dimethylamino)methyl]phenyl]-1,4-benzoquinone, 102780-74-5; 2,5-dichloro-3,6-bis(4-tolyl)-1,4-benzoquinone, 28293-34-7.