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Effect of Methoxyl Group Position on the Regioselectivity of Ammonia Substitution Reactions Involving 3,3′-Dichloro-2,2′-binaphthoquinones

Kenneth W. Stagliano,*,† Zhenhai Lu,† Ashkan Emadi,† John S. Harwood,‡ and Cynthia A. Harwood‡

Department of Biological, Chemical, and Physical Sciences, Illinois Institute of Technology, Chicago, Illinois 60616, and Department of Chemistry, University of Illinois at Chicago, Chicago, Illinois 60607

stagliano@iit.edu

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Abstract: A series of methoxyl-substituted 3,3′-dichloro-2,2′-binaphthoquinones **2** were prepared and evaluated for regioselectivity in ammonia substitution reactions. Biquinone **2b** underwent regiospecific amination at the unsubstituted chloronaphthoquinone unit whereas the isomeric biquinone, **2c**, produced moderate regioselectivity (85:15). Biquinone **2d**, however, showed no level of regioselectivity demonstrating that the position of the methoxyl group influences the regiochemistry. The intramolecular hydrogen bond in biquinone **5** altered the regioselectivity. Semiempirical calculations revealed comparatively larger LUMO coefficients at the chlorinated carbons that underwent preferential substitution.

The presence of the biquinone moiety in biologically significant natural products,[1] as well as its emerging use as a ligand in catalysis,[2] has stimulated interest in the development of methods for its construction. The original biomimetic route to biquinones utilized oxidative phenolic coupling reactions to form the key quinone−quinone bond.[3] Palladium-catalyzed coupling approaches involving quinonylstannanes[4] and quinonylboronic esters[5] have also been developed which lead directly to the biquinone. Recently, we reported a synthesis of hydroxybinaphthoquinones based on the substitution of a halogen in 2,3-dihalonaphthoquinones by hydroxyquinone anions.[6] However, attempts to extend the reaction to 2-aminonaphthoquinones yielded *N*,*N*-bis(quinonyl)amines as opposed to the aminobiquinone derivatives.[7]

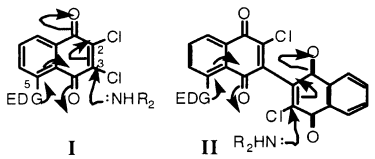

FIGURE 1. Electron donating groups (EDG) control regiochemistry in substitution reactions.

To gain access to aminobiquinones to study their potential antiviral properties,[8] we have prepared a series of methoxyl-substituted 3,3′-dichlorobiquinones and examined their regioselectivity in substitution reactions with ammonia. Here we report that when a *peri*-methoxyl group is present on the aryl ring of one of the chloronaphthoquinone units of the biquinone, regiospecific substitution of chlorine by ammonia proceeds at the unsubstituted chloronaphthoquinone unit. We also demonstrate how changing the position of the methoxyl group effects the regioselectivity of the reaction.

The electronic effects of the *peri*-methoxyl group present in derivatives of juglone methyl ether (5-methoxy-1,4-naphthoquinone) have been extensively utilized in total syntheses to control regiochemistry in reactions involving the quinone double bond.[9] For example, in 5-methoxy-2,3-dichloronaphthoquinone **I** (EDG = OCH_3) nucleophilic substitution of chlorine proceeds with high selectivity at the C-3 position, Figure 1.[10] By analogy, however, it is not known what regiochemical effects, if any, the presence of a *peri*-methoxyl group would exert in substitution reactions involving dichlorobiquinone systems **II** (EDG = OCH_3). Considering that the methoxyl is an electron-donating group (EDG),[11] oxygen n-donation to a carbonyl π-system would render the carbonyl less electron withdrawing, making the double bond of that quinone unit less electrophilic toward nucleophilic attack. Substitution should proceed (by default) at the unsubstituted chloronaphthoquinone unit.

To test this hypothesis, the *peri*-methoxyl-substituted dichlorobiquinone **2b**[12] was prepared by reaction of the readily available hydroxybiquinone **1b** with oxalyl chloride,[6] Scheme 1. Isomeric biquinones **2** were prepared in a similar manner. Our first goal was to optimize conditions for monosubstitution of one of the chlorine atoms using a suitable ammonia source. When a solution of the unsubstituted dichlorobiquinone **2a**[12] in CH_2Cl_2 was

† Illinois Institute of Technology.
‡ University of Illinois at Chicago.

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(3) For a review, see: Laatsch, H. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 423−424.

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(5) Davies, M. W.; Johnson, C. N.; Harrity, J. P. A. *J. Org. Chem.* **2001**, *66*, 3525−3532.

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(7) Bittner, S.; Meenakshi, C.; Temtsin, G. *Tetrahedron* **2001**, *57*, 7423−7429.

(8) We have demonstrated that biquinone derivatives possess anti-HIV activity in the MTT cytoprotection assay.

(9) (a) Naruta Y.; Maruyama, K. In *The Chemistry of the Quinonoid Compounds*; Patai, S., Rappoport Z., Eds.; John Wiley & Sons: New York, 1988; Vol. 2, pp 292−303. (b) Kelly, T. R.; Parekh, N.; Trachtenberg, E. N. *J. Org. Chem.* **1982**, *47*, 5009−5013 and references therein.

(10) (a) Cameron, D. W.; Riches, A. G. *Aust. J. Chem.* **1999**, *52*, 1165−1171. (b) Belitskaya, L. D.; Kolesnikov, V. T. *Zh. Org. Khim. Engl. Transl.* **1984**, *20*, 1920−1925.

(11) Gordon, A. J.; Ford, R. A. *The Chemist's Companion*; Wiley-Interscience: New York, 1972.

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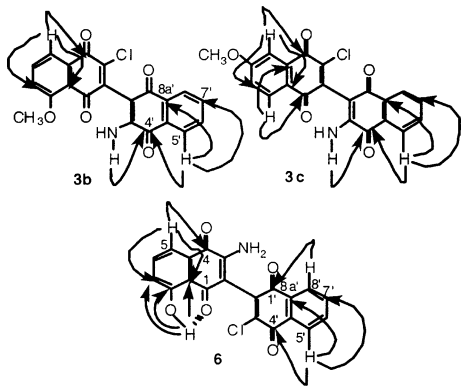
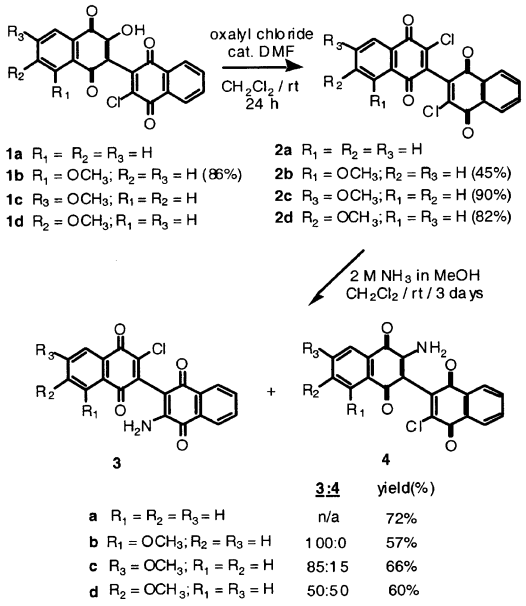


FIGURE 2. Important HMBC correlations in aminobiquinones.

SCHEME 1

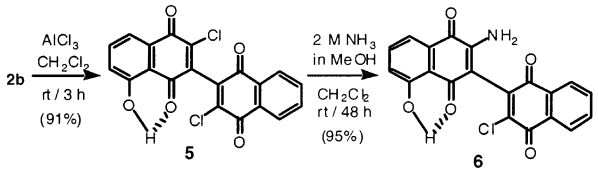


treated with 2 equiv of 2 M ammonia in methanol, the aminochlorobiquinone **3a** was isolated in 72% yield as a brilliant orange solid. Attempts to improve the yield by increasing the equivalents of ammonia resulted in disubstitution to form the symmetrical 3,3′-diamino-2,2′-binaphthoquinone[13] as a side product.

We then set out to demonstrate whether the *peri*-methoxyl group in **2b** could indeed promote regioselective substitution of one of the chlorine atoms. Reaction of **2b** with 2.5 equiv of ammonia in CH_2Cl_2 at room temperature for 3 days afforded a single substitution product (by TLC) along with starting material. The substitution product was easily separated by flash chromatography to afford a stable orange solid in 57% yield. The ^1H and ^{13}C NMR spectra indicated that a single regioisomer had formed.

The structure was assigned by using HMBC NMR spectroscopy, Figure 2.[14] Observation of three bond correlations of the amine proton[15] *and* the C-5′ aromatic ring proton to the C-4′ carbonyl group confirmed that substitution occurred exclusively at the unsubstituted quinone unit to yield **3b**. This conclusion was further corroborated by the additional long-range coupling of the C-5′ aromatic proton to C-8a′ and C-7′.

SCHEME 2



Experiments were also performed to determine whether the observed regioselectivity could be extended to dichlorobiquinones that possessed the methoxyl group at other positions on the aromatic ring. Treatment of dichlorobiquinone **2c** with ammonia was moderately regioselective providing an 85:15 mixture of biquinones **3c** and **4c**.[17] The structure of the major regioisomer **3c** was also confirmed by HMBC, Figure 2.

Whereas ammonia substitution proceeded with high regioselectivity in dichlorobiquinones **2b** and **2c**, amination of the isomeric quinone **2d** was not regioselective and provided a 50:50 mixture of aminobiquinones **3d** and **4d**.[17] These observations demonstrate that the position of the methoxyl group plays an important role in the regioselectivity of ammonia substitution in these systems. Apparently, to avoid amination of the methoxyl-substituted chloroquinone unit, the methoxyl group must be in a position to donate its electrons directly to the carbonyl group that would otherwise be involved in the conjugate addition step of the substitution process.

Based on the well-precedented regiochemical directing effects of the *peri*-hydroxyl group of juglone,[16] we also prepared biquinone **5** by demethylation of **2b** with aluminum chloride, Scheme 2. The Lewis acid character imparted by the intramolecular hydrogen bond was expected to alter the regioselectivity in favor of substituton of the chlorine attached to the juglone unit.[16] Treatment of biquinone **5** with ammonia did yield a single product in 95% overall yield.

However, determination of which regioisomer had formed was not straightforward since correlation of the amine proton to a carbonyl carbon was not observed in the HMBC. The structure was confirmed by HMBC correlation of the C-4′ carbonyl carbon[18] to the C-5′ aromatic proton (Figure 2) indicating that amine substitution must have occurred on the chlorojuglone unit. Further support was provided by correlation of the carbonyl carbon at C-4 to the C-5 aromatic proton on the juglone unit, Figure 2.

We turned to semiempirical calculations (Table 1) to determine whether the regioselectivities might be predictable, using the assumption that the polarization of

(13) Martins, F. J. C.; Viljoen, A. M.; Strydom, S. J.; Fourie, L. F.; Wessels, P. L. *Tetrahedron* **1991**, *47*, 8373−8378.

(14) Bax, A.; Summers, M. F. *J. Am. Chem. Soc.* **1986**, *108*, 2093−2094.

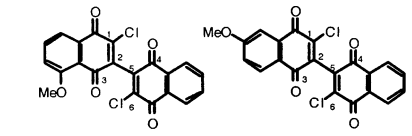
(15) The critical three-bond correlation of the N−H proton to the C-4′ carbonyl group was only detected when DMSO-d_6 was used as the NMR solvent. In $CDCl_3$, the amine peak broadened in the ^1H NMR and long-range couplings were not detected in the HMBC.

(16) Cameron, D. W.; Crosby, I. T.; Feutrill, G. I. *Tetrahedron Lett.* **1992**, *33*, 2855−2856.

(17) Ratios of isomeric products were measured directly from the integration of ^1H NMR absorptions of the methoxyl group protons, which are common to both of the regioisomers.

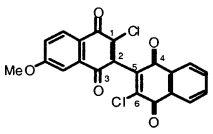
(18) The chemical shift of the carbonyl carbon vicinal to the chlorinated carbon appeared at 177−178 ppm in all of the prepared biquinones, see Table 4 in the Supporting Information.

TABLE 1. LUMO/SLUMO Coefficients and Charges for the Substitutionally Labile Chloroenone Carbons of Biquinones 2b−d and 5 Determined by Semiempirical (PM3) Calculations[a]

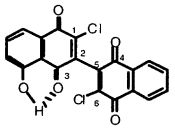


2b

2c



2d



5

	LUMO/SLUMO[b] (charge)			
C	**2b**	**2c**	**2d**	**5**
1	−0.1228/−0.1828 (*−0.2060*)	0.0545/−0.1750 (*−0.1989*)	0.0516/0.6703 (*−0.1917*)	**0.3648/0.0271** (***−0.1849***)
2	−0.0266/0.1404 (*−0.1037*)	−0.0872/0.4542 (*−0.1031*)	0.0170/−0.6550 (*−0.1132*)	−0.3597/−0.0021 (*−0.1096*)
3	−0.0213/−0.0170 (*0.4215*)	−0.1386/−0.3374 (*0.4163*)	−0.1176/−0.3444 (*0.4085*)	−0.2418/−0.1547 (*0.4399*)
4	−0.4088/−0.1191 (*0.4079*)	−0.3055/0.1185 (*0.4082*)	−0.0221/−0.1456 (*0.4082*)	−0.1117/−0.2851 (*0.4084*)
5	−0.6532/0.0188 (*−0.1252*)	−0.3495/−0.0149 (*−0.1247*)	−0.1956/−0.0573 (*−0.1232*)	−0.0604/−0.5327 (*−0.1217*)
6	**0.6944/−0.1009** (***−0.1829***)	**0.3751/−0.0424** (***−0.1817***)	0.2461/0.0058 (*−0.1828*)	0.0687/0.5799 (*−0.1822*)

[a] Using Gaussian 98. PM3 calculations using Cerius[2] and the MOPAC suite revealed similar trends. [b] Numbers in bold correspond to experimentally observed sites of nucleophilic substitution. Raw coefficients must be squared for comparison.

the accepting chloroenone in the ground state could be extrapolated to the energies of the ammonia−chloroenone Michael adduct.[19] The nearly identical charges of the two carbonyl groups at C-3 and C-4 revealed that oxygen n-donation to the carbonyl π-system was not detected in these calculations. Furthermore, the nearly identical charges of the chlorinated carbons at C-1 and C-6 did not predict site selectivity. The high degree of regioselectivity observed for quinones **2b** and **2c** was supported by the larger LUMO coefficient at C-6 relative to C-1. However, the large LUMO coefficient at C-6 (relative to C-1) in **2d** and the lack of regioselectivity observed experimentally suggested that other orbital interactions might be involved.

Calculation of the SLUMO (second lowest unoccupied molecular orbital)[19] of the biquinones (Table 1) revealed a narrow LUMO/SLUMO orbital energy gap possibly making the SLUMO also accessible to a reacting nucleophile. The lack of regiocontrol observed for **2d** might then be explained by the observation of large LUMO and SLUMO coefficients at C-6 and C-1, respectively. Similarly, the high regioselectivity observed in quinones **2b** and **2c** was supported by the significantly larger LUMO coefficient at C-6 compared to both the LUMO and SLUMO coefficients at C-1. Interestingly, the large SLUMO coefficient at C-6 calculated for biquinone **5** apparently had no influence on the regioselectivity. The LUMO and SLUMO orbital pictures located in the Supporting Information further supported this explanation. In biquinones **2c** and **2d**, the LUMO is localized on one of the quinone rings and the SLUMO is localized on the other. Therefore, both the LUMO and SLUMO are required to complete the reactivity picture for these two biquinones. The situation for **2b** is somewhat more complicated as the LUMO and the SLUMO are both slightly delocalized over both biquinone rings. However, this observation does not alter the proposed reasoning for the reactivity of **2b** since the LUMO coefficient at C-6 is much larger than that at C-1 as mentioned earlier.

In closing, unsymmetrical dichlorobiquinones have been prepared which underwent ammonia substitution with high (100:0) to moderate (85:15) regioselectivity to yield aminobinaphthoquinone derivatives. This study extends the well-precedented regiodirective influences of *peri*-methoxyl and *peri*-hydroxyl groups in quinone substitution reactions from mononaphthoquinone to binaphthoquinone systems.

Experimental Section

3′-Chloro-3-hydroxy-8-methoxy-2,2′-binaphthalenyl-1,4,1′,4′-tetraone (1b). 2,3-Dichloro-1,4-naphthoquinone (0.227 g, 1.00 mmol), 2-hydroxy-5-methoxy-1,4-naphthoquinone (0.204 g, 1.00 mmol), and Cs_2CO_3 (0.652 g, 2.00 mmol) were placed in a 25-mL round-bottom flask fitted with a T-bore stopcock. After three vacuum and nitrogen cycles, 15 mL of anhydrous CH_3CN was added and the suspension was stirred at rt for 3 d. The dark red mixture was acidified with concentrated HCl to pH 2 (litmus), and the resulting yellow suspension was poured into 100 mL of water, and the mixture was stirred for 1 h. The yellow precipitate was extracted with $CHCl_3$, dried ($MgSO_4$), filtered, and evaporated. The crude product was purified by flash chromatography on oxalic acid coated silica gel eluting with 50% EtOAc in hexanes to yield 0.339 g (86%) of the biquinone **1b** as a bright yellow solid: mp 198−200 °C; R_f 0.15 (50% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.99 (s, 3H), 7.39−7.41 (d, J = 10.0 Hz, 1H), 7.49 (s, 1H, broad), 7.69−7.73 (t, J = 9.7 Hz, 1H), 7.76−7.81 (m, 2H), 7.85−7.87 (d, J = 9.5 Hz, 1H), 8.12−8.14 (m, 1H), 8.21−8.23 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 56.6, 116.8, 119.4, 119.6, 120.2, 127.3, 127.4, 131.4, 131.5, 131.9, 134.1, 134.4, 134.6, 139.4, 145.6, 151.3, 160.2, 177.4, 180.4, 181.2 (2C); FT-IR 3260, 1674, 1661, 1637, 1587, 1458, 1360, 1324, 1298, 1270, 1221, 1130, 1042, 1012 cm^{-1}. Repeated attempts to detect a molecular ion in the high-resolution mass spectra by using both EI and FAB conditions were unsuccessful. The ^{1}H NMR and ^{13}C NMR are attached for support of the structure. The use of **1b** in subsequent reactions yielded the expected products, which were fully characterized.

3,3′-Dichloro-8-methoxy-2,2′-binaphthalenyl-1,4,1′,4′-tetraone (2b). To a solution of the biquinone **1b** (0.500 g, 1.27 mmol) in anhydrous CH_2Cl_2 (20 mL) was added 0.22 mL of oxalyl chloride (0.322 g, 2.54 mmol) followed by 3 drops of anhydrous DMF. The reaction mixture was stirred for 24 h at rt and then slowly poured into 100 mL of water (CAUTION!). The mixture was extracted with $CHCl_3$ and the organic layer was washed with brine, dried ($MgSO_4$), filtered, and evaporated. The crude solid was purified by flash chromatography on silica eluting with 30% EtOAc in hexanes to yield 0.235 g (45%) of the dichlorobiquinone **2b** as a yellow solid: mp 193−195 °C; R_f 0.25 (30% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.99 (s, 3H), 7.37−7.39 (d, J = 10.6 Hz, 1H), 7.75−7.79 (t, J = 10.3 Hz, 1H), 7.79−7.85 (m, 2H), 7.90−7.92 (d, J = 9.5 Hz, 1H), 8.13−8.15 (m, 1H), 8.24−8.26 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 56.6, 118.8, 118.9, 120.5, 127.4, 127.6, 131.2, 131.5, 133.3, 134.4, 134.7, 135.6, 140.5, 141.3, 142.6, 144.7, 160.5, 177.0, 177.4, 178.8, 179.8; FT-IR 2930, 1680, 1656, 1585, 1471, 1464, 1275, 1260, 1239, 1154, 1046 cm^{-1}; MS (FAB) m/z (rel intensity) 413 [(M + H)$^+$, 46], 379 (40), 343 (5), 231 (14), 154 (42), 136 (36), 117 (100); HRMS (FAB) calcd for $C_{21}H_{11}{}^{35}Cl_2O_5$ (M + H)$^+$ 412.9984, found 412.9998.

3,3′-Dichloro-6-methoxy-2,2′-binaphthalenyl-1,4,1′,4′-tetraone (2c). Reaction of the biquinone **1c** (0.738 g, 1.87 mmol)

(19) (a) Rozeboom, M. D.; Tegmo-Larsson, I.-M.; Houk, K. N. *J. Org. Chem.* **1981**, *46* (11), 2338−2345. (b) Cox, A. L.; Johnston, J. N. *Org. Lett.* **2001**, *3* (23), 3695−3697.

with oxalyl chloride (1.092 g (0.75 mL), 8.60 mmol), as described above for the preparation of **2b**, yielded 0.693 g (90%) of the dichlorobiquinone **2c** as a yellow solid: mp 216−217 °C; R_f 0.37 (30% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.99 (s, 3H), 7.26−7.29 (dd, J = 10.8, 3.2 Hz, 1H), 7.67−7.68 (d, J = 3.4 Hz, 1H), 7.81−7.86 (m, 2H), 8.07−8.10 (d, J = 10.8 Hz, 1H), 8.14−8.16 (m, 1H), 8.25−8.27 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 56.2, 111.2, 121.2, 124.8, 127.4, 127.7, 129.9, 131.3, 131.5, 133.3, 134.5, 134.7, 139.9, 140.0, 144.3, 144.9, 164.7, 176.9, 177.1, 178.7, 179.7; FT-IR 2943, 1677, 1655, 1585, 1575, 1497, 1347, 1300, 1276, 1236, 1132, 1073, 1021 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 413 [(M + H)$^+$, 10], 391 (3), 379 (5), 231 (7), 154 (100), 136 (100), 117 (62); HRMS (FAB) calcd for $C_{21}H_{11}{}^{35}Cl_2O_5$ (M + H)$^+$ 412.9984, found 412.9977.

3,3′-Dichloro-7-methoxy-2,2′-binaphthalenyl-1,4,1′,4′-tetraone (2d). Reaction of the biquinone **1d** (0.500 g, 1.27 mmol) with oxalyl chloride (0.806 g (0.55 mL), 6.35 mmol), as described above for the preparation of **2b**, yielded 0.433 g (82%) of the dichlorobiquinone **2d** as a yellow solid: mp 212−213 °C; R_f 0.37 (30% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.97 (s, 3H), 7.26−7.29 (dd, J = 10.9, 3.1 Hz, 1H), 7.56 (d, J = 3.3 Hz, 1H), 7.81−7.86 (m, 2H), 8.14−8.17 (m, 1H), 8.19−8.21 (d, J = 10.7 Hz, 1H), 8.25−8.27 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 56.1, 111.0, 121.0, 124.6, 127.4, 127.7, 130.3, 131.3, 131.5, 133.6, 134.5, 134.8, 139.3, 139.8, 145.1, 145.6, 164.8, 175.7, 176.9, 179.7, 179.8; FT-IR 2945, 1676, 1657, 1587, 1576, 1496, 1344, 1301, 1279, 1235, 1173, 1144, 1090, 1071, 1018 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 413 [(M + H)$^+$, 8], 391 (5), 379 (5), 231 (14), 154 (100), 136 (91), 117 (89); HRMS (FAB) calcd for $C_{21}H_{11}{}^{35}Cl_2O_5$ (M + H)$^+$ 412.9984, found 412.9977.

3′-Amino-3-chloro-2,2′-binaphthalenyl-1,4,1′,4′-tetraone (3a). To a solution of the dichlorobiquinone **2a** (0.300 g, 0.78 mmol) in 20 mL of anhydrous CH_2Cl_2 in a 50-mL pressure tube, at rt, was added 0.78 mL (0.027 g, 1.56 mmol) of a 2 M solution of ammonia in methanol. The flask was immediately sealed with a Teflon screw cap and the reaction mixture was stirred at rt for 3 d. The resulting suspension was concentrated, and the precipitate was filtered to yield a crude solid that was purified by flash chromatography on silica eluting with 30% EtOAc in hexane to yield 0.205 g (72%) of the aminochlorobiquinone **3a** as an orange solid: mp 211−212 °C; R_f 0.36 (30% EtOAc in hexanes); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.47 (s, 2H, broad), 7.78−7.80 (dt, J = 9.4, 1.6 Hz, 1H), 7.84−7.88 (dt, J = 9.4, 1.5 Hz, 1H), 7.92−7.96 (m, 3H), 8.04−8.06 (m, 2H), 8.14−8.16 (m, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 107.0, 126.1, 126.6, 127.1, 127.2, 130.5, 131.7, 132.3, 133.2 (2C), 134.8, 135.2, 135.7, 141.7, 145.7, 147.1, 177.9, 179.1, 181.1, 181.5; FT-IR 3438 (N−H), 3326 (N−H), 2923, 2852, 1683, 1674, 1616, 1593, 1575, 1539, 1506, 1436, 1394, 1348, 1274, 1122, 1004 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 364 [(M + H)$^+$, 3], 338 (4), 220 (5), 154 (100), 136 (90); HRMS (FAB) calcd for $C_{20}H_{11}{}^{35}ClNO_4$ (M + H)$^+$ 364.0377, found 364.0307.

3′-Amino-3-chloro-8-methoxy-2,2′-binaphthalenyl-1,4,1′,4′-tetraone (3b). Reaction of the dichlorobiquinone **2b** (0.200 g, 0.48 mmol) with ammonia (0.020 g (0.60 mL), 1.20 mmol), as described above for the preparation of **3a**, yielded 0.108 g (57%) of the aminochlorobiquinone **3b** as an orange solid: mp 161−163 °C; R_f 0.23 (30% EtOAc in hexanes); ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.91 (s, 3H), 7.42 (s, 2H, broad), 7.61−7.63 (d, J = 8.6 Hz, 1H), 7.74−7.80 (m, 2H), 7.84−7.88 (m, 2H), 7.93−7.94 (dd, J = 7.7, 1.1 Hz, 1H), 8.04−8.06 (dd, J = 7.7, 1.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 56.9, 107.8, 119.5, 119.8, 119.9, 126.0, 126.6, 130.5, 133.1, 133.2, 133.6, 135.7 (2C), 142.8, 143.2, 146.9, 160.0, 178.3, 179.2, 179.4, 181.5; FT-IR 3438 (N−H), 3336 (N−H), 1676, 1668, 1615, 1583, 1471, 1404, 1348, 1270, 1251, 1153, 1003 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 394 [(M + H)$^+$, 8], 359 (14), 358 (13), 261 (6), 232 (7), 217 (8), 154 (100), 136 (88); HRMS (FAB) calcd. for $C_{21}H_{13}{}^{35}ClNO_5$ (M+ H)$^+$ 394.0482, found 394.0481.

3′-Amino-3-chloro-6-methoxy-2,2′-binaphthalenyl-1,4,1′,4′-tetraone (3c). Reaction of the dichlorobiquinone **2c** (0.188 g, 0.45 mmol) with ammonia (0.019 g (0.57 mL), 1.13 mmol), as described above for the preparation of **3a**, yielded 0.116 g (66%) of an orange solid as a 85:15 mixture of regioisomers **3c** and **4c** as measured from the integration of ^{1}H NMR absorptions of the methoxyl group protons which are common to both of the regioisomers: mp 197−199 °C; R_f 0.38 (40% EtOAc in hexanes); ^{1}H NMR [85:15 mixture] (500 MHz, DMSO-d_6) δ 3.97 (s, 3H), 7.42−7.44 (dd, J = 8.6, 2.7 Hz, 1H), 7.45 (s, 2H, broad), 7.56−7.57 (d, J = 2.7 Hz, 1H), 7.77−7.80 (dt, J = 7.5, 1.3 Hz, 1H), 7.85−7.88 (dt, J = 7.6,1.3 Hz, 1H), 7.93−7.95 (dd, J = 7.6, 1.3 Hz, 1H), 7.99−8.01 (d, J = 8.6 Hz, 1H), 8.04−8.06 (dd, J = 7.6, 1.1 Hz, 1H); ^{13}C NMR [85:15 mixture] (125 MHz, DMSO-d_6) δ 56.5, 107.0, 111.0, 120.7, 125.5, 125.9, 126.4, 129.5, 130.4, 133.0, 133.0, 133.5, 135.5, 141.6, 144.9, 146.8, 164.0, 177.8, 178.9, 179.9, 181.3; FT-IR 3430 (N−H), 3327 (N−H), 1668, 1662, 1618, 1612, 1593, 1575, 1559, 1568, 1397, 1351, 1279, 1082, 1022, 857, 725 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 394 [(M + H)$^+$, 39], 359 (30), 358 (43), 261 (4), 232 (6), 154 (100), 136 (84); HRMS (FAB) calcd for $C_{21}H_{13}{}^{35}ClNO_5$ (M + H)$^+$ 394.0482, found 394.0499.

Regioisomeric Mixture of 3′-Amino-3-chloro-7-methoxy-2,2′-binaphthalenyl-1,4,1′,4′-tetraone (3d) and 3-Amino-3′-chloro-7-methoxy-2,2′-binaphthalenyl-1,4,1′,4′-tetraone (4d). Reaction of the dichlorobiquinone **2d** (0.200 g, 0.48 mmol) with ammonia (0.020 g (0.60 mL), 1.20 mmol), as described above for the preparation of **3a**, yielded 0.116 g (61%) of an orange solid as a 50:50 mixture of regioisomers **3d** and **4d** as measured from the integration of ^{1}H NMR absorptions of the methoxyl group protons which are common to both of the regioisomers.

3,3′-Dichloro-8-hydroxy-2,2′-binaphthalenyl-1,4,1′,4′-tetraone (5). To a solution of the biquinone **2b** (0.100 g, 0.24 mmol) in anhydrous CH_2Cl_2 (6 mL), under nitrogen, was added aluminum chloride (0.645 g, 4.84 mmol). The purple reaction mixture was stirred at rt, under N_2, for 3 h. The reaction was acidified to pH =2−3 with 10% aq HCl and extracted with $CHCl_3$. The organic layer was dried ($MgSO_4$), filtered, and evaporated to yield 0.087 g (91%) of the juglonic biquinone **5** as an orange solid: mp 216−218 °C; R_f 0.40 (30% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35−7.37 (d, J = 10.6 Hz, 1H), 7.70−7.74 (t, J = 10.2 Hz, 1H), 7.82−7.88 (m, 3H), 8.16−8.18 (m, 1H), 8.26−8.29 (m, 1H), 11.6 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 114.3, 121.0, 125.6, 127.5, 127.8, 131.1, 131.2, 131.4, 134.7, 134.9, 136.9, 139.1, 139.7, 145.4, 145.9, 162.1, 176.2, 176.8, 179.7, 184.8; FT-IR 3419, 1684, 1664, 1634, 1589, 1454, 1369, 1304, 1269, 1234, 1144 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 399 [(M + H)$^+$, 37], 365 (35), 231 (13), 167 (25), 154 (100), 136 (89), 117 (75); HRMS (FAB) calcd for $C_{20}H_9{}^{35}Cl_2O_5$ (M + H)$^+$ 398.9827, found 398.9843.

3-Amino-3′-chloro-8-hydroxy-2,2′-binaphthalenyl-1,4,1′,4′-tetraone (6). Reaction of the dichlorobiquinone **5** (0.100 g, 0.25 mmol) with ammonia (0.011 g (0.32 mL), 0.625 mmol) for 48 h, as described above for the preparation of **3a**, yielded 0.074 g (95%) of the aminochlorobiquinone **6** as an orange solid: mp 148−152 °C; R_f 0.31 (30% EtOAc in hexanes); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.32−7.34 (dd, J = 8.2, 1.2 Hz, 1H), 7.60−7.61 (dd, J = 7.5, 1.2 Hz, 1H), 7.64−7.67 (t, J = 7.9 Hz, 1H), 7.84−7.88 (d, J = 17 Hz, broad, 2H), 7.92−7.96 (m, 2H), 8.06−8.08 (m, 1H), 8.15−8.16 (m, 1H), 12.93 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 105.2, 114.0, 119.0, 125.7, 126.6, 126.8, 130.2, 131.2, 131.7, 134.4, 134.8 (2C), 140.1, 145.7, 147.9, 160.3, 177.4, 180.2, 180.6, 184.8; FT-IR 3624 (sharp), 3427 (N−H), 3323 (N−H), 1734, 1717, 1666, 1640, 1612, 1553, 1507, 1462, 1407, 1382, 1270, 1243, 1157, 1121, 1080, 1053 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 380 [(M + H)$^+$, 5], 307 (21), 289 (13), 220 (13), 205 (7), 154 (100), 136 (67); HRMS (FAB) calcd for $C_{20}H_{11}{}^{35}ClNO_5$ (M + H)$^+$ 380.0326, found 380.0305.

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Supporting Information Available: General experimental, ^{1}H and ^{13}C NMR spectra for **1b**, **2b**−**d**, **3a**−**c**, **5**, and **6**, HMBC spectra of **3b**,**c** and **6**, and results of semiempirical calculations of **2a**−**c** including images of the calculated LUMO and second LUMO (SLUMO) for **2b**−**d** and **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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