Unprecedented Directing Effect of Bromine on the Regioselectivity of Addition of Stannylated Oxazolines to Substituted 2-Bromo-1,4-naphthoquinones. Synthesis of 4-Oxazolinyl-1,2-Naphthoquinones

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Introduction

In recent years, the utility of the halogen atom as a control element for directing regiochemistry in quinone systems[1] has been extended to include reactions between organometallics and bromoquinones.[2−8] The reaction can lead to addition of the organometallic to either the quinone carbonyl groups or the vinylic carbons on the quinone core. Both palladium "catalyzed" and "uncatalyzed" versions of the reaction are known. For all practical purposes, regiospecific functionalization of the vinylic carbons can be achieved by palladium-catalyzed coupling of organotins[3] or organoboronic acids[4] to the halogenated carbon of the bromoquinone. In contrast to these catalyzed reactions, where regiochemistry is invariably controlled by the position of the bromine atom,[5] the elements that control regiochemistry during uncatalyzed addition of organometallics to bromoquinones are less well defined. For example, lithiated glycals add to bromobenzoquinones at the carbonyl most distant from the bromine atom,[6] while dialkylcuprates[7] and heteroarylstannanes[8] undergo reaction at the vinylic carbon bearing the bromine.

Here, we report an unprecedented mode of addition in which stannylated oxazolines **II** add to bromonaphthoquinones **I** at the carbonyl group that is *vicinal* to the bromine atom (Figure 1)! We also demonstrate that the position of electron-donating methoxyl groups on the aryl ring of the bromonaphthoquinone has no effect on the regioselectivity of the reaction. Extensive spectroscopic and crystallographic analyses were required to differentiate the bromoquinols **V** from other products (**III**, **IV**, **VI**) that may have formed. Regiospecific conversion of the bromoquinols **V** to novel 4-oxazolinyl-1,2-naphthoquinones is also described.

Results and Discussion

Our interest in both racemic and chiral 2-quinonyloxazolines **III** for use in nitrogen-directed addition of organometallics to quinone carbonyl groups[9] led us to explore the palladium-catalyzed cross-coupling of stannylated oxazolines **2**[10] to bromonaphthoquinones **1**[11] (Scheme 1). The requisite stannylated oxazoline **2** was prepared by lithiation of the corresponding oxazoline followed by transmetalation with trimethyltin chloride.[10] Best results were obtained when the crude reaction mixture was filtered under nitrogen and the product distilled prior to use.

Attempts to optimize the cross-coupling of stannane **2** to bromoquinones **1a**−**c** by varying the catalyst, cocatalyst, solvent, and temperature invariably resulted in an intractable mixture of products. During these optimization studies, we were surprised to learn that after omission of the palladium catalyst the reaction of stannane **2** with quinone **1a** at room temperature afforded a mixture consisting of a single addition product and unreacted bromoquinone **1a**. The product was easily separated from the starting material by flash chromatography yielding a stable colorless solid in 43% yield. We were unable to improve the yield of the addition product even after increasing the reaction time and using excess of the stannane **2**. Remarkably, no bisoxazoline adducts were detected even when a 10-fold molar excess of the stannane was used.

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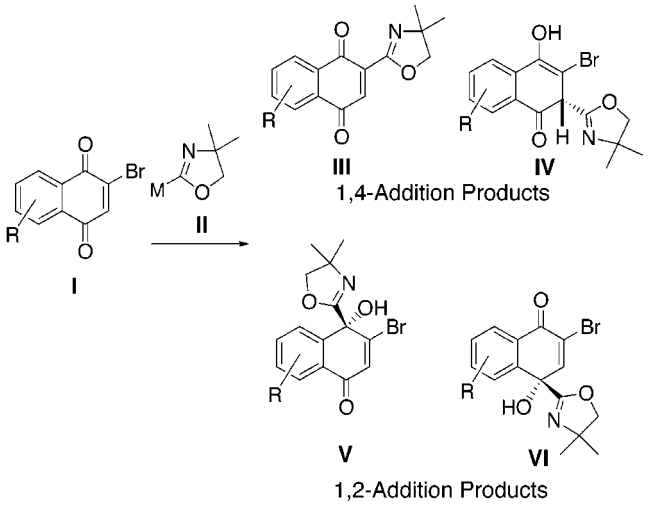
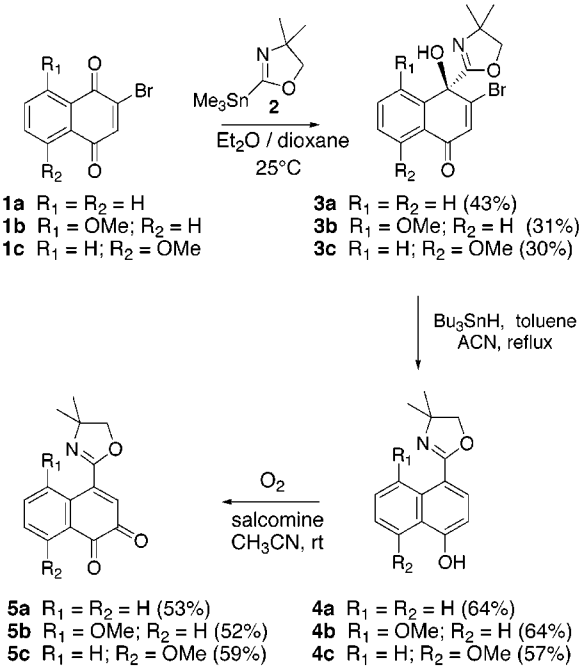


Figure 1.

Scheme 1



To study the synthetic potential of the reaction, we examined the regioselectivity of the reaction between stannane **2** and substituted quinones **1b** and **1c**. Again, only a single product was detected along with the starting bromoquinones. The addition products were remarkably stable under mildly acidic and basic conditions. Although the yields were moderate (30−43%), production of quinols **3a**−**c** could be scaled-up to multigram quantities and the yields brought up to 90% by recovering and recycling the unreacted bromoquinones.

Unequivocal structure assignment of the addition products **3a**−**c** was accomplished using 2D-NMR and X-ray crystallography. Of the four possible products, **III**−**VI**, shown in Figure 1, formation of quinone **III** was easily ruled out based on color and the results of IR, ^{1}H NMR, and MS analyses. To differentiate the vicinal 1,4-addition product **IV** from bromoquinols **V** and **VI**, the ^{13}C NMR spectra of the adducts, including data from a DEPT experiment, were examined. The spectrum of adduct **3a** indicated the presence of five sp^2-hybridized

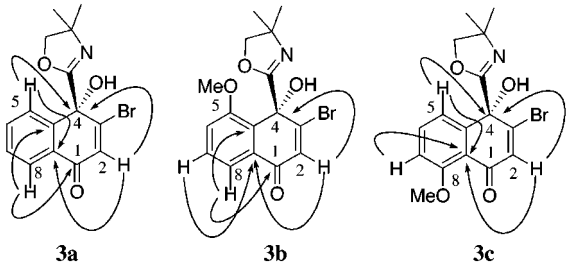


Figure 2. Important HMBC correlations for bromoquinols **3a**−**c**.

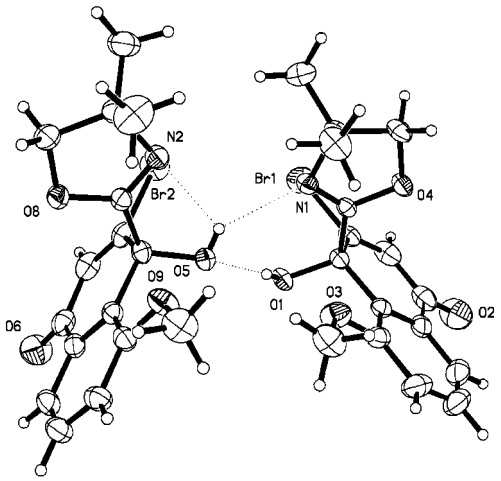


Figure 3. ORTEP drawing of the hydrogen-bonded dimer of quinol **3b** at a 30% probability level.

C−H carbons with chemical shifts in the range 128.0−136.4 ppm. The spectra of the substituted adducts **3b** and **3c** contained four sp^2-hybridized C−H carbons with chemical shifts between 113.6 and 135.6 ppm. The conspicuous absence of an upfield signal for an sp^3-hybridized C−H carbon in **IV** further confirmed our suspicion that **IV** was not the structure of the addition product formed.

To determine whether quinol **V** or **VI** was obtained, we examined long-range ^{1}H−^{13}C connectivities of the quinols **3a**−**c** obtained from HMBC 2D-NMR experiments[12] (Figure 2). For all the quinols **3**, long-range coupling between the vinylic proton at C-2 and the sp^3 carbon at C-4 were detected indicating that addition occurred at the carbonyl group that was vicinal to the bromine atom. This conclusion was further corroborated in compound **3c** with the observed long-range coupling of the proton at C-5 to the sp^3 carbon at C-4. Coupling of the proton at C-8 to the carbonyl carbon at C-1, in **3b**, offered additional support.

The structure assignment was also confirmed by X-ray crystallography. Quinol **3b** was slowly crystallized from an ether/hexane solution to provide the hydrogen-bonded dimer shown in Figure 3.

Although more studies are needed to elucidate the exact source of the observed regioselectivity, competition between steric and electronic factors is undoubtedly involved. The steric effects include an interplay between the steric environment of the carbonyl groups and the steric bulk of the approaching stannylated oxazoline,

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including its solvation sphere.[2f] The effect of electron donation by the bromine[13] and methoxyl[14] groups on the electrophilicity of the carbonyl groups, together with the inductive withdrawing effects exerted by bromine, must also be considered. It is noteworthy that in bromoquinone **1b** addition occurs exclusively at the C-1 carbonyl group, which is more sterically hindered than C-4 and, in the absence of bromine, expected to be less electrophilic due to electron donation by the methoxyl group. Apparently, under the reaction conditions employed, the electronic effects of bromine are more significant in controlling regiochemistry than steric hindrance and resonance effects of the remote methoxyl group.

With the bromoquinols in hand, we envisioned that we still might be able to introduce the oxazoline ring onto an *o*-quinone skeleton by reductive aromatization[6] to the naphthol followed by oxidation. To remove the bromine substituent in the same operation, conditions capable of concomitant debromination and reduction were sought. Reaction of quinol **3a** with excess tributyltin hydride[15] in boiling toluene in the presence of the radical initiator 1,1′-azobis(cyclohexanecarbonitrile) (ACN) afforded the desired naphthol **4a** in 64% yield. The regiochemistry of the reduction reaction was confirmed by analysis of the ^{1}H NMR coupling constants. All of the aromatic protons in the naphthol **4a** displayed ortho coupling. Reduction of the quinols **3b** and **3c** proceeded in a similar fashion to give good yields of naphthols **4b** and **4c**, respectively.

The naphthols **4a**−**c** were cleanly oxidized to the orthoquinones **5a**−**c** under neutral conditions using salcomine-catalyzed air oxidation.[16] Isolation of the quinones **5a**−**c** was accomplished by trituration of the crude product with a small quantity of ether/hexane followed by filtration of the brilliant red-orange precipitate. We noted that facile reduction of the unsubstituted orthoquinone **5a** (yellow spot on TLC) to the hydroquinone (green spot on TLC) occurred readily in solution or when in contact with silica.

Conclusions

In conclusion, the uncatalyzed addition of stannylated oxazolines to substituted bromonaphthoquinones occurs regiospecifically to the carbonyl group vicinal to the bromine atom. To the best of our knowledge, the preparation of bromoquinols **3** represents the first example of the regiospecific formation of stable bromoquinols using organotin derviatives. Our observations that remote methoxyl groups, which are known to influence the electrophilicity of quinone carbonyl groups,[14] had no effect on the regioselectivity of the reaction, is yet another illustration of the powerful regiochemical directing effects of halogens in quinone chemistry. The potential usefulness of the bromoquinols **3** for the fomation of novel quinone frameworks was demonstrated by their two step conversion to 4-oxazolinyl-1,2-naphthoquinones **5**. We continue to explore the organometallic chemistry of quinones and are actively pursuing new applications of bromoquinols **3** in organic synthesis.

Experimental Section

General Methods. Unless otherwise indicated, all NMR data were collected at room temperature in $CDCl_3$ with $CHCl_3$ as the internal reference standard (δ 7.26 ppm for ^{1}H and 77.23 ppm for ^{13}C). Two-dimensional NMR spectra were obtained using a 5 mm TBI Z-gradient probe. Samples were dissolved in acetone-d_6 and were run at 300 K. Two-dimensional magnitude-mode gradient-enhanced COSY, HMQC and HMBC spectra were obtained using standard Bruker pulse sequences. COSY spectra generally employed one scan per increment for 256 increments, while HMQC and HMBC spectra used four scans and 256 increments. Two HMBC experiments were run for each sample, one being optimized for long-range couplings (generally $^2J_{C-H}$ or $^3J_{C-H}$) of 16 Hz and the other optimized for 10 or 12 Hz. Data processing was done using the standard Bruker software. IR spectra were measured in KBr pellets. Melting points were taken in open capillary tubes and are uncorrected. MS were measured under electron impact (EI) conditions. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN. Analytical thin-layer chromatography (TLC) was carried out on commercial Analtech silica gel plates, 250 μm thickness, with fluorescent indicator (F-254). Column chromatography was performed with 35−70 μm silica gel (Acros). Diethyl ether and tetrahydrofuran (THF) were freshly distilled from a sodium/benzophenone still immediately prior to use. Toluene and dichloromethane were distilled from CaH_2 and stored over 4 Å molecular sieves under an atmosphere of dry nitrogen. Unless otherwise specified, all manipulations involving air-sensitive reagents were carried out under an atmosphere of dry nitrogen in oven dried (at least 6 h at 140 °C) glassware. Bromonaphthoquinones **1a**−**c** were prepared as reported.[11] The stannlyated oxazoline **2** was obtained by a modification of the published procedure[10] and distilled under dry nitrogen immediately prior to use.

4,4-Dimethyl-2-trimethylstannanyl-4,5-dihydroxazole (2). To a stirred solution of 4,5-dihydro-4,4-dimethyloxazoline[17] (12.08 g, 122.0 mmol) in dry diethyl ether (600 mL) at −78 °C and under N_2 was added, via cannula, *n*-BuLi (91 mL of a 1.6 M solution in hexane, 145.6 mmol). The resulting white suspension was stirred for 30 min at −78 °C. Me_3SnCl (123 mL of a 1 M solution in THF, 123 mmol) was added via cannula. The clear solution was stirred for another 30 min at −78 °C and slowly warmed to room temperature over a period of 3−4 h, during which time a white precipitate formed. The suspension was filtered under an atmosphere of dry N_2 through a pad of Celite deposited on a double-ended filter funnel. (*NOTE*: It was critical to avoid exposing the filtrate to air.) The solvents were removed under reduced pressure (25 mmHg) to afford a viscous residue that was immediately transferred, via syringe (avoid air!), to a short-path distillation apparatus. Vacuum distillation, using an oil bath temperature of 90−130 °C and a vacuum pressure of 2−5 mmHg, afforded the stannylated oxazoline **2** 15.93 g (50%) as a clear oil.

General Procedure for the Synthesis of Bromoquinols (3). To a stirred suspension of the bromonaphthoquinone **1** (1.0 mmol) in dry ether (8 mL per 1 mmol) at room temperature and under N_2 was added dry dioxane, dropwise, until a yellow to orange solution formed and the final dioxane/ether ratio was 1/3 v/v. A solution of the stannylated oxazoline **2** (1.5 mmol) in dry ether (4 mL per 1.0 mmol of oxazoline **2**) was added dropwise via cannula to the bromonaphthoquinone solution. The resulting brown solution was stirred at room temperature for the indicated period of time (16−22 h). Solvents were removed under reduced pressure yielding a mixture of the quinol **3** and the starting bromonaphthoquinone **1**. Purification by flash chromatography on silica eluting with ether/hexane yielded a slightly colored solid. Trituration with a minimum quantity of cold ether yielded the quinols **3** as white solids which could be further purified by crystallization from ether/hexane. Unreacted bromonaphthoquinones **1** were recycled.

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3-Bromo-4-(4,4-dimethyl-4,5-dihydroxazol-2-yl)-4-hydroxy-4*H*-naphthalen-1-one (3a). Reaction of the bromoquinone **1a** (2.20 g, 9.32 mmol) with the stannylated oxazoline **2** (4.10 g, 15.65 mmol) for 19 h, according to the general procedure above, followed by flash chromatography on silica eluting with ether/hexane (3:7) yielded 1.354 g (43%) of the quinol **3a** as a white solid: mp = 130−132 °C; R_f = 0.35 (ether/hexane 1:1); ^{1}H NMR (300 MHz) δ 1.31 (s, 3H), 1.38 (s, 3H), 3.93 (d, J = 8.4 Hz, 1H), 4.09 (d, J = 8.4 Hz, 1H), 5.11 (s, 1H), 7.01 (s, 1H), 7.52 (td, J = 7.8, 1.5 Hz, 1H), 7.62 (dd, J = 8.4, 1.5 Hz, 1H), 7.68 (td, J = 8.1, 1.5 Hz, 1H), 8.12 (dd, J = 7.8, 0.9 Hz, 1H); ^{13}C NMR (100 MHz) δ 27.9, 28.1, 67.6, 71.8, 82.5, 126.9, 127.4, 128.1, 129.5, 133.7, 134.1, 140.8, 147.7, 165.7, 181.8; FT-IR 3156, 2960, 1660, 1616, 1597,1361, 1341, cm^{-1}; MS (EI) *m*/*z* (intensity) 337 (M^{2+}, 2.3), 335 (M^+, 2.7), 318 (2.3), 257 (17.6), 256 (100), 238 (20.5), 211 (7.5), 199 (8.7), 184 (16.2), 157 (45.5), 129 (40.6), 101 (50.5); HRMS (EI) calcd for $C_{15}H_{14}BrNO_3$ (M^+) 335.0157, found (M^+) 335.0156. Anal. Calcd for $C_{15}H_{14}BrNO_3$: C, 53.73; H, 4.21; N, 4.18. Found: C, 52.09; H, 4.30; N, 4.18.

3-Bromo-4-(4,4-dimethyl-4,5-dihydroxazol-2-yl)-4-hydroxy-5-methoxy-4*H*-naphthalen-1-one (3b). Reaction of the bromoquinone **1b** (0.326 g, 1.22 mmol) with the stannylated oxazoline **2** (0.479 g, 1.83 mmol) for 16 h, according to the general procedure above, followed by flash chromatography on silica eluting with ether/hexane (1:1) yielded 0.138 g (31%) of the quinol **3b** as a white solid: mp = 204−205 °C; R_f = 0.37 (ether); ^{1}H NMR (300 MHz) δ 1.32 (s, 3H), 1.37 (s, 3H), 3.90 (s, 3H), 3.99 (dd, J = 8.4, 8.1 Hz, 2H), 5.01 (s, 1H), 7.00 (s, 1H), 7.15 (dd, J = 8.1, 0.90 Hz, 1H), 7.49 (t, J = 7.8 Hz, 1H), 7.78 (dd, J = 7.8, 1.5 Hz, 1H); ^{13}C NMR δ 28.0, 28.1, 55.9, 67.8, 71.1, 81.5, 115.8, 119.6, 129.3, 130.4, 130.8, 134.0, 147.3, 157.1, 164.2, 181.7; FT-IR 3401, 2964, 1667, 1593, 1476, 1365, 1351 cm^{-1}; MS (EI) *m*/*z* (intensity) 367 (M^{2+}, 9.3), 365 (M^+, 11.9), 320 (7.8), 286 (100), 267 (23.5) 258 (15.5), 214 (23.6), 187 (14.8), 173 (13.6), 159 (10.7), 145 (16.6), 129 (19.1), 131 (61.7); HRMS (EI) calcd for $C_{16}H_{16}BrNO_4$ (M^+) 365.0263, found (M^+) 365.0271. Anal. Calcd for $C_{16}H_{16}BrNO_4$: C, 52.48; H, 4.40; N, 3.82. Found: C, 51.38; H, 4.79; N, 3.94.

3-Bromo-4-(4,4-dimethyl-4,5-dihydroxazol-2-yl)-4-hydroxy-8-methoxy-4*H*-naphthalen-1-one (3c). Reaction of the bromoquinone **1c** (1.46 g, 5.51 mmol) with the stannylated oxazoline **2** (2.16 g, 8.26 mmol) for 22 h, according to the general procedure above, followed by flash chromatography on silica eluting with ether/hexane (6:4) yielded 0.603 g (30%) of the quinol **3c** as a white solid: mp = 164−165 °C; R_f = 0.46 (ether); ^{1}H NMR (300 MHz) δ 1.28 (s, 3H), 1.36 (s, 3H), 3.92 (d, J = 8.4 Hz, 1H), 3.96 (s, 3H), 4.08 (d, J = 7.8 Hz, 1H), 4.99 (s, 1H), 6.89 (s, 1H), 7.03 (dd, J = 8.1, 0.90 Hz, 1H), 7.31 (dd, J = 8.25, 1.5 Hz, 1H), 7.56 (t, J = 7.8 Hz, 1H); ^{13}C NMR (75 MHz) δ 27.8, 28.1, 56.5, 67.6, 71.8, 82.4, 112.7, 118.9, 119.6, 134.5, 135.6, 143.6, 143.8, 160.4, 165.8, 181.2; FT-IR 3236, 2975, 1654, 1623, 1471, 1436, 1364 cm^{-1}; MS (EI) *m*/*z* (intensity) 367 (M^{2+}, 18.4), 365 (M^+, 18.6), 348 (9.8), 286 (100), 258 (19.4), 214 (10.5), 187 (18.2), 159 (8.9), 116 (11.2), 100 (27.55), 55 (15.1), 41 (14.25), 28 (18.1); HRMS (EI) calcd for $C_{16}H_{16}BrNO_4$ (M^+) 365.0262, found (M^+) 365.0241. Anal. Calcd for $C_{16}H_{16}BrNO_4$: C, 52.48; H, 4.40; N, 3.82. Found: C, 52.78; H, 4.60; N, 3.94.

General Procedure for the Synthesis of Naphthols (4). To a refluxing solution of the quinols **3** (1.0 mmol) and tributyltin hydride (10 mmol) in dry toluene (54 mL per 1.0 mmol) under N_2 was added 1,1′-azobis(cyclohexanecarbonitrile) (ACN) (0.5 mmol). The resulting yellow solution was stirred at reflux and the progress of the reaction monitored by TLC. After reaction of all the quinol **3**, the solvents were removed under reduced pressure and the crude naphthols **4** purified by flash chromatography on silica eluting with ether/hexane. The naphthols **4** could be further purified by trituration with cold ether/hexane to remove final traces of colored impurities.

4-(4,4-Dimethyl-4,5-dihydroxazol-2-yl)naphthalen-1-ol (4a). Reaction of the quinol **3a** (0.352 g, 1.05 mmol) with tributyltin hydride (2.38 g, 8.2 mmol) for 5 h at reflux, according to the general procedure above, followed by flash chromatography on silica eluting with ether/hexane (3:7) yielded 0.161 g (64%) of the naphthol **4a** as a light pink solid that was triturated with ether/hexane to yield a white solid: mp = 187−188 °C; R_f = 0.38 (ether/hexane 1:1); ^{1}H NMR (300 MHz) δ 1.50 (s, 6H), 4.23 (s, 2H), 6.35 (d, J = 7.8 Hz, 1H), 7.40 (td, J = 7.2, 0.90 Hz, 1H), 7.51 (td, J = 6.9, 1.5 Hz, 1H), 7.64 (d, J = 8.1 Hz, 1H), 8.28 (d, J = 7.8 Hz, 1H), 8.60 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz) δ 28.6 (two carbons), 67.1, 79.4, 107.3, 114.8, 122.9, 124.8, 125.2, 125.4, 127.5, 130.7, 132.5, 157.0, 165.2; FT-IR 2968, 1631, 1576, 1519, 1362 cm^{-1}; MS (EI) *m*/*z* (intensity) 241 (M^+, 52.3), 226 (100.0), 198 (17.9), 170 (21.2), 140 (11.7), 115 (9.5), 28 (8.3); HRMS (EI) calcd for $C_{15}H_{15}NO_2$ (M^+) 241.1103, found (M^+) 241.1117. Anal. Calcd for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.80. Found: C, 73.40; H, 6.43; N, 5.61.

4-(4,4-Dimethyl-4,5-dihydroxazol-2-yl)-5-methoxynaphthalen-1-ol (4b). Reaction of the quinol **3b** (0.268 g, 0.734 mmol) with tributyltin hydride (2.16 g, 7.43 mmol) for 3 h at reflux, according to the general procedure above, followed by flash chromatography on silica eluting with ether/hexane (8:2) yielded 0.127 g (64%) of the naphthol **4b** as a light yellow solid that was triturated with ether/hexane to yield a white solid: mp = 246−248 °C; R_f = 0.45 (ether); ^{1}H NMR (300 MHz) δ 1.52 (s, 6H), 3.93 (s, 3H), 4.20 (s, 2H), 6.42 (d, J = 7.8 Hz, 1H), 6.80 (d, J = 8.4 Hz, 1H), 7.02 (d, J = 7.8 Hz, 1H), 7.22 (d, J = 8.1 Hz, 1H), 7.76 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz) δ 28.4 (two carbons), 56.3, 66.8, 80.1, 106.8, 108.8, 113.9, 115.8, 124.3, 124.9, 127.3, 129.1, 154.9, 155.8, 168.6; FT-IR 3421, 3097, 2960, 1657, 1596, 1525, 1391, 1366 cm^{-1} MS (EI) *m*/*z* (intensity) 271 (M^+, 9.4), 240 (100), 198 (13.0), 187 (21.6), 156 (8.0), 128 (5.5), 115 (6.9); HRMS (EI) calcd for $C_{16}H_{17}NO_3$ (M^+) 271.1208, found (M^+) 271.1204. Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.45; H, 6.52; N, 5.03.

4-(4,4-Dimethyl-4,5-dihydroxazol-2-yl)-8-methoxynaphthalen-1-ol (4c). Reaction of the quinol **3c** (0.533 g, 1.46 mmol) with tributyltin hydride (4.22 g, 14.5 mmol) at reflux for 1h, according to the general procedure above, followed by flash chromatography on silica eluting with ether/hexane (7:3) yielded 0.225 g (57%) of the naphthol **4c** as a light yellow solid that on trituration with ether/hexane yielded a white solid: mp = 140−141 °C; R_f = 0.63 (ether); ^{1}H NMR (300 MHz) δ 1.45 (s, 6H), 4.08 (s, 5H), 6.85 (d, J = 7.8 Hz, 1H), 6.86 (d, J = 8.4 Hz, 1H), 7.44 (t, J = 8.4, 7.8 Hz, 1H), 7.96 (d, J = 8.4 Hz, 1H), 8.79 (d, J = 8.4 Hz, 1H), 9.88 (s, 1H); ^{13}C NMR (75 MHz) δ 28.8 (two carbons), 56.4, 68.4, 78.1, 104.5, 109.8, 115.1, 116.0, 120.6, 127.2, 131.6, 134.9, 156.2, 157.6, 162.0; FT-IR 3327, 2959, 1635, 1605, 1584, 1465 cm^{-1}; MS (EI) *m*/*z* (intensity) 271 (M^+, 64.0), 256 (100.0), 241 (11.3), 228 (8.3), 199 (25.7), 184 (6.3), 156 (14.7), 140 (3.9), 128 (5.7), 102 (4.7), 63 (3.5), 41 (6.9), 29 (6.2); HRMS (EI) calcd for $C_{16}H_{17}NO_3$ (M^+) 271.1208, found (M^+) 271.1203. Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.80; H, 6.40; N, 5.05.

General Procedure for the Synthesis of 4-Oxazolyl-1,2-naphthoquinones (5). To a stirred suspension of the naphthol **4** (1.0 mmol) and salcomine (0.2 mmol) in acetonitrile (100 mL per 1.0 mmol of naphthol) at room temperature was bubbled oxygen for 15 min. The reaction was subsequently stirred at room temperature in the open air for 16 h. Unique isolation procedures were required for each of the quinones **5**.

4-(4,4-Dimethyl-4,5-dihydroxazol-2-yl)-1,2-dihydro-1,2-naphthalenedione (5a). The naphthol **4a** (0.462 g, 1.92 mmol) was oxidized according to the general procedure above using 0.120 g (0.369 mmol) of salcomine. The reaction mixture was filtered through a small plug of silica gel, and the filtrate was concentrated under reduced pressure at 25 °C (NO HEAT!) yielding a brown oil. Ether (2 mL) was added and the resulting suspension filtered to yield 0.260 g (53%) of the quinonyl oxazoline **5a** as a light orange solid: mp =117−119 °C; R_f = 0.80 (ether); ^{1}H NMR (400 MHz) δ 1.44 (s, 6H); 4.11 (s, 2H), 6.94 (s, 1H), 7.53 (td, J = 7.3 and 1.1 Hz, 1H), 7.68 (td, J = 7.7 and 1.5 Hz, 1H), 8.15 (dd, J = 7.7 and 1.1 Hz, 1H), 8.61 (dd, J = 7.9 and 1.1 Hz, 1H); ^{13}C NMR (100 MHz) δ 28.3 (two carbons), 69.7, 78.5, 129.4, 130.0, 130.8, 130.9, 131.6, 132.2, 135.6, 141.2, 158.6, 178.2, 180.9; FT-IR 2960, 1700, 1665, 1582, 1361, 1341, 1287 cm^{-1}; MS (EI) *m*/*z* (intensity) 255 (M^+, 100), 212 (81.2), 200 (11.9), 184 (19.6), 155 (60.2), 101 (26.8); HRMS (EI) calcd for $C_{15}H_{13}NO_3$ (M^+) 255.0895, found (M^+) 255.0886.

4-(4,4-Dimethyl-4,5-dihydroxazol-2-yl)-5-methoxy-1,2-dihydro-1,2-naphthalenedione (5b). The naphthol **4b** (0.338 g, 1.25 mmol) was oxidized according to the general procedure above using 0.128 g of salcomine (0.394 mmol). The reaction mixture was filtered through a small plug of silica gel and the filtrate concentrated under reduced pressure at 25 °C (NO

HEAT!) to a volume of ~2 mL. Ether (3 mL) was added and the resulting suspension filtered yielding 0.185 g (52%) of the quinonyl oxazoline **5b** as a light orange solid: mp = 147−148 °C; R_f = 0.30 (ether); ^{1}H NMR (300 MHz) δ 1.41 (s, 6H), 3.91 (s, 3H), 4.14 (s, 2H), 6.50 (s, 1H); 7.23 (d, J = 8.0 Hz, 1H), 7.51 (t, J = 8.4 and 7.8 Hz, 1H), 7.70 (d, J = 7.7 Hz, 1H); ^{13}C NMR (100 MHz) δ 28.4 (two carbons), 56.7, 69.6, 78.8, 115.8, 122.8, 129.5, 143.3, 136.9, 142.1, 141.4, 159.5, 163.4, 178.1, 181.8; FT-IR 2960, 1695, 1670, 1596, 1362, 1339, 1289 cm^{-1}; MS (EI) *m*/*z* (intensity) 285 (M^+, 100.0), 242 (19.7), 230 (30.9), 185 (25.3), 170 (19.8); HRMS (EI) calcd for $C_{16}H_{15}NO_4$ (M^+) 285.1001, found (M^+) 285.1006. Anal. Calcd for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 66.94; H, 5.50; N, 4.81.

4-(4,4-Dimethyl-4,5-dihydroxazol-2-yl)-8-methoxy-1,2-dihydro-1,2-naphthalenedione (5c). The naphthol **4c** (0.324 g, 1.19 mmol) was oxidized according to the general procedure above using 0.108 g of salcomine (0.332 mmol). The reaction mixture was filtered through a small plug of silica gel, and the filtrate was concentrated under reduced pressure at 25 °C (NO HEAT!) to a volume of ~10 mL. The resulting suspension was filtered yielding 0.200 g (59%) of the quinonyl oxazoline **5c** as a red-orange solid: mp = 173−175 °C; R_f = 0.26 (ether); ^{1}H NMR (300 MHz) δ 1.45 (s, 6H), 4.00 (s, 3H), 4.12 (s, 2H), 6.90 (s, 1H), 7.15 (d, J = 9.0 Hz, 1H), 7.62 (t, J = 7.8 Hz, 1H), 8.02 (d, J = 7.8 Hz, 1H); FT-IR (KBr) 2968, 1685, 1663, 1635, 1576, 1471, 1387, 1354 cm^{-1}; ^{13}C NMR (75 MHz) δ 28.5 (two carbons), 56.9, 68.1, 80.4, 119.8, 120.6, 123.8, 128.5, 132.7, 132.8, 142.5, 156.9, 162.1, 178.6, 180.4; MS (EI) *m*/*z* (intensity) 285 (M^+, 100.0), 242 (67.7), 215 (27.8), 186 (20.5), 127 (19.9), 101 (11.9); HRMS (EI) calcd for $C_{16}H_{15}NO_4$ (M^+) 285.1001, found (M^+) 285.0982. Anal. Calcd for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 66.99; H, 5.28; N, 5.07.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of quinols **3**, naphthols **4**, and 1,2-naphthoquinones **5**; a complete description of X-ray crystallographic data for quinol **3b** and HMBC spectra and tables summarizing the observed long-range connectivities for quinols **3a**−**c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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