Regiospecific Synthesis of 2,3-Bisnaphthopyranyl Quinones Related to Conocurvone. Effect of Substituents on Palladium-Catalyzed Cross-Coupling of Organostannanes to Naphthopyranyl Hydroxyquinone Triflates

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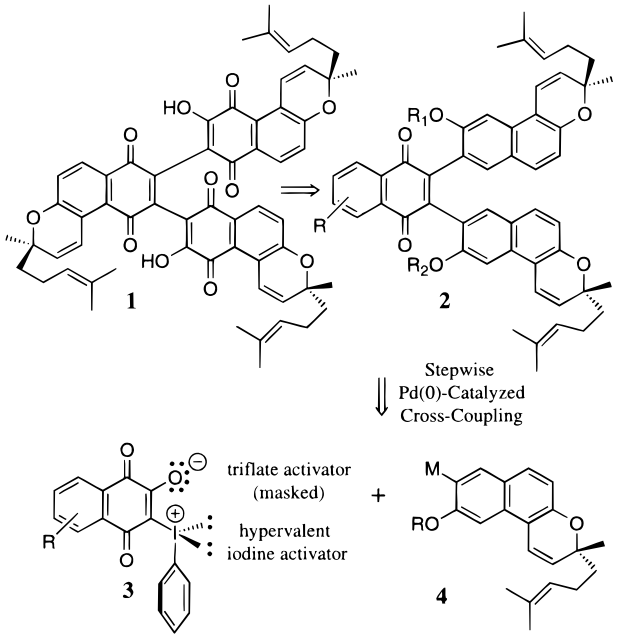
Introduction

Our interest in conocurvone **1**, a plant-derived trimeric quinone possessing potent anti-HIV activity,[1] has led us to explore the synthetic potential of quinone 1,4-dipoles[2] in palladium-catalyzed cross-coupling reactions.[3] We reasoned that the dipoles **3** could serve as doubly activated quinone equivalents in regiocontrolled palladium-catalyzed arylation reactions since they were armed with both a hypervalent iodine and a triflate (in masked form). In particular, we envisioned that if metalated naphthopyrans **4** could be coupled to the carbon bearing the hypervalent iodine,[4] the resulting naphthopyranyl hydroxyquinone could be activated as the triflate and subjected to a second coupling reaction. Subsequent oxidation of the 2,3-bisnaphthopyranyl quinone **2**[5] would lead to a convergent approach for constructing the trimeric quinone framework of conocurvone.[6] Given the significant therapeutic potential of conocurvone for the treatment of HIV-infection, this strategy could serve as a useful entry into a wide range of symmetrical and *unsymmetrical* analogues with potentially improved biological properties.[7]

Here we report the successful implementation of this strategy for the regiocontrolled synthesis of 2,3-bisnaphthopyranyl quinones. We also describe the unprecedented effect of a quinone substituent in controlling triflate decomposition during palladium-catalyzed cross-coupling of metalated naphthopyrans to naphthopyranyl hydroxyquinone triflates.



Results and Discussion

In an effort to expand the application of our doubly activated quinone concept[2] to the synthesis of 2,3-bisnaphthopyranyl quinones, we recently developed conditions for the regiospecific metalation of naphthopyrans.[8] As model compounds for the present cross-coupling experiments, the MOM and *N,N*-diethylcarbamate stannanes **6** were prepared starting from racemic 9-hydroxynaphthopyran **5a** (Scheme 1).[9] Protection of the phenol as the MOM ether **5b**[10] (or carbamate **5c**[11]) followed by

(1) Decosterd, L. A.; Parsons, I. C.; Gustafson, K. R.; Cardellina, J. H., II; McMahon, J. B.; Cragg, G. M.; Murata, Y.; Pannell, L. K.; Steiner, J. R.; Clardy, J.; Boyd, M. R. *J. Am. Chem. Soc.* **1993**, *115*(15), 6673−6679.

(2) Stagliano, K. W.; Malinakova, H. C. *Tetrahedron Lett.* **1997**, *38*(38), 6617−6620.

(3) Both haloquinones and stannylquinones have been employed in palladium-catalyzed cross-coupling reactions, see: (a) Haloquinones: Tamayo, N.; Echavarren, A. M.; Paredes, M. C. *J. Org. Chem.* **1991**, *56*(23), 6488−6491. Echavarren, A. M.; Tamayo, N.; Paredes, M. C. *Tetrahedron Lett.* **1993**, *34*(29), 4713−4716. Fukuyama, Y.; Kiriyama, Y.; Kodama, M. *Tetrahedron Lett.* **1993**, *34*(47), 7637−7638. Chan, K. S.; Mak, C. C. *Tetrahedron* **1994**, *50*(7), 2003−2016. Rama Devi, A.; Iyengar, D. S.; Pardhasaradhi, M. *Tetrahedron* **1994**, *50*(8), 2543−2550. Echavarren, A. M.; Tamayo, N.; Cárdenas, D. J. *J. Org. Chem.* **1994**, *59*, 9(20), 6075−6083. Gothelf, K. V.; Torssell, K. B. G. *Acta Chem. Scand.* **1994**, *48*, 61−67. Graham, A. E.; McKerrecher, D.; Davies, D. H.; Taylor, R. J. K. *Tetrahedron Lett.* **1996**, *37*(41), 7445−7448. de Frutos, O.; Echavarren, A. M. *Tetrahedron Lett.* **1996**, *37*(49), 8953−8956. Yoshida, S.; Kubo, H.; Saika, T.; Katsumura, S. *Chem. Lett.* **1996**, 139−140. Mohri, S.; Stefinovic, M.; Snieckus, V. *J. Org. Chem.* **1997**, *62*(21), 7072−7073. (b) Stannylquinones: Liebeskind, L. S.; Riesinger, S. W. *J. Org. Chem.* **1993**, *58*(2), 408−413 and references therein. Kelly, T. R.; Bringmann, G.; Götz, R.; Keller, P. A.; Walter, R.; Boyd, M. R.; Lang, F.; Garcia, A.; Walsh, J. J.; Tellitu, I.; Bhaskar, K. V. *J. Org. Chem.* **1998**, *63*(4), 1090−1097. (c) The Heck reaction has also been used to arylate quinones, see: Itahara, T. *J. Org. Chem.* **1985**, *50*(26), 5546−5550.

(4) Pd(II)-mediated coupling of alkynes to quinone 1,4-dipoles was examined; see: Kobayashi, K.; Uneda, T.; Kawakita, M.; Morikawa, O.; Konishi, H. *Tetrahedron Lett.* **1997**, *38*(5), 837−840.

(5) Differential protection of the hydroxyl groups in bisnaphthopyranylquinone **2** will allow us to oxidize the two naphthopyranyl subunits in separate synthetic steps, thus circumventing the undesired cyclotrimerization reaction, see: Laatsch, H. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*(4), 422−424.

(6) For syntheses of trimeric and higher oligomeric quinones, see: (a) Pummerer, R.; Lüttringhaus, A.; Fick, R.; Pfaff, A.; Riegelbauer, G.; Rosenhauer, E. *Chem. Ber.* **1938**, *71*(12), 2569−2583. (b) Laatsch, H. *Liebigs Ann. Chem.* **1990**, 433−440. (c) Liebeskind, L. S.; Yin, J. *J. Org. Chem.* **1998**, *63*(17), 5726−5727.

(7) It has been suggested that the low solubility of conocurvone requires the preparation of analogues with more favorable physical properties which will ultimately improve its bioavailability: Armstrong, J. A.; Baker, R. W.; Best, W. M.; Byrne, L. T.; Cannon, J. R.; Colegate, S. M.; Gray, A. R.; Marchant, N. G.; Rothnie, N.; Sargent, M. V.; Sims, C. G.; Spadek, Z. E.; Trengove, R. D. *Aust. J. Chem.* **1999**, *52*(1), 57−62.

(8) Stagliano, K. W.; Malinakova, H. C. *Tetrahedron Lett.* **1998**, *39*(28), 4941−4944.

(9) Both racemic and optically active 9-hydroxynaphthopyrans are known: (a) Racemic: Cannon, J. R.; Joshi, K. R.; McDonald, I. A.; Retallack, R. W.; Sierakowski, A. F.; Wong, L. C. H. *Tetrahedron Lett.* **1975**, *32*, 2795−2798. (b) Optically Active: Jacobsen, E. N.; Vander Velde, S. L. *J. Org. Chem.* **1995**, *60*(17), 5380−5381.

(10) Ramakrishnan, V. T.; Kagan, J. *J. Org. Chem.* **1970**, *35*(9), 2901−2904.

(11) Lustig, E.; Benson, W. R.; Duy, N. *J. Org. Chem.* **1967**, *32*, 851−852.

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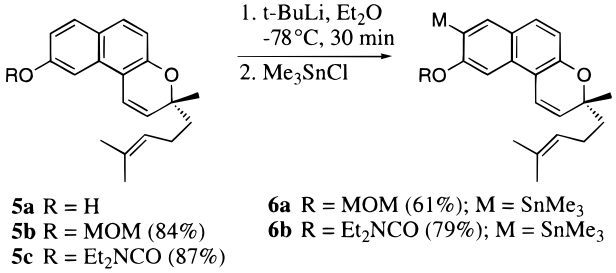
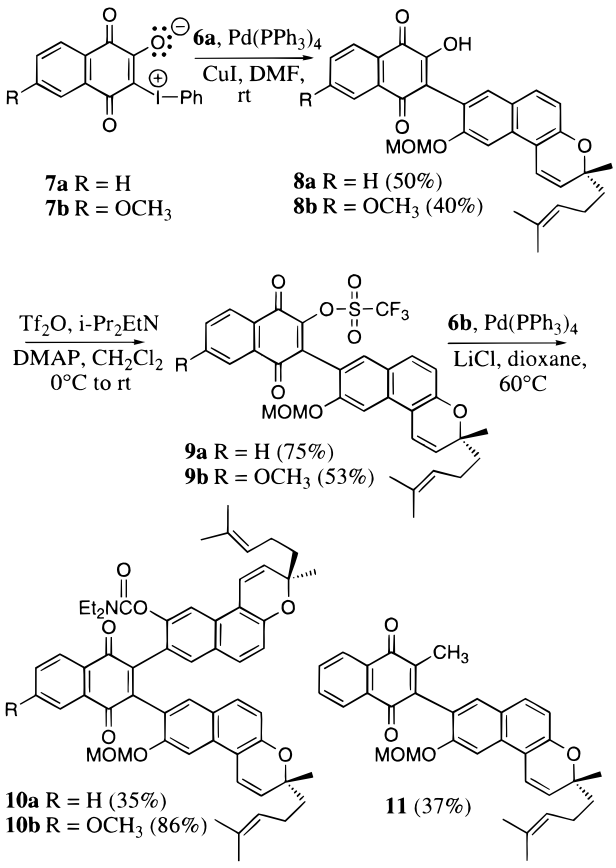
Scheme 1



Scheme 2



regiospecific directed ortho lithiation with *t*-BuLi and reaction with trimethylstannyl chloride provided the stannanes **6a** and **6b** in respectable yields as viscous oils after column chromatography.[8]

Initial screening of the reaction conditions revealed that the cross coupling of naphthopyranyl stannane **6a** to the dipole **7a**[12] proceeded at room temperature to give **8a** in 50% yield as a red glassy solid (Scheme 2).[2] The optimized procedure required the presence of both tetrakis(triphenylphosphine) palladium *and* cocatalytic copper iodide. Contributing to the moderate yield was the formation of 2-hydroxy-3-methyl-1,4-naphthoquinone,[13] produced in 20% yield by methyl transfer from the trimethyltin group of **6a**.[14]

Since the present cross-coupling reaction afforded 3-naphthopyranyl hydroxyquinone **8a** in a single step,[15] this opened up a new synthetic option for further functionalization of the quinone core. Activation of the free hydroxyl in **8a** as the triflate, using triflic anhydride in the presence of catalytic DMAP and Hünig's base (5 equiv) provided **9a** as an isomerically pure red solid that was stable to both aqueous workup and chromatography.

In contrast to our previous report on the facile coupling of aryl stannanes to aryl hydroxyquinone triflates,[2] the coupling of naphthopyranyl stannanes to naphthopyranyl hydroxyquinone triflates proved problematic. When a mixture of the triflate **9a**, 4 equiv of the stannane **6b**, 18 mol % of $Pd(PPh_3)_4$, and 3 equiv of LiCl[14] was heated at 80 °C in dioxane, no coupled product was detected. Under these reaction conditions, only the hydroxyquinone **8a** could be isolated. However, when the reaction temperature was decreased to 60 °C, low yields of the desired coupled product **10a** (35%), along with the hydroxyquinone **8a** (25%) and the methyl transfer product **11** (37%),[14] were isolated.

In an attempt to suppress decomposition of the triflate **9a** to the hydroxyquinone **8a**, we explored the potential of room-temperature cross-coupling conditions. Coupling of the naphthopyran **6b** to the triflate **9a** using the ligandless catalytic system ($Pd_2(dba)_3$, NMP)[16] at room temperature resulted in no reaction. However, when the temperature was raised to 60 °C, with added $AsPh_3$[17] and excess LiCl, the reaction proceeded, but only to give the methyl transfer product **11**.[14] Interestingly, none of the hydroxyquinone **8a** was detected in the reaction mixture.

To minimize the alkyl transfer process,[14] we performed a comparative study using different metalated naphthopyrans. Reaction of the triflate **9a** with the tributylstannyl derivative of **6** (M = $SnBu_3$; R = Et_2NCO)[8] using standard Stille conditions ($Pd(PPh_3)_4$/LiCl/dioxane/60 °C) afforded the hydroxyquinone **8a** as the major product. Similarly, the use of the boronic acid derivative of **6** (M = $B(OH)_2$, R = Et_2NCO)[8] under Suzuki conditions[18] ($Pd(PPh_3)_4/K_3PO_4$/DMF/ 60 °C), provided a 20% yield of the coupled product **10a** along with 70% of the hydroxyquinone **8a**.

In light of these results, we turned our attention to experiments that might provide insight into the cause of triflate decomposition. Initially, we examined the stability of the triflate **9a** to heat. Heating the triflate in dioxane to 80 °C did not lead to decomposition even after extended periods of time. Moreover, no decomposition to the hydroquinone **8a** was observed when a series of solutions of the triflate in dioxane at 80 °C were treated separately with (1) the catalyst ($Pd(PPh_3)_4$), (2) LiCl, (3) both $Pd(PPh_3)_4$ and LiCl, and (4) an excess of the stannane **6b**. Although cleavage of enol triflates derived from 1,3-dicarbonyl compounds has been observed as a

(12) Varvoglis, A.; Hatzigrigoriou, E.; Spyroudis, S. *Liebigs Ann. Chem.* **1989**, 167−170.

(13) Weygand, F.; Weber, H.; Maekawa, E. *Chem. Ber.* **1957**, *90*, 1879−1895.

(14) The effect of the nature of the alkyl groups on the stannane, the solvent and the added LiCl on aryl vs alkyl transfer in Stille coupling reactions has been described; see: Farina, V.; Krishnan, B.; Marshall, D. R.; Roth, G. P. *J. Org. Chem.* **1993**, *58*(20), 5434−5444, and references therein.

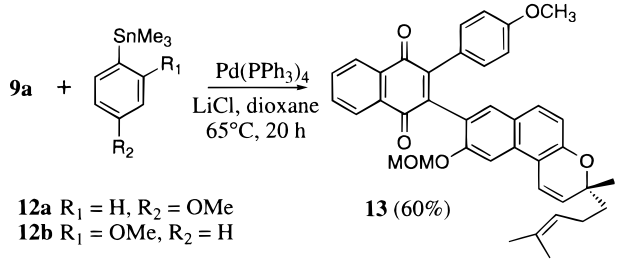
(15) Previously reported palladium-catalyzed cross-coupling of organostannanes to 2-acetoxy-3-bromoquinones proved to be of limited synthetic value. Consequently, functionalized arylhydroxyquinones were prepared by a sequence involving palladium-catalyzed cross-coupling to bromoquinones followed by *t*-BuOOH/$HClO_4$ mediated hydroxylation; see: Echavarren, A. M.; Tamayo, N.; Cardenas, D. J. *J. Org. Chem.* **1994**, *59*(20), 6075- 6083.

(16) Echavarren, A. M.; de Frutos, O.; Tamayo, N.; Noheda, P.; Calle, P. *J. Org. Chem.* **1997**, *62*(13), 4524−4527.

(17) Acceleration of Stille coupling reactions has been observed when the Ph_3P ligand is replaced with the more nucleophilic Ph_3As ligand, see: Farina, V.; Krishnan, B. *J. Am. Chem. Soc.* **1991**, *113*(25), 9585−9595.

(18) Suzuki, A.; Miyaura, N.; Watanabe, T. *Synlett* **1992**, 207−210.

Scheme 3

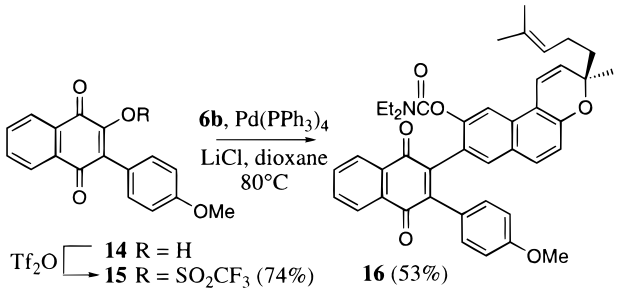


side reaction in several palladium-catalyzed reactions,[19] attributed to the added halide, the current process required all components of the catalytic system, including the stannane![20] It had been reported that in the presence of excess LiCl the palladium-catalyzed coupling of organostannanes to hydroxyquinone triflates led to formation of 2-chloro-1,4-naphthoquinone via an addition−elimination reaction.[16] We did not observe chlorination of triflate **9a** presumably due to the presence of the naphthopyran ring, which stabilized the quinone core toward nucleophilic addition of chloride.[21]

At this stage, we speculated that steric hindrance about the cross-coupling site in the ortho-substituted stannane **6b** may have a role in the decomposition reaction.[22] When we tried to couple the unhindered *p*-anisylstannane **12a**[23] to the triflate **9a**, the coupled product **13** was isolated in a respectable yield (Scheme 3). In contrast, reaction of **9a** with the hindered *o*-anisylstannane **12b**[24] under identical conditions at 65 °C did not proceed. When the temperature was raised to 80 °C, hydroxyquinone **8a** was detected as the only product. This demonstrated that the triflate **9a** could be efficiently processed through the catalytic cycle when there was a sufficiently reactive (in this case unhindered) arylmetal species present to capture the intermediate naphthopyranylquinonylpalladium complex.

Considering our previous success at cross-coupling of the hindered stannane **12b** to various aryl hydroxyquinone triflates,[2] we suspected that additional factors might be responsible for the poor yield of **10a** obtained during coupling of **6b** to **9a**. In a complementary series of studies, we investigated whether the substitution pattern of the aryl group attached to the hydroxyquinone triflate had an influence on the coupling yields (Scheme 4). When we tried the coupling of the naphthopyran **6b** to the triflate **15**,[2] which possessed no substituent in the vicinity of the quinone−aryl bond, the coupled product **16** was isolated in reasonable yield along with only trace

Scheme 4



amounts of the hydroxyquinone **14**. This observation, in conjunction with results of related experiments,[2,25] suggested that triflates that possessed aromatic rings substituted with alkoxy groups ortho to the quinone−aryl bond were more likely to undergo triflate decomposition during coupling reactions with hindered stannanes.

It was evident from the studies above that triflate decomposition could be minimized by using suitably substituted arylhydroxyquinone triflates and/or unhindered aryl stannanes as coupling partners. We assumed that triflate decomposition was a competing side reaction that occurred during the long reaction times required to couple our unreactive (i.e., hindered) substrates **9a** and **6b**. However, it was unclear from these studies how the substitution pattern of the aryl group attached to the triflates influenced the cross-coupling reaction.[26]

We speculated that a potential mechanism for decomposition of **9a** into **8a** might involve reduction of the quinone core by the catalytic system[27] followed by elimination of trifluoromethanesulfinate from oxygen.[28] The resulting anion of 4-hydroxy-3-naphthopyranyl-1,2-naphthoquinone would eventually provide the *p*-hydroxyquinone **8a** on workup.

We rationalized that one approach to testing this hypothesis and potentially controlling the reductive-elimination process would be to introduce electron-releasing groups onto the quinone, thereby decreasing the tendency of the quinone nucleus toward reduction,[29] hence, allowing for the triflate to remain intact for participation in cross-coupling. To accomplish this, we used the substituted dipole **7b**, which possessed a strategically placed electron-donating methoxyl group on the aryl ring of the quinone (Scheme 2). The position of the oxygen atom was consistent with that of the oxygen on the central quinone core of conocurvone **1**.

(19) (a) Neel, D. A., Jirousek, M. R.; McDonald, J. H., III. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 47−50. (b) Farina, V.; Baker, S. R.; Benigni, D. A.; Hauck, S. I.; Sapino, C. *J. Org. Chem.* **1990**, *55*(23), 5833−5847.

(20) Intramolecular migration of a trifluoromethanesulfonyl group in calixarene systems was reported to proceed only in the presence of a palladium catalyst, LiCl, and at least a catalytic amount of vinyltributyl stannane. See: Echavarren, A. M.; Gonzalez, J. J.; Nieto, P. M.; Prados, P.; de Mendoza, J. *J. Org. Chem.* **1995**, *60*(23), 7419−7423.

(21) For an example of decreased reactivity toward *ipso*-substitution of methoxide due to the presence of an aryl ring on the quinone core, see: Liebeskind, L. S.; Yu, M. S.; Yu, R. H.; Wang, J.; Hagen, K. S. *J. Am. Chem. Soc.* **1993**, *115*(20), 9048−9055.

(22) Differences in reactivity between hindered and unhindered substrates used in palladium mediated synthesis of hindered biaryls related to the michellamines have been observed: Hoye, T. R.; Chen, M. *J. Org. Chem.* **1996**, *61*(22), 7940−7942.

(23) Buchman, O.; Grosjean, M.; Nasielski, J. *Bull. Soc. Chim. Belg.* **1962**, *71*, 467−472.

(24) Bishop, M. E.; Schaeffer, C. D., Jr.; Zuckerman, J. J. *Spectrochim. Acta* **1976**, *32A*(8), 1519−1537.

(25) Cross-coupling of the hindered arylstannane **12b** to 2-(2-methoxyphenyl)-3-[(trifluoromethanesulfonyl)oxy]-1,4-naphthoquinone[2] afforded the hydroxyquinone resulting from triflate decomposition as the major product accompanied by 11% of the diarylquinone. Unpublished results.

(26) Presumably, increased steric hindrance about the cross-coupling site and/or chelation of the MOM group in **9** to palladium could be responsible for the observed phenomenon. Chelation of an electron-donor group to palladium is known to give rise to stable cyclometalated complexes; see: Bruce, M. I. *Angew. Chem., Int. Ed. Engl.* **1997**, *16*, 73−86.

(27) The reduction of electron-deficient quinone electrophiles during the Stille coupling leading to recovery of the uncoupled hydroquinone has been observed; see: Chan, K. S.; Mak, C. C. *Tetrahedron* **1994**, *50*(7), 2003−2016.

(28) Loss of trifluoromethanesulfinate ion from aryl triflates has been observed; see: Creary, X.; Benage, B.; Hilton, K. *J. Org. Chem.* **1983**, *48*(17), 2887−2891.

(29) For a discussion of substituent effects on reversible half-wave potentials of quinone/hydroquinone couples, see: Chambers, J. Q. In *The Chemistry of the Functional Groups. The Chemistry of the Quinonoid Compounds*; Patai, S., Ed.; John Wiley & Sons: New York, 1974; Part 2, Chapter 14.

As anticipated, cross-coupling of naphthopyran **6a** to the more electron-rich dipole **7b**[4] proceeded at a slower rate as compared to the unsubstituted dipole **7a**. The time required for completion of the coupling reaction was 48 h at room temperature. The hydroxyquinone **8b** was isolated in moderate yield and immediately converted to the triflate **9b**. When standard Stille conditions[2] were employed, we were delighted to observe that the cross-coupling of naphthopyranyl stannane **6b** to the triflate **9b** provided quinone **10b** in 86% yield after chromatography. Remarkably, neither the hydroxyquinone **8b** nor the methyl transfer side product were detected in the reaction mixture contributing to the good yield of **10b**. The absence of **8b** supports our mechanistic hypothesis for triflate decomposition.

Conclusions

In conclusion, Pd^0-mediated cross-coupling reactions to construct hindered 2,3-bisnaphthopyranyl quinone model systems relevant to conocurvone synthesis were studied. To the best of our knowledge, the synthesis of bisnaphthopyranyl quinone **10b** represents the first regiocontrolled approach to an unsymmetrical 2,3-diaryl naphthoquinone possessing substituents on the quinone moiety. Our observation of substituent effects on palladium-catalyzed cross-coupling reactions involving quinone systems has also been reported. Although the effect of remote substituents on the chemistry of quinones is well documented,[30] the studies described herein are the first examples of their influence on palladium-catalyzed cross-coupling chemistry. We continue to explore the effect of remote substituents on palladium-catalyzed cross-coupling reactions to quinones and are actively pursuing strategies for the oxidation of 2,3-bisnaphthopyranyl quinones **10** to conocurvone derivatives.

Experimental Section

General Methods. All manipulations involving air-sensitive reagents were carried out under dry nitrogen using standard Schlenck techniques in oven-dried glassware. Flash chromatography was carried out using Acros 0.035−0.07 mm silica gel as the stationary phase. Preparative thin-layer chromatography was performed with Analtech silica gel glass plates (1000 μmn). Diethyl ether and tetrahydrofuran (THF) were distilled under nitrogen from sodium/benzophenone immediately prior to use. Toluene and methylene chloride (CH_2Cl_2) were distilled from calcium hydride and stored over 4-Å molecular sieves prior to use. Reagents were used as received from commercial suppliers. Extracts were dried with anhydrous magnesium sulfate and concentrated under reduced pressure with a rotary evaporator. Unless otherwise indicated, IR spectra were of thin films on NaCl plates, NMR spectra were measured in $CDCl_3$. The NMR chemical shifts are reported in ppm of the δ scale using $CHCl_3$ as an internal reference. Melting points were measured in open capillary tubes and are uncorrected.

9-(Methoxymethoxy)-3-methyl-3-(4-methyl-3-pentenyl)-3*H*-naphtho[2,1-*b*]pyran (5b). To sodium hydride (7.22 g of an 80% mineral oil dispersion, 240.7 mmol), previously washed with hexane (3 × 50 mL), under nitrogen and at room temperature was added 60 mL of THF and 18 mL of DMF. The suspension was cooled to 0 °C, and a solution of the hydroxynaphthopyran **5a**[9] (5.152 g, 17.5 mmol) in 15 mL of THF was slowly added. The resulting fluorescent green suspension was stirred for an additional 1 h at 0 °C. Chloromethyl methyl ether (4.0 mL, 53 mmol) was injected into the reaction mixture, during which time the fluorescent green color changed to dark gray. The mixture was stirred at room temperature for 8−12 h. The reaction mixture was cooled in an ice bath, and excess sodium hydride was quenched by dropwise addition of methanol. The reaction mixture was poured into 500 mL of 50% aqueous NH_4OH and the mixture stirred for 30 min. The mixture was extracted with EtOAc, and the combined organic layers were washed with water, dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by filtration through a short column of silica eluting with EtOAc/hexane (1:9) to afford 4.99 g (84%) of the known MOM ether **5b**[9a] as a light yellow oil: $R_f = 0.76$ (ether/hexane, 1:3); ^{1}H NMR (300 MHz) δ 1.43 (s, 3H), 1.57 (s, 3H), 1.65 (s, 3H), 1.71−1.77 (m, 2H), 2.12−2.16 (m, 2H), 3.5 (s, 3H), 5.08−5.10 (m, 1H), 5.29 (s, 2H), 5.64 (d, 1H, J = 10.2 Hz), 6.91 (d, 1H, J = 9.3 Hz), 6.97 (d, 1H, J = 10.2 Hz), 7.05 (dd, 1H, J = 9.2, 2.4 Hz), 7.46 (s, 1H), 7.55 (d, 1H, J = 8.8 Hz), 7.65 (d, 1H, J = 8.8 Hz); FT-IR 1620, 1247, 1183 cm^{-1}.

9-(*N*,*N*-Diethylcarbamoyloxy)-3-methyl-3-(4-methyl-3-pentenyl)-3*H*-naphtho[2,1-*b*]pyran (5c). To a stirred solution of the hydroxynaphthopyran **5a**[9] (5.21 g, 17.7 mmol), Et_3N (2.6 mL, 1.89 g, 18.7 mmol), and DMAP (0.395 g, 3.23 mmol) in 50 mL of toluene at room temperature under N_2 was added *N*,*N*-diethylcarbamoyl chloride (2.31 mL, 2.47 g, 18.2 mmol). The reaction mixture was refluxed for 16 h, cooled to room temperature, and washed with water. The organic layer was dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by filtration through a short column of silica eluting with ether/hexane (1:4) to yield 5.29 g (87%) of the pure carbamate **5c** as a yellow oil: $R_f = 0.34$ (ether/hexane, 1:3); ^{1}H NMR (300 MHz) δ 1.25 (t, 3H, J = 7.2 Hz), 1.32 (t, 3H, J = 6.9 Hz), 1.45 (s, 3H), 1.59 (s, 3H), 1.67 (s, 3H), 1.71−1.86 (m, 2H), 2.16 (dd, 2H, J = 15.9, 7.8 Hz), 3.48 (hept, 4H, J = 6.9 Hz), 5.12 (tt, 1H, J = 7.2, 1.3 Hz), 5.67 (d, 1H, J = 9.9 Hz), 6.98 (d, 1H, J = 10.2 Hz), 7.02 (d, 1H, J = 9.0 Hz), 7.12 (dd, 1H, J = 8.7, 2.2 Hz), 7.63 (d, 1H, J = 9.0 Hz), 7.65 (d, 1H, J = 2.4 Hz), 7.72 (d, 1H, J = 8.7 Hz); ^{13}C NMR (75 MHz) δ 13.76, 14.62, 17.93, 23.02, 25.95, 26.27, 41.03, 42.18, 42.49, 78.61, 112.60, 113.51, 117.89, 118.88, 118.98, 124.17, 126.87, 128.27, 129.10, 129.75, 130.69, 131.78, 150.13, 151.68, 154.43; FT-IR 1716, 1261 cm^{-1}; MS (FAB) *m*/*z* (relative intensity) 394 (MH^+, 19), 310 (100); HRMS (FAB) calcd for $C_{25}H_{32}NO_3$ $(M + H)^+$ 394.2383, found 394.2367. Anal. Calcd for $C_{25}H_{31}NO_3$: C, 76.30; H, 7.94; N, 3.56. Found: C, 76.53; H, 7.84; N, 3.53.

9-(Methoxymethoxy)-3-methyl-3-(4-methyl-3-pentenyl)-8-trimethylstannyl-3*H*-naphtho[2,1-*b*]pyran (6a). To a stirred solution of the naphthopyran **5b** (0.294 g, 0.869 mmol) in 8.8 mL of diethyl ether at −25 °C was added *t*-BuLi (1.0 mL of a 1.7 M solution in pentane, 1.7 mmol). The resulting red mixture was stirred for 1 h at −25 °C, during which time a precipitate formed. Me_3SnCl (2.6 mL of a 1 M solution in THF, 2.6 mmol) was added. The reaction mixture was stirred for another 10 min at −25 °C and slowly warmed to room temperature over a period of 3−4 h. The reaction was poured into saturated NH_4Cl. The organic layer was washed with saturated NH_4Cl, dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by flash chromatography on silica eluting with ether/hexane/TEA (10:500:5) to afford 0.267 g (61%) of the stannylated naphthopyran **6a** as a colorless oil: $R_f = 0.60$ (ether/hexane, 0.5:9.5); ^{1}H NMR (300 MHz) δ 0.35 (s, 9H), 1.45 (s, 3H), 1.58 (s, 3H), 1.67 (s, 3H), 1.73−1.87 (m, 2H), 2.16 (dd, 2H, J = 15.9, 7.8 Hz), 3.52 (s, 3H), 5.11 (tt, 1H, J = 7.2, 1.3 Hz), 5.32 (s, 2H), 5.66 (d, 1H, J = 9.9 Hz), 6.92 (d, 1H, J = 8.7 Hz), 7.01 (d, 1H, J = 9.9 Hz), 7.42 (s, 1H), 7.56 (d, 1H, J = 8.7 Hz), 7.73 (s, 1H); ^{13}C NMR (75 MHz) δ −8.64 (three carbons), 17.95, 23.04, 25.98, 26.24, 40.98, 56.28, 78.44, 94.25, 100.87, 113.16, 116.18, 119.03, 124.26, 125.56, 127.98, 128.89, 129.67, 131.75, 131.79, 137.62, 151.80, 160.14; FT-IR 1608, 1151 cm^{-1}; MS (FAB) *m*/*z* (relative intensity) 502 (M^+, 38), 487 (64), 419 (100); HRMS (FAB) calcd for $C_{25}H_{34}O_3Sn$ 502.1530, found 502.1513. Anal. Calcd for $C_{25}H_{34}O_3Sn$: C, 59.91; H, 6.84. Found: C, 60.37; H, 7.15.

9-(*N*,*N*-Diethylcarbamoyloxy)-3-methyl-3-(4-methyl-3-pentenyl)-8-trimethylstannyl-3*H*-naphtho[2,1-*b*]pyran (6b). To a stirred solution of the naphthopyran **5c** (0.505 g, 1.28 mmol) in 13 mL of diethyl ether at −78 °C was added *t*-BuLi (1.3 mL of a 1.7 M solution in pentane, 2.21 mmol). The resulting orange-

(30) The use of remote substituents to control the regiochemistry of the Diels−Alder reaction in naphthoquinone systems has been summarized: Naruta Y.; Maruyama, K. In *The Chemistry of the Quinonoid Compounds*; Patai, S., Rappoport, Z., Ed.; John Wiley & Sons: New York, 1988; Vol. 2, pp 292−303.

brown colored mixture was stirred for 30 min at −78 °C. Me_3SnCl (4.5 mL of a 1 M solution in THF, 4.5 mmol) was added. The reaction mixture was stirred for another 10 min at −78 °C and slowly warmed to room temperature over a period of 3−4 h. The reaction was quenched by pouring the mixture into 50 mL of saturated NH_4Cl. The organic layer was washed with saturated NH_4Cl, dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by flash chromatography on silica eluting with ether/hexane/TEA (100:600:7) to afford 0.563 g (79%) of the stannylated naphthopyran **6b** as a colorless oil: $R_f = 0.74$ (ether/hexane, 1:1); ^{1}H NMR (300 MHz) δ 0.36 (s, 9H), 1.25 (t, 3H, $J = 7.2$ Hz), 1.32 (t, 3H, $J = 7.2$ Hz), 1.44 (s, 3H), 1.58 (s, 3H), 1.67 (s, 3H), 1.70−1.84 (m, 2H), 2.15 (dd, 2H, $J = 15.6$, 7.8 Hz), 3.49 (dq, 4H, $J = 21.9$, 7.2 Hz), 5.10 (tt, 1H, $J = 7.2$, 1.3 Hz), 5.65 (d, 1H, $J = 9.9$ Hz), 6.98 (d, 1H, $J = 9.9$ Hz), 7.00 (d, 1H, $J = 8.4$ Hz), 7.59 (s, 1H), 7.62 (d, 1H, $J = 9.0$ Hz), 7.81 (s, 1H); ^{13}C NMR (75 MHz) δ −8.59 (three carbons), 13.66, 14.57, 17.94, 23.00, 25.96, 26.20, 40.97, 41.87, 42.21, 78.60, 112.43, 113.44, 117.79, 119.04, 124.19, 127.30, 128.02, 128.93, 131.06, 131.33, 131.76, 137.72, 151.64, 154.68, 154.84; FT-IR 1715, 1613, 1273, 1152 cm^{-1}; MS (FAB) *m*/*z* (relative intensity) 558 (MH^+, 19), 542 (100), 474 (11); HRMS (FAB) calcd for $C_{28}H_{39}NO_3SnLi$ $(M + Li)^+$ 564.2112, found 564.2114. Anal. Calcd for $C_{28}H_{39}NO_3Sn$: C, 60.45; H, 7.07; N, 2.52. Found: C, 60.80; H, 7.19; N, 2.48.

1,4-Dihydro-2-hydroxy-3-[9-(methoxymethoxy)-3-methyl-3-(4-methyl-3-pentenyl)-3*H*-naphtho[2,1-*b*]pyran-8-yl]-1,4-naphthalenedione (8a). To a stirred suspension of the dipole **7a**[12] (0.587 g, 1.56 mmol), $Pd(PPh_3)_4$ (0.242 g, 0.2095 mmol), and CuI (0.337 g, 1.76 mmol) dissolved in 14 mL of anhydrous DMF at room temperature was added a solution of the stannane **6a** (2.28 g, 4.56 mmol) in 6 mL of anhydrous DMF. The resulting red suspension was stirred at room temperature for 12 h. The mixture was extracted with 60 mL of ether and the organic layer washed with 5% $NaHCO_3$ to remove the 2-methyl-3-hydroxy-1,4-naphthoquinone byproduct. The organic layer was dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by filtration through a short column of silica eluting with ether/hexane (1:3) to afford 0.395 (50%) of the hydroxyquinone **8a** as a red oil that turned into a red glass upon prolonged drying under high vacuum: $R_f = 0.23$ (ether/hexane, 1:1); ^{1}H NMR (400 MHz) δ 1.45 (s, 3H), 1.59 (s, 3H), 1.67 (s, 3H), 1.70−1.85 (m, 2H), 2.11−2.18 (m, 2H), 3.46 (s, 3H), 5.07−5.12 (m, 1H), 5.25 (d, 2H, $J = 7.2$ Hz), 5.67 (d, 1H, $J = 10.0$ Hz), 6.94 (d, 1H, $J = 8.8$ Hz), 7.01 (d, 1H, $J = 10.0$ Hz), 7.48 (s, 1H), 7.58 (d, 1H, $J = 8.8$ Hz), 7.64 (d, 2H, $J = 4.4$ Hz), 7.75 (t, 1H, $J = 7.2$ Hz), 7.81 (t, 1H, $J = 7.2$ Hz), 8.19 (t, 2H, $J = 6.8$ Hz); ^{13}C NMR (100 MHz) δ 17.86, 22.93, 25.90, 26.19, 40.96, 56.32, 78.63, 95.09, 104.13, 113.22, 116.95, 117.10, 118.73, 119.07, 121.08, 124.30, 124.77, 126.47, 127.36, 128.27, 129.61, 129.74, 131.69, 131.92, 133.21, 133.32, 135.35, 152.41, 153.18, 154.10, 181.99, 183.53; FT-IR 3362, 1660, 1652 cm^{-1}; MS (FAB) *m*/*z* (relative intensity) 510 (M^+, 22), 427 (100); HRMS (FAB) calcd for $C_{32}H_{30}O_6Na$ $(M + Na)^+$ 533.1940, found 533.1948. Repeated attempts at elemental analysis yielded unsatisfactory results.

1,4-Dihydro-2-hydroxy-6-methoxy-3-[9-(methoxymethoxy)-3-methyl-3-(4-methyl-3-pentenyl)-3*H*-naphtho[2,1-*b*]pyran-8-yl]-1,4-naphthalenedione (8b). To a stirred suspension of the dipole **7b**[4] (1.307 g, 3.20 mmol), $Pd(PPh_3)_4$ (0.513 g, 0.444 mmol), and CuI (0.562 g, 2.95 mmol) in 15 mL of anhydrous DMF at room temperature was added a solution of the stannane **6a** (3.31 g, 6.62 mmol) in 30 mL of anhydrous DMF. The resulting red suspension was stirred at room temperature for 48 h. The mixture was extracted with ether and the organic layer washed with water. The organic layer was dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by filtration through a short column of silica eluting with ether/hexane mixtures (gradient from 1/10 to 10/0) to afford 0.692 g (40%) of the hydroxyquinone **8b** as a red powder: mp = 97−101 °C; $R_f = 0.51$ (ether/hexane, 2:1); ^{1}H NMR (300 MHz) δ 1.47 (s, 3H), 1.61 (s, 3H), 1.69 (s, 3H), 1.71−1.82 (m, 2H), 2.13−2.22 (m, 2H), 3.48 (s, 3H), 3.97 (s, 3H), 5.11−5.15 (m, 1H), 5.26 (d, 2H, $J = 7.2$ Hz), 5.68 (d, 1H, $J = 9.9$ Hz), 6.95 (d, 1H, $J = 8.4$ Hz), 7.03 (d, 1H, $J = 10.2$ Hz), 7.17 (d, 1H, $J = 2.7$ Hz), 7.20 (d, 1 H, $J = 2.7$ Hz), 7.59 (d, 1H, $J = 9.0$ Hz), 7.65−7.66 (m, 2H), 7.69 (s, 1H), 8.12 (d, 1H, $J = 8.7$ Hz); ^{13}C NMR (75 MHz) δ 17.94, 23.00, 25.96, 26.25, 40.99, 55.87, 56.28, 78.56, 95.04, 104.06, 111.26, 113.08, 116.79, 118.87, 118.96, 119.26, 122.85, 124.20, 124.68, 128.10, 129.00, 129.44, 130.12, 131.47, 131.76, 132.16, 135.74, 152.16, 153.42, 154.00, 165.40, 180.31, 183.19; FT-IR 3339, 1657, 1246, 1149 cm^{-1}; MS (FAB) *m*/*z* (relative intensity) 540 (M^+, 50), 457 (100); HRMS (FAB) calcd for $C_{33}H_{32}O_7Na$ $(M + Na)^+$ 563.2046, found 563.2048. Repeated attempts at elemental analysis yielded unsatisfactory results.

1,4-Dihydro-2-[9-(methoxymethoxy)-3-methyl-3-(4-methyl-3-pentenyl)-3*H*-naphtho[2,1-*b*]pyran-8-yl]-3-[(trifluoromethanesulfonyl)oxy]-1,4-naphthalenedione (9a). To a solution of the hydroxyquinone **8a** (0.176 g, 0.345 mmol), DMAP (0.015 g, 0.123 mmol), and $(i\text{-Pr})_2EtN$ (0.3 mL, 0.22 g, 1.72 mmol) in 10 mL of dry CH_2Cl_2 at 0 °C was added trifluoromethanesulfonic anhydride (0.1 mL, 0.168 g, 0.594 mmol). The resulting dark brown solution was stirred for 20−30 min at 0 °C and then concentrated. The crude product was purified by flash chromatography on silica eluting with ether/hexane (1:3) to yield 0.165 g (75%) of the triflate **9a** as a red oil that solidified into a red fluffy powder upon drying on high vacuum: mp = 127−129 °C dec; $R_f = 0.51$ (ether/hexane, 1:1); ^{1}H NMR (300 MHz)[31] δ 1.46 (d, 3H, $J = 13.4$ Hz), 1.57 (s, 3H), 1.66 (s, 3H), 1.71−1.82 (m, 2H), 2.14−2.17 (m, 2H), 3.44 (s, 3H), 5.10−5.17 (m, 1H), 5.23 (dd, 2H, $J = 15.6$, 6.9 Hz), 5.68 (dd, 1H, $J = 10.4$, 1.8 Hz), 6.95−7.01 (m, 2H), 7.57−7.63 (m, 3H), 7.84−7.87 (m, 2H), 8.18−8.21 (m, 1H), 8.26−8.29 (m, 1H); ^{13}C NMR (75 MHz)[31] δ 17.96 (17.93), 22.97 (23.20), 25.98, 26.47 (26.70), 41.20 (41.38), 56.47, 78.99, 95.07, 103.85, 113.05 (113.01), 115.78, 117.38 (117.47), 118.68 (118.79), 120.31, 124.11, 124.18, 127.25, 127.58, 128.31, 129.79, 130.36, 131.96, 132.06, 132.37, 134.60, 135.07, 137.57, 148.86, 153.08 (153.12), 153.31, 167.19, 177.67, 182.39; FT-IR 1683, 1427, 1212, 1138 cm^{-1}; MS (FAB) *m*/*z* (relative intensity) 642 (M^+, 36), 559 (100), 427 (17); HRMS (FAB) calcd for $C_{33}H_{29}O_8SF_3$ 642.1535, found 642.1538. Anal. Calcd for $C_{33}H_{29}O_8SF_3$: C, 61.68; H, 4.55. Found: C, 61.83; H, 4.70.

1,4-Dihydro-6-methoxy-3-[9-(methoxymethoxy)-3-methyl-3-(4-methyl-3-pentenyl)-3*H*-naphtho[2,1-*b*]pyran-8-yl]-2-[(trifluoromethanesulfonyl)oxy]-1,4-naphthalenedione (9b). To a solution of the hydroxyquinone **8b** (0.250 g, 0.462 mmol), DMAP (0.030 g, 0.245 mmol), and $(i\text{-Pr})_2EtN$ (0.45 mL, 0.33 g, 2.58 mmol) in 15 mL of dry CH_2Cl_2 at 0 °C was added trifluoromethanesulfonic anhydride (0.150 mL, 0.251 g, 0.891 mmol). The resulting dark brown solution was stirred for 45 min at 0 °C and then concentrated. The crude product was purified by flash chromatography on silica eluting with ether/hexane (1:3) to yield 0.163 g (53%) of the triflate **9b** as a red fluffy solid: mp = 53−55 °C; $R_f = 0.59$ (ether/hexane, 1:1); ^{1}H NMR (300 MHz)[31] δ 1.46 (d, 3H, $J = 12.5$ Hz), 1.57 (s, 3H), 1.66 (s, 3H), 1.74−1.84 (m, 2H), 2.14−2.16 (m, 2H), 3.44 (s, 3H), 3.97 (s, 3H), 5.09−5.14 (m, 1H), 5.24 (dd, 2H, $J = 16.5$, 6.9 Hz), 5.67 (dd, 1H, $J = 9.9$, 2.2 Hz), 6.94−7.01 (m, 2H), 7.30 (dd, 1H, $J = 9.0$, 2.7 Hz), 7.56−7.63 (m, 4H), 8.20 (d, 1H, $J = 8.4$ Hz); ^{13}C NMR (75 MHz)[31] δ 17.92 (17.96), 22.98 (23.20), 25.98, 26.47 (26.69), 41.20 (41.37), 56.43 (two carbons), 78.96, 95.05, 103.83, 111.27, 112.99 (113.03), 115.91, 116.07, 117.33 (117.42), 118.69 (118.79), 120.31, 120.89, 123.69, 124.12 (124.20), 128.29, 129.75 (128.80), 131.87, 131.94, 132.30, 134.24, 136.95, 149.18, 153.00, 153.05, 153.34, 165.13, 176.51, 182.49; FT-IR 1678, 1426, 1226 cm^{-1}; MS (FAB) *m*/*z* (relative intensity) 672 (M^+, 38), 589 (100), 457 (21); HRMS (FAB) calcd for $C_{34}H_{31}O_9SF_3Na$ $(M + Na)^+$ 695.1539, found 695.1522.

1,4-Dihydro-2-[9-(methoxymethoxy)-3-methyl-3-(4-methyl-3-pentenyl)-3*H*-naphtho[2,1-*b*]pyran-8-yl]-3-[9-(*N*,*N*-diethylcarbamoyloxy-3-methyl-3-(4-methyl-3-pentenyl)-3*H*-naphtho[2,1-*b*]pyran-8-yl]-1,4-naphthalenedione (10a) and 1,4-Dihydro-2-[9-(methoxymethoxy)-3-methyl-3-(4-methyl-3-pentenyl)-3*H*-naphtho[2,1-*b*]pyran-8-yl]-3-methyl-1,4-naphthalenedione (11). To a stirred suspension of the triflate **9a** (0.103 g, 0.160 mmol), $Pd(PPh_3)_4$ (0.033 g, 0.0285 mmol), and

(31) Because of hindered rotation about the bond joining the naphthopyran to the quinone core in compounds **9**, **10**, **11**, **13**, and **16**, the ^{1}H NMR spectra are complex. This is also the reason for the very large number of peaks in the ^{13}C NMR spectra. The spectra are still useful for identification of the structure of these compounds. Chemical shifts of the satellite peaks arising from the hindered rotation are indicated in parentheses following the parent signals.

LiCl (0.020 g, 0.471 mmol) in 2 mL of anhydrous dioxane at room temperature was added stannane **6b** (0.345 g, 0.620 mmol) dissolved in 7 mL of anhydrous dioxane. The resulting red reaction mixture was stirred for 6 h at 60 °C. The mixture was cooled to room temperature and extracted with ether. The organic layer was washed with water, dried over $MgSO_4$, filtered, and concentrated. Purification by flash chromatography on silica eluting with ether/hexane (1:2) provided 0.050 g (35%) of the bisnaphthopyranyl quinone **10a** as a red solid, 0.030 g (37%) of **11** as an orange oil, and 0.020 g (25%) of **8a**.

Analytical data for **10a**: mp = 82−86 °C; R_f = 0.43 (ether/hexane, 1:1); ^{1}H NMR (500 MHz)[31] δ 1.01 (t, 3H, J = 6.8 Hz), 1.10 (t, 3H, J = 6.8 Hz), 1.36−1.39 (m, 6H), 1.48 (s, 3H), 1.54 (s, 3H), 1.59 (s, 3H), 1.64−1.68 (m, 5H), 1.72−1.74 (m, 2H), 2.06−2.10 (m, 4H), 3.17−3.37 (m, 4H), 3.23 (s, 0.5 H), 3.56 (s, 2.5H), 5.03−5.07 (m, 2H), 5.27 (d, 1H, J = 6.6 Hz), 5.37 (d, 1H, J = 6.6 Hz), 5.56−5.60 (m, 2H), 6.74 (d, 1H, J = 8.7 Hz), 6.82 (d, 1H, J = 8.8 Hz), 6.89−6.93 (m, 2H), 7.24−7.28 (m, 1H), 7.31−7.35 (m, 2H), 7.39 (d, 1H, J = 1.8 Hz), 7.51 (s, 1H), 7.61 (s, 0.5 H), 7.75−7.79 (m, 2H), 7.95 (s, 0.5 H), 8.16−8.22 (m, 2H); ^{13}C NMR (125 MHz)[31] δ 13.25, 14.11 (13.93), 17.58, 17.62, 22.69 (22.77), 22.82, 25.60, 25.65, 26.09, 26.16, 40.83, 40.91, 41.71 (41.45), 42.08 (41.91), 56.30 (55.77), 78.36, 78.60, 95.04 (94.84), 102.98 (103.87), 112.41, 112.63 (112.75), 113.28, 116.41, 116.66, 117.82, 118.81, 122.55, 124.06, 124.12, 124.39, 124.64, 126.17, 126.51, 126.67, 127.75, 127.98, 129.10, 129.82, 129.86, 130.49, 130.73, 131.17, 131.27, 131.63, 132.38, 133.60, 133.65, 144.12, 145.02 (145.43), 146.70, 148.09 (147.60), 152.02 (151.94), 152.82 (153.05), 153.37, 154.23, 183.79 (184.59) (two carbons); FT-IR 1725, 1668, 1291 cm^{-1}; MS (FAB) m/z (relative intensity) 885 (M^+, 25), 854 (25), 802 (80); HRMS (FAB) calcd for $C_{57}H_{59}NO_8Li$ $(M + Li)^+$ 892.4240, found 892.4398.

Analytical data for **11**: R_f = 0.66 (ether/hexane, 1:1); ^{1}H NMR (400 MHz)[31] δ 1.45 (d, 3H, J = 4.0 Hz), 1.58 (s, 3H), 1.66 (s, 3H), 1.71−1.81 (m, 2H), 2.08 (s, 3H), 2.13−2.19 (m, 2H), 3.42 (s, 3H), 5.11 (tq, 1H, J = 7.2 Hz, 1.2 Hz), 5.22 (dd, 2H, J = 25.4 Hz, 7.2 Hz), 5.68 (d, 1H, J = 10.4 Hz), 6.95 (d, 1H, J = 8.8 Hz), 7.00 (d, 1H, J = 10.0 Hz), 7.45 (s, 1H), 7.56 (d, 1H, J = 8.8 Hz), 7.61 (s, 1H), 7.73−7.76 (m, 2H), 8.10−8.13 (m, 1H), 8.16−8.19 (m, 1H); ^{13}C NMR (100 MHz)[31] δ 14.79, 17.86, 22.98 (22.91), 25.89, 26.29 (26.23), 40.98 (41.03), 56.37, 78.71, 94.91, 103.93, 113.20, 117.11, 118.95 (118.93), 122.46, 124.30 (124.25), 124.67, 126.51, 126.77, 128.38 (128.42), 129.44, 130.50, 131.56, 131.95, 132.49, 132.60, 133.60, 133.78, 144.63, 145.33, 152.40, 153.62, 183.87, 185.95; FT-IR 1663, 1292, 1150, cm^{-1}; MS (FAB) m/z (relative intensity) 508 (M^+, 22), 425 (100); HRMS (FAB) calcd for $C_{33}H_{32}O_5Na$ $(M + Na)^+$ 531.2147, found 531.2150. Repeated attempts at elemental analysis yielded unsatisfactory results.

1,4-Dihydro-6-methoxy-3-[9-(methoxymethoxy)-3-methyl-3-(4-methyl-3-pentenyl)-3*H*-naphtho[2,1-*b*]pyran-8-yl]-2-[9-(*N*,*N*-diethylcarbamoyloxy-3-methyl-3-(4-methyl-3-pentenyl)-3*H*-naphtho[2,1-*b*]pyran-8-yl]-1,4-naphthalenedione (10b). To a stirred suspension of the triflate **9b** (0.060 g, 0.089 mmol), $Pd(PPh_3)_4$ (0.038 g, 0.0329 mmol), and LiCl (0.030 g, 0.707 mmol) in 2.0 mL of anhydrous dioxane was added the stannane **6b** (0.290 g, 0.521 mmol) dissolved in 3.0 mL of anhydrous dioxane. The reaction mixture was stirred for 13 h at 60 °C. The suspension was cooled to room temperature and filtered through a small plug of cotton. The filtrate was concentrated and the product purified by flash chromatography on silica eluting with ether/hexane (2:3) to afford 0.070 g (86%) of the bisnaphthopyranyl quinone **10b** as a red solid: mp = 86−89 °C; R_f = 0.24 (ether/hexane, 1:1); ^{1}H NMR (500 MHz)[31] δ 1.02 (t, 3H, J = 6.7 Hz), 1.12 (t, 3H, J = 6.7 Hz), 1.35−1.39 (m, 6H), 1.48 (s, 3H), 1.54 (d, 3H, J = 2.9 Hz), 1.58 (s, 3H), 1.63−1.67 (m, 5H), 1.69−1.76 (m, 2H), 2.04−2.09 (m, 4H), 3.23 (s, 0.5H), 3.30−3.40 (m, 4H), 3.56 (s, 2.5H), 3.96 (s, 3H), 5.04−5.06 (m, 2H), 5.27 (d, 1H, J = 6.6 Hz), 5.38 (d, 1H, J = 6.6 Hz), 5.56−5.60 (m, 2H), 6.74 (d, 1H, J = 8.7 Hz), 6.81 (d, 1H, J = 8.6 Hz), 6.90 (d, 1H, J = 9.9 Hz), 6.92 (d, 1H, J = 10.0 Hz), 7.23−7.25 (m, 2H), 7.30−7.34 (m, 2H), 7.37 (d, 1H, J = 1.6 Hz), 7.51 (s, 1H), 7.60 (d, 1H, J = 2.8 Hz), 7.76 (s, 1H), 8.14 (d, 1H, J = 8.6 Hz); ^{13}C NMR (125 MHz)[31] δ 13.29, 14.13 (13.97), 17.57, 17.62, 22.64 (22.70), 22.77 (22.82), 25.60, 25.65, 26.09, 26.16 (26.22), 40.83, 40.91, 41.71 (41.45), 42.08 (41.90), 55.92 (55.73), 56.27, 78.33 (78.35, 78.24) 78.58, 95.08 (94.82), 103.00 (103.87), 109.72, 112.31, 112.60, 113.24, 113.32, 116.38 (116.65), 117.76, 118.84, 120.40, 122.67, 124.07 (124.12), 124.57 (124.67), 125.41 (125.52), 125.96, 126.16, 127.73, 127.94, 129.01 (129.08), 129.23, 129.79, 130.48, 130.70, 131.11 (131.23), 131.63, 132.12, 134.35, 143.76, 145.19, 146.28 (145.65), 148.13 (147.68), 151.95 (151.89, 151.99), 152.04 (152.11), 152.83 (152.07), 153.38, 154.29, 163.99, 182.85 (182.76), 183.88 (184.67); FT-IR 1718, 1666, 1295 cm^{-1}; MS (FAB) m/z (relative intensity) 915 (M^+, 18), 884 (23), 832 (100); HRMS (FAB) calcd for $C_{58}H_{61}NO_9Na$ $(M + Na)^+$ 938.4244, found 938.4225. Anal. Calcd for $C_{58}H_{61}NO_9$: C, 76.04; H, 6.71. Found: C, 75.50; H, 6.78.

1,4-Dihydro-2-[4-methoxyphenyl]-3-[9-(methoxymethoxy)-3-methyl-3-(4-methyl-3-pentenyl)-3*H*-naphtho[2,1-*b*]pyran-8-yl]-1,4-naphthalenedione (13). To a suspension of the triflate **9a** (0.509 g, 0.793 mmol), $Pd(PPh_3)_4$ (0.241 g, 0.208 mmol), and LiCl (0.253 g, 0.596 mmol) in 20 mL of anhydrous dioxane was added the stannane **12a**[23] (1.17 g, 4.12 mmol) dissolved in 20 mL of anhydrous dioxane. The resulting suspension was stirred for 20 h at 65 °C. The mixture was cooled to room temperature and filtered through a small plug of cotton. The filtrate was concentrated and the residue purified by flash chromatography on silica eluting with ether/hexane (1:3), providing 0.286 g (60%) of the arylnaphthopyranyl quinone **13** as a red powder: mp = 72−75 °C; R_f = 0.38 (ether/hexane, 1:1); ^{1}H NMR (300 MHz)[31] δ 1.42 (d, 3H, J = 10.3), 1.56 (d, 3H, J = 3.6 Hz), 1.65 (d, 3H, J = 1.2 Hz), 1.71−1.82 (m, 2H), 2.09−2.19 (m, 2H), 3.42 (s, 3H), 3.71 (s, 3H), 5.08−5.14 (m, 1H), 5.09 (d, 1H, J = 6.9 Hz), 5.20 (d, 1H, J = 6.6 Hz), 5.64 (dd, 1H, J = 10.7, 1.5 Hz), 6.70 (dd, 2H, J = 9.0, 0.9 Hz), 6.84 (d, 1H, J = 8.7 Hz), 6.95 (d, 1H, J = 10.5 Hz), 7.12 (d, 2H, J = 8.4 Hz), 7.22 (s, 1H), 7.37 (d, 1H, J = 9.0 Hz), 7.51 (s, 1 H), 7.76−7.78 (m, 2H), 8.14−8.19 (m, 1H), 8.21−8.24 (m, 1H); ^{13}C NMR (75 MHz)[31] δ 17.95, 22.96 (23.19), 25.97, 26.31 (26.53), 41.06 (41.24), 55.33, 56.41, 78.66, 95.18, 103.56, 112.91, 113.26, 116.62, 116.70, 118.85 (118.95), 123.00, 124.15, 124.24, 124.51, 125.66, 126.56, 126.81, 128.04, 128.10, 129.42, 131.07, 131.28, 131.61, 132.43, 132.55, 133.65, 133.76, 143.97, 146.09, 152.13, 154.27, 159.54, 184.21, 185.05; FT-IR 1664, 1288 cm^{-1}; MS (EI) m/z (relative intensity) 602 ($M+2H^+$, 14), 517 (100); HRMS (EI) calcd for $C_{39}H_{36}O_6$ 600.2512, found 600.2497.

1,4-Dihydro-2-hydroxy-3-(4-methoxyphenyl)-1,4-naphthalenedione (14). To a suspension of the dipole **7a**[12] (0.159 g, 0.42 mmol), $Pd(PPh_3)_4$ (0.054 g, 0.046 mmol), and CuI (0.059 g, 0.31 mmol) in 3.5 mL of anhydrous DMF at room temperature was added the 4-methoxyphenyltrimethyl stannane **12a**[23] (0.70 g, 2.58 mmol) dissolved in 5.0 mL of anhydrous DMF. The suspension was stirred for 16 h at room temperature. Ether (10 mL) was added, and the mixture was extracted with 5% aqueous $NaHCO_3$ (5 × 20 mL) until the aqueous extract was almost colorless. The combined aqueous layer was acidified to pH = 2 with concentrated HCl and the mixture extracted with CH_2Cl_2. The combined organic layers were washed with water, dried over $MgSO_4$, filtered, and concentrated to yield a dark red solid. The product was recrystallized from ether/hexane yielding 0.090 g (76%) of the hydroxyquinone **14** as red needles: mp = 170−172 °C (lit.[32] mp 175−176 °C); R_f = 0.37 (ether/hexane, 1:1); ^{1}H NMR (300 MHz) δ 3.86 (s, 3H), 6.99 (d, 2H, J = 8.3 Hz), 7.51 (d, 2H, J = 8.8 Hz), 7.57 (s, 1H), 7.72−7.82 (m, 2H), 8.12−8.20 (m, 2H); FT-IR 3362, 1653 cm^{-1}.

1,4-Dihydro-2-(4-methoxyphenyl)-3-[(trifluoromethanesulfonyl)oxy]-1,4-naphthalenedione (15). To a solution of the hydroxyquinone **14** (0.160 g, 0.571 mmol) and Et_3N (0.10 mL, 0.072 g, 0.170 mmol) in 7 mL of dry CH_2Cl_2 at 0 °C was added trifluoromethanesulfonic anhydride (0.15 mL, 0.251 g, 0.89 mmol). The resulting purple reaction mixture was stirred for 20 min at 0 °C and then concentrated using a minimum amount of external heat to avoid decomposition (30−40 °C). Purification of the residue by flash chromatography on silica eluting with ether/hexane (1:4) provided 0.173 g (74%) of the triflate **15** as yellow needles: mp = 158−160 °C; R_f = 0.50 (ether/hexane, 1:1); ^{1}H NMR (300 MHz) δ 3.89 (s, 3H), 7.02 (d, 2H, J = 8.8 Hz), 7.39 (d, 2H, J = 8.8 Hz), 7.83−7.86 (m, 2H), 8.19−8.26 (m, 2H); ^{13}C NMR (75 MHz) δ 55.67, 114.02 (two carbons), 119.32, 120.30, 127.09, 127.67, 130.23, 131.81, 132.53 (two carbons), 134.75,

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135.07, 137.89, 147.78, 161.66, 177.73, 183.29; FT-IR 1674, 1426, 1211, 1155 cm^{-1}; MS (EI) *m/z* (relative intensity) 412 (M^+, 8), 279 (5), 251 (100). Anal. Calcd for $C_{18}H_{11}F_3O_6S$: C, 52.43; H, 2.69. Found: C, 52.61; H, 2.71.

1,4-Dihydro-2-[4-methoxyphenyl]-3-[9-(*N*,*N*-diethylcarbamoyloxy-3-methyl-3-(4-methyl-3-pentenyl)-3*H*-naphtho-[2,1-*b*]pyran-8-yl]-1,4-naphthalenedione (16). To a suspension of the triflate **15** (0.078 g, 0.189 mmol), $Pd(PPh_3)_4$ (0.061 g, 0.052 mmol), and LiCl (0.05 g, 1.17 mmol) in 1.0 mL of anhydrous dioxane at room temperature was added stannane **6b** (0.473 g, 0.852 mmol) dissolved in 2.0 mL of anhydrous dioxane. The resulting suspension was stirred for 8 h at 80 °C. The temperature was then raised to 95−100 °C, and stirring was continued for an additional 22 h. The reaction was cooled to room temperature and extracted with 10 mL of ethyl acetate. The organic layer was washed with water, dried over $MgSO_4$, filtered, and concentrated to yield a brown oil. The residue was purified by flash chromatography on silica eluting with ethyl acetate/hexane (1:4) to provide 0.065 g (53%) of the arylnaphthopyranyl quinone **16** as a red powder: mp = 80−83 °C; R_f = 0.19 (ether/hexane, 1:4); ^{1}H NMR (300 MHz)[31] δ 0.95−1.20 (m, 6H), 1.42 (d, 3H, J = 9.5 Hz), 1.56 (s, 3H), 1.65 (s, 3H), 1.69−1.78 (m, 2H), 2.08−2.12 (m, 2H), 3.12−3.32 (m, 4H), 3.71 (s, 3H), 5.06−5.13 (m, 1H), 5.62 (d, 1H, J = 9.5 Hz), 6.73 (d, 2H, J = 8.0 Hz), 6.89−6.95 (m, 2H), 7.18−7.24 (m, 3H), 7.36 (d, 1H, J = 8.8 Hz), 7.76−7.79 (m, 3H), 8.16−8.18 (m, 2H); ^{13}C NMR (75 MHz)[31] δ 13.41, 14.34, 17.98, 22.97 (23.15), 25.97, 26.41 (26.50), 41.13 (41.19), 41.88, 42.19, 55.33, 78.85, 113.38 (two carbons), 118.05, 118.11, 118.96, 124.13, 124.21, 124.48, 125.02, 126.29, 126.48, 126.82, 128.21, 129.37, 130.67, 131.44, 131.84, 132.15, 132.27, 132.41, 133.73, 133.83, 143.29, 146.24, 148.24, 152.10, 153.39, 159.65, 164.97, 183.85, 184.97; FT-IR 1718, 1664, 1287, 1165 cm^{-1}; MS (FAB) *m/z* (relative intensity) 656 (M + H^+, 51), 572 (100), 473 (12); HRMS (FAB) calcd for $C_{42}H_{42}O_6N$ (M + H)$^+$ 656.3012, found 656.2987. Anal. Calcd for $C_{42}H_{41}NO_6$: C, 76.92; H, 6.30. Found: C, 77.09; H, 6.29.

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Supporting Information Available: FT-IR, ^{1}H NMR, and ^{13}C NMR spectra of compounds **5c**, **6a**,**b**, **8a**,**b**, **9a**,**b**, **10a**,**b**, **11**, **13**, **15**, and **16**. This material is available free of charge via the Internet at http://pubs.acs.org.

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