Synthesis of Hydroxylated Naphthoquinone Derivatives

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The use of the Stobbe condensation for the synthesis of juglone derivatives is presented, together with studies towards their further functionalization. The regiospecific oxidation of the above products to *o*- or *p*-naphthoquinones was also investigated. Finally, the preparation of useful intermediates for the synthesis of related natural products such as alkannin and shikonin is proposed.

Introduction

Hydroxylated naphthoquinone derivatives constitute a very important class of biologically active compounds including juglones and naphthazarines. Even the simplest homologues of this class are challenging synthetic targets, due to their high chemical reactivity and polyoxygenated nature. Consequently, several diversified synthetic approaches such as Diels–Alder reaction,[1–4] Fischer carbene complexes,[5–8] Hauser annulation,[9–11] *o*-substituted tertiary benzamide chemistry,[12,13] cyclobutenedione chemistry,[14,15] Stobbe condensation,[16] naphthol oxidation,[17,18] etc. have been reported. The most common synthetic problems associated with these compounds involve low yields in the final deprotection steps and constraints on the functionalization of the aromatic skeleton. Stobbe condensation of various benzaldehydes (**1**, Scheme 1) with diethyl succinate (**2**), employing simple and often commercially available starting materials, may address both problems. By this approach, the formation of a highly functionalized aromatic skeleton (**3**) may be achieved in two steps. These useful synthetic intermediates may, after regioselective oxidization, be successfully converted into *p*- and *o*-naphthoquinones **4** and **5**, respectively, of which the former could be further transformed to the naturally occurring compounds alkannin and shikonin. This strategy allows orthogonal protection of hydroxyl groups, a crucial prerequisite for efficient deprotection in the final steps. Additionally, by taking advantage of the carboxyl moiety of key intermediate **3**, several side chains, including β-keto allyl derivatives (**6**, Scheme 1), may be constructed. The results of our related studies are presented here.

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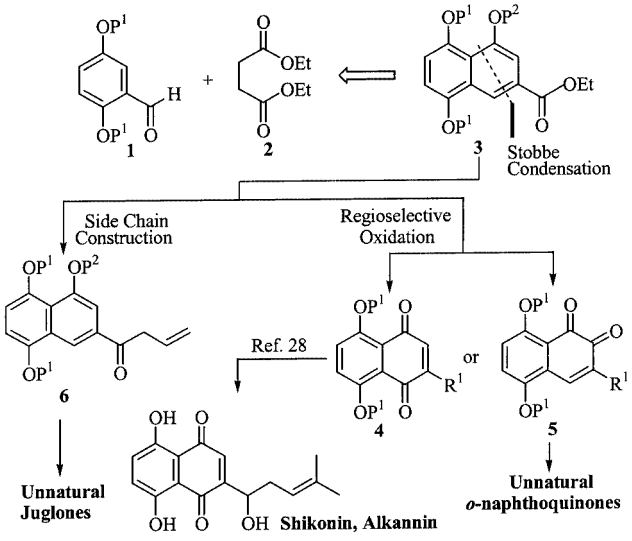
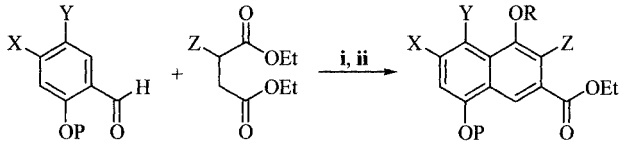


Scheme 1. Target key intermediates and final products (P^1, P^2 = protective groups, R^1 = carboxylated or aliphatic side chain)

Results and Discussion

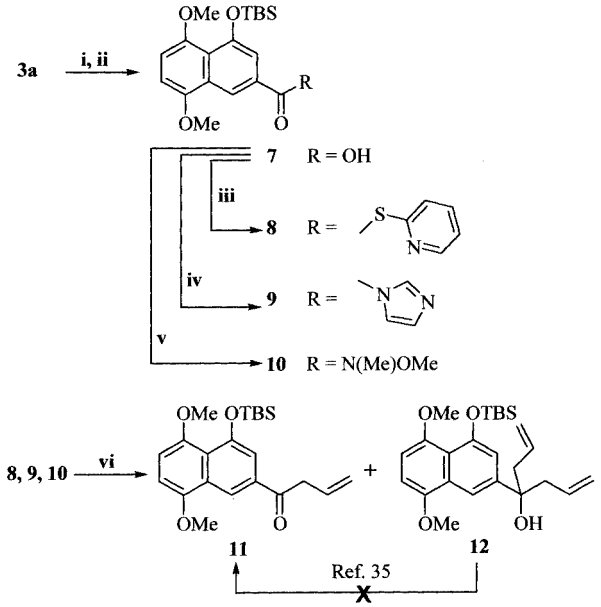
The protected juglone derivatives **3a**, **3b**, and **3d** were prepared by application of standard Stobbe conditions[19] to benzaldehydes **1a**, **1b**, and **1d** (Scheme 2). This method was found to be unsuitable for the preparation of silylated juglones, since benzaldehyde **1c** afforded only the peracetylated compound **3c**.

Side chain modifications followed preparation of the aromatic core. Attachment of the prenyl group was considered to be of high priority, since this group appears in the structure of many natural products, including the title compounds. However, most reported syntheses concerning α-prenylation[20–27] of aldehydes or acid derivatives were expected to result in multistep and "tricky" synthetic procedures. On the other hand, it has been demonstrated[28] that

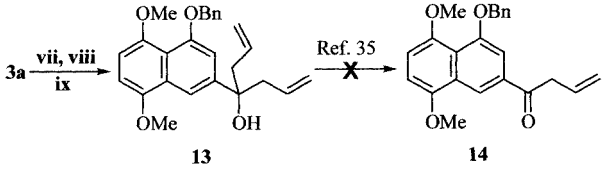


Compnd	P	X	Y	Z	Yield of **3** (based on **1**)
1a	Me	H	OMe	H	**3a**: 50%
1b	Bn	H	OBn	H	**3b**: 53%
1c	TBS	H	OTBS	H	**3c**: 55%
1d	Me	OMe	H	Me	**3d**: 37%

Scheme 2. Preparation of juglone derivatives; reagents and conditions: i) NaH, cat. EtOH, PhMe or *t*BuOK, *t*BuOH, 1 h, then conc. HCl (or AcOH for substrate **1c**); ii) Ac_2O, AcONa, 120 °C, 5 h, 37−55% (based on **1**)



Compnd	Y	Yield % **11**, **12**		Conditions
8	Y=MgBr	0	87	Et_2O, −20 °C
9	Y=Li	20	55	Et_2O, −100 °C
9	Y=MgBr	63	15	Et_2O, −100 °C
10	Y=MgBr	94	Trace	THF, −20 °C

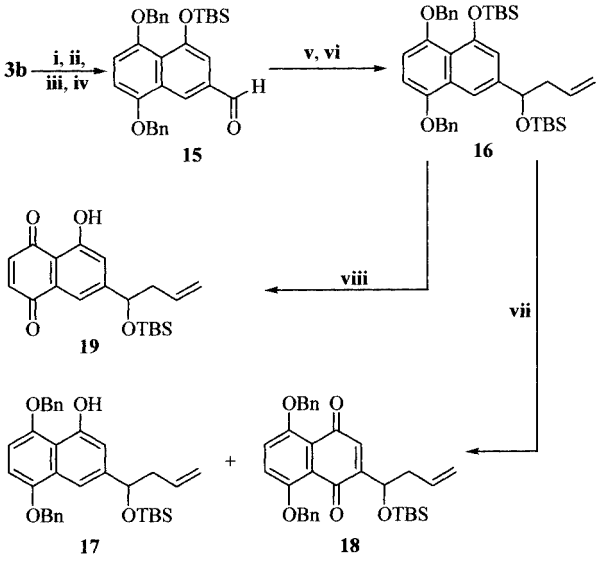


Scheme 3. Functionalization of carboxylates; reagents and conditions: i) LiOH aq. 3 N/THF/MeOH, 1:1:1, 60 °C, 2 h; ii) TBSCl, imidazole, cat. DMAP, DMF, 70% (based on **3a**); iii) Aldrithiol-2™, PPh_3, CH_3CN, 1 h, 90%; iv) Im_2CO, THF, 10 min, 94%; v) MeONHMe·HCl, CBr_4, pyridine, PPh_3, CH_2Cl_2, 30 min, 87%; vi) Organometallic reagent, Et_2O or THF, −100 or −20 °C, for yields see table; vii) EtONa, EtOH, reflux 1 h, 89%; viii) $PhCH_2Br$, Cs_2CO_3, DMF, cat. Bu_4NI, 5 h, 87%; ix) Excess allylmagnesium bromide, Et_2O, 0 °C, 94%. TBSCl = *tert*-butylclorodimethylsilane, DMAP = 4-dimethylaminopyridine, Aldrithiol-2™ = 2,2′-dipyridyl disulfide, Im_2CO = carbonyldiimidazole

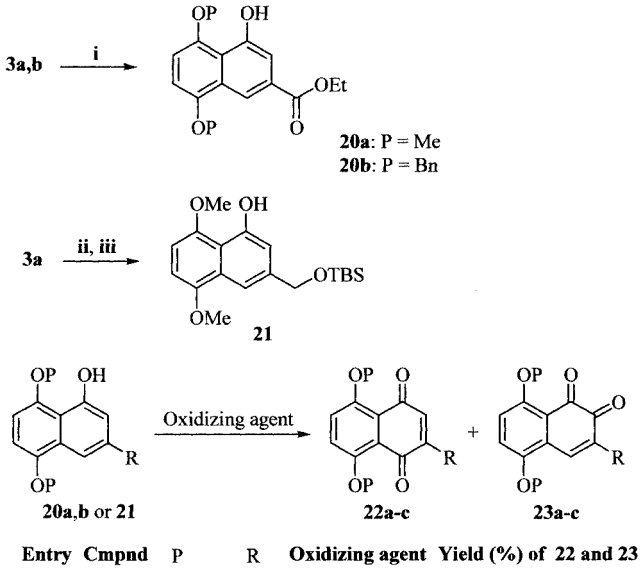
the allyl moiety in compounds such as **11** (Scheme 3) is efficiently transformed into the respective prenyl component. Thus, compound **3a**, after saponification and subsequent selective silylation, was converted through carboxylic acid **7** into the *S*-pyridin-2-yl ester **8**,[29,30] the imidazolide **9**,[31,32] or the Weinreb amide **10**,[33,34] functionalities suitable for monoalkylation (Scheme 3). Controlled allylation of substrates **9** and **10** at low temperature afforded the desired compound **11** in good to excellent chemical yields. In contrast, *S*-pyridin-2-yl ester **8** remained completely unreactive at low temperature, while at higher temperature it exclusively furnished the disubstituted derivative **12**. Although it has been reported[35] that such derivatives can be transformed into the corresponding propenyl ketones (similar to **11**) upon treatment with a strong base (e.g., *t*BuOK, DMF, 60 °C), that was not the case with compound **12**. Under the same reaction conditions, benzylated analogue **13** (prepared in three steps from naphthol **3a**) was also unreactive.

The use of benzyl ether as a protective group was thought to be a highly promising alternative to methyl ether protection, due to its mild deprotection conditions. Thus, the model compound **16** was synthesized in high yield (77%) from **3b** (Scheme 4). Treatment of **16** with CAN at 25 °C afforded a mixture of products, among which structures **17** and **18** were identified (yields 20−40%). The **17**/**18** ratio varied according to reaction time and molar equivalents of CAN. It should be noted that substrates **20b** and **21** (Scheme 5) under the same conditions afforded the corresponding *p*-quinones **22b** and **22c**, respectively, in less than 10% yield, among many other unidentified products. On the other hand, under radical conditions generated by use of 4,4′-di-*tert*-butylbiphenyl or naphthalene and lithium metal,[36−38] complete cleavage of the benzyl ether groups and the aromatic silyl ether occurred, affording juglone derivative **19** in 25−30% yield after aerial oxidation. Several other trials were even more disappointing, and so the use of benzyl ethers was not studied further.

The preparation of *o*- and/or *p*-naphthoquinone derivatives by the regiospecific oxidation of the corresponding juglones was also investigated. Treatment of acetates **3a** and **3b** with alkaline ethanol furnished naphthols **20a** and **20b** in almost quantitative yields, whereas exhaustive DIBAL reduction of acetate **3a** and subsequent selective silylation provided naphthol **21** (Scheme 5). According to the literature, all these juglone derivatives should be transformable into the respective naphthazarines upon salcomine-catalyzed oxidation.[39] In this respect, the presented synthetic approach should give rise to either juglone or naphthazarine derivatives. However, as has been recently reported by



Scheme 4. Deprotection attempts on substrate **16**; reagents and conditions: i) EtONa, EtOH, reflux 1 h, 93%; ii) TBSCl, imidazole, cat. DMAP, DMF, 2 h, 97%; iii) DIBAL, CH_2Cl_2, −78 °C, 20 min, 98%; iv) NMO, cat. TPAP, CH_2Cl_2, 2 h, 98%; v) allylmagnesium bromide, Et_2O, 0 °C, 15 min; vi) TBSCl, imidazole, cat. DMAP, DMF, 1.5 h, 89% (based on **15**); vii) CANaq., CH_3CN; viii) Li, DTBBP, THF, −78→0 °C or Li, naphthalene, THF, −20→0 °C; DIBAL = diisobutylaluminium hydride, NMO = 4-methylmorpholine *N*-oxide, TPAP = tetrapropylammonium perruthenate, CAN = ammonium cerium(IV) nitrate, DTBBP = 4,4′-di-*tert*-butylbiphenyl

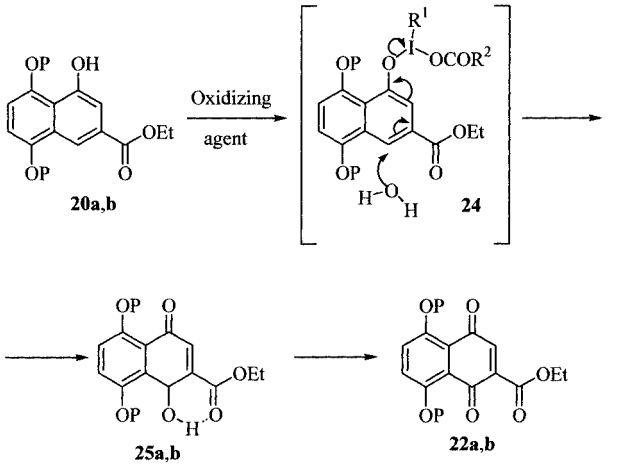


Entry	Cmpnd	P	R	Oxidizing agent	Yield (%) of 22 and 23
1	**20a**	Me	CO_2Et	Salcomine	**22a**: - **23a**: 90%
2	**20a**	Me	CO_2Et	Fremy's salt	**22a**: - **23a**: 78%
3	**20a**	Me	CO_2Et	$Ph_2Se_2O_3$	**22a**: - **23a**: 80%
4	**20b**	Bn	CO_2Et	Salcomine	**22b**: - **23b**: 90%
5	**21**	Me	CH_2OTBS	$Ph_2Se_2O_3$	**22c**: - **23c**: 75%
6	**21**	Me	CH_2OTBS	Fremy's salt	**22c**: Trace **23c**: 70%
7	**21**	Me	CH_2OTBS	$PhI(CF_3CO_2)_2$	**22c**: 53% **23c**: Trace
8	**21**	Me	CH_2OTBS	Salcomine	**22c**: - **23c**: 93%

Scheme 5. Oxidation of juglone derivatives to *p*- or *o*-quinones; reagents and conditions: i) EtONa, EtOH, reflux 1 h, 89−93%; ii) DIBAL, CH_2Cl_2, −78 °C, 2 h, 95%; iii) 1.1 equiv. TBSCl, imidazole, DMF, 12 h, 85%

our group,[40] this is not the case, and the corresponding *o*-naphthoquinones are exclusively formed in high yields (Scheme 5; entries 1,4,8). After a number of attempts with various oxidants on both electron-rich and electron-poor substrates, it was evident that only hypervalent iodide reagents[41] could oxidize the *p*-position regiospecifically. According to the most widely accepted mechanism,[41,42] hypervalent iodide oxidations take place through intermediate **24** (Scheme 6), which is attacked by a molecule of water, preferably at the *para* position. Thus, the alkyl derivative **21**, upon oxidation with PIFA, furnished the expected quinone **22c** (Scheme 5, entry 7). Surprisingly, oxidation of the carboxylated analogues **20a** and **20b** proceeded only up to the intermediate hydroxy-enones **25a** and **25b** (Scheme 6; entries 9, 11−13).[43] Several attempts to force this oxidation to quinones **22a** and **22b** respectively, by changing the reaction conditions, were unsuccessful, and the use of a second oxidant as well as the addition of a strong mineral acid was necessary. After experimentation with CAN, CrO_3, HgO, and DDQ, the combination of ferric chloride and HCl provided the best results (Scheme 6; entries 10,14).

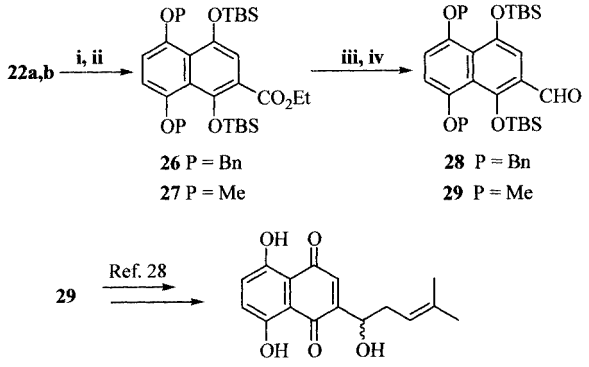
These compounds were efficiently transformed into useful and versatile synthetic intermediates. From quinones **22a** and **22b**, for example, esters **26** and **27**, respectively (Scheme 7), were produced after reduction with $Na_2S_2O_4$ and protection of the phenolic groups as silyl ethers. Reduction of **26** and **27** with DIBAL and subsequent oxidation of the resulting benzyl alcohols with NMO/TPAP afforded aldehydes **28** and **29**, respectively, in high yields (based on



Entry	Cmpnd	P	Oxidizing agent	Yield (%) of 22 or 25
9	**20a**	Me	$PhI(CF_3CO_2)_2$ (PIFA)	**25a**: 55%
10	**20a**	Me	PIFA then H^+ / $FeCl_3$	**22a**: 48%
11	**20a**	Me	$C_6F_{13}I(CF_3CO_2)_2$	**25a**: 45%
12	**20a**	Me	$PhI(OAc)_2$	**25a**: 37%
13	**20b**	Bn	$PhI(CF_3CO_2)_2$	**25b**: 75%
14	**20b**	Bn	PIFA then H^+ / $FeCl_3$	**22b**: 67%

Scheme 6. Oxidation of juglone derivatives to *p*-quinones with hypervalent iodine reagents

22a and **22b**). These aldehydes resemble the common intermediate of most synthetic schemes so far reported for alkannin and shikonin,[44] with the additional advantage of orthogonal protection of the aromatic hydroxyl groups. As has recently been demonstrated,[28] intermediate **29** has been converted into the above natural products in good yields.



Scheme 7. Preparation of aldehyde **29**; reagents and conditions: i) $Na_2S_2O_4$, $CHCl_3/H_2O$, 15 min; ii) TBSCl, imidazole, cat. DMAP, DMF, 89% (**22a**→**27**); iii) DIBAL, CH_2Cl_2, −78 °C, 1 h, 93%; iv) NMO, cat. TPAP, CH_2Cl_2, 3 h, 97%

Conclusion

In conclusion, the utility of the Stobbe condensation for the preparation of naphthoquinone derivatives has been demonstrated. Functionalization of the side chain and regiospecific oxidation of various naphthols was also thoroughly investigated. These functionalized and orthogonally protected naphthoquinones are useful synthetic intermediates for biologically important classes of compounds. Furthermore, several juglone derivatives, as well as *o*- and *p*-naphthoquinones and the naturally occurring alkannin and shikonin, have been successfully synthesized by this route.

Experimental Section

General Remarks: All reactions were carried out under anhydrous conditions and argon atmosphere, using dry, freshly distilled solvents, unless otherwise noted. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were distilled from sodium/benzophenone, dichloromethane (CH_2Cl_2) from P_2O_5, and toluene from sodium. Yields refer to chromatographically and spectroscopically (^1H NMR) homogeneous materials, unless otherwise stated. All reagents were purchased at highest commercial quality and used without further purification, unless otherwise stated. Compound **3a** was prepared according to ref.[19] All reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica gel plates (60 F_{254}), with use of UV light as visualizing agent and ethanolic phosphomolybdic acid or *p*-anisaldehyde solution and heat as developing agents. Merck silica gel (60, particle size 0.040−0.063 mm) was used for flash column chromatography. NMR spectra were recorded on Bruker AMX 500 or AC 250 instruments. The following abbreviations are used to denote NMR signal multiplicities: s = singlet, d = doublet, t = triplet, q = quadruplet, m = multiplet, dd = doublet of doublets. IR spectra were recorded on a Nicolet Magna system 550 FT-IR instrument. High-resolution mass spectra (HRMS) were recorded on a VG ZAB-ZSE mass spectrometer under fast atom bombardment (FAB) conditions, and matrix-assisted (MALDI-FTMS) mass spectra were recorded on a PerSeptive Biosystems Voyager IonSpect mass spectrometer. Melting points (m.p.) are uncorrected and were recorded on a Gallenkamp melting point apparatus.

General Procedure for the Preparation of Compounds 3b−3d: *t*BuOK (2.1 g, 18.8 mmol) was added portionwise to a stirred solution of benzaldehyde **1b** (3.0 g, 9.4 mmol) and diethyl succinate (4.1 g, 23.6 mmol) in *t*BuOH (35 mL). Upon completion of the addition, the mixture was stirred at 25 °C for 1 h, and was then poured into HCl solution (1 N, 60 mL) and extracted with EtOAc (2 × 40 mL). The organic layer was separated and treated with saturated aqueous Na_2CO_3 solution. The aqueous layer was extracted with EtOAc (30 mL) and then acidified with concentrated hydrochloric acid until pH = 2. Finally the aqueous layer was extracted with EtOAc (3 × 30 mL), and the organic extracts were washed with brine (50 mL), dried with Na_2SO_4, and evaporated under reduced pressure to afford crude 4-[2,5-bis(benzyloxy)-phenyl]-3-(ethoxycarbonyl)-3-butenoic acid. The crude carboxylic acid was cyclized in boiling acetic anhydride (2.9 g, 28.4 mmol) and anhydrous sodium acetate (927.0 mg, 11.3 mmol) for 5 h. The mixture was allowed to cool overnight and then poured into ice/water (150 mL). The yellow-orange amorphous solid was filtered and washed with water (4 × 80mL). The air-dried crude product was finally recrystallized from EtOAc and Et_2O to afford **3b** as a pale orange, crystalline solid (2.4 g, 53% yield based on **1b**). **3b:** R_f = 0.55 (hexanes/EtOAc, 8:2); m.p. 178−180 °C. IR (KBr): $\tilde{\nu}$ = 2930, 1751, 1720, 1608, 1454, 1363, 1264, 1225, 1023, 752 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 1.39 (t, *J* = 7.1 Hz, 3 H, CH_2CH_3), 1.66 (s, 3 H, OAc), 4.39 (q, *J* = 7.1 Hz, 2 H, CH_2CH_3), 5.01 (s, 2 H, OCH_2Ph), 5.22 (s, 2 H, OCH_2Ph), 6.83 (AB_q, *J* = 8.8 Hz, Δ*v* = 23.3 Hz, 2 H, CH_{naphth}), 7.26−7.56 (m, 10 H, CH_{ar}), 7.64 (s, 1 H, CH_{naphth}), 9.00 (s, 1 H, CH_{naphth}) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 14.3, 20.2, 61.2, 70.7, 71.6, 106.7, 109.5, 119.7, 127.2, 127.9, 128.4, 128.6, 128.7, 128.8, 136.4, 136.9, 146.6, 148.4, 149.5, 165.9, 170.2 ppm. HRMS (MALDI) calcd. for $C_{29}H_{26}O_6$ ($[M + Na]^+$): 493.1621; found 493.1631.

When the above conditions were applied to benzaldehyde **1c** (acetic acid was used instead of hydrochloric acid during the acidification step), the only isolated product was triacetate **3c**, as a white solid (55% yield based on **1c**). **3c**: R_f = 0.40 (hexanes/EtOAc, 8:2); m.p. 154−156 °C. IR (KBr): $\tilde{\nu}$ = 2992, 1772, 1724, 1466, 1366, 1283, 1188, 1032, 897 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 1.38 (t, *J* = 7.1 Hz, 3 H, CH_2CH_3), 2.34 (s, 3 H, OAc), 2.36 (s, 3 H, OAc), 2.44 (s, 3 H, OAc), 4.39 (q, *J* = 7.1 Hz, 2 H, CH_2CH_3), 7.26 (AB_q, *J* = 8.4 Hz, Δ*v* = 31.1 Hz, 2 H, CH_{ar}), 7.73 (d, *J* = 1.5 Hz, 1 H, CH_{ar}), 8.55 (d, *J* = 1.5 Hz, 1 H, CH_{ar}) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 14.2, 21.0, 61.5, 119.2, 120.6, 122.4, 122.8, 128.6, 128.9, 142.5, 145.5, 165.1, 168.8, 169.1, 169.2 ppm. HRMS (MALDI) calcd. for $C_{19}H_{18}O_8$ ($[M + Na]^+$): 397.0894; found 397.0898.

For the preparation of compound **3d**, sodium hydride was used instead of *t*BuOK. A catalytic amount of ethanol (0.1 mL) was added to a stirred solution of sodium hydride (345.6 mg, 14.4 mmol) in toluene (10 mL), followed by dropwise addition of a solution of benzaldehyde **1d** (1 g, 6.0 mmol) in diethyl 2-methylsuccinate (2.8 g, 15.0 mmol). The reaction mixture was further

treated as above to afford **3d** as pale orange crystalline solid (737.8 mg, 37% yield based on **1d**). **3d**: R_f = 0.40 (hexanes/EtOAc, 8:2); m.p. 128−130 °C. IR (KBr): $\tilde{\nu}$ = 2943, 1764, 1718, 1635, 1430, 1249, 1207, 1156, 1052 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 1.40 (t, J = 7.1 Hz, 3 H, CH_2CH_3), 2.45 (s, 3 H, $C_{ar}Me$), 2.48 (s, 3 H, OAc), 3.87 (s, 3 H, OMe), 3.94 (s, 3 H, OMe), 4.37 (q, J = 7.1 Hz, 2 H, CH_2CH_3), 6.44 (d, J = 2.2 Hz, 1 H, CH_{ar}), 6.51 (d, J = 2.2 Hz, 1 H, CH_{ar}), 8.65 (s, 1 H, CH_{ar}) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 14.0, 14.4, 20.6, 55.3, 55.7, 60.8, 91.4, 97.8, 120.0, 123.9, 125.6, 128.4, 130.7, 144.1, 157.6, 161.0, 167.5, 168.8 ppm.

Preparation of Acid 7: An aqueous solution of LiOH (3 M, 15 mL) was added to a stirred solution of **3a** (700.0 mg, 2.19 mmol) in a 1:1 mixture of THF/MeOH (30 mL) and the mixture was heated to 60 °C for 2 h. The organic solvents were then evaporated under reduced pressure and the residue was acidified to pH = 2 with 1 M HCl solution, to form a pale brown solid, which was filtered. The crude acid was air-dried for 1 h, and then dried under high vacuum at 40 °C overnight and used in the next step without further purification. The crude product was dissolved in anhydrous DMF (4.0 mL) and cooled to 0 °C, followed by addition of imidazole (374.4 mg, 5.50 mmol) and TBSCl (497.4 mg, 3.30 mmol). The ice bath was removed and the reaction mixture was stirred overnight at 25 °C. Upon consumption of the starting material (monitored by TLC) the reaction was quenched with methanol (1.0 mL) and a saturated aqueous solution of NH_4Cl was added (15 mL), followed by addition of EtOAc (25 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (2 × 15 mL). The combined organic extracts were washed with brine (20 mL) and the solvent was evaporated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, hexanes/EtOAc, 7:3) to afford **7** as a white solid (556.2 mg, 70% yield from **3a**). R_f = 0.50 (hexanes/EtOAc, 7:3); m.p. 225−226 °C. IR (KBr): $\tilde{\nu}$ = 2931, 1681, 1598, 1463, 1383, 126, 1065, 838, 784 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 0.24 (s, 6 H, Me_2Si), 1.04 (s, 9 H, tBuSi), 3.84 (s, 3 H, OMe), 3.94 (s, 3 H, OMe), 6.76 (AB_q, J = 8.6 Hz, $\Delta\nu$ = 19.4 Hz, 2 H, CH_{ar}), 7.48 (s, 1 H, CH_{ar}), 8.71 (s, 1 H, CH_{ar}) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 2.7, 18.6, 25.9, 55.9, 104.6, 107.7, 115.7, 119.2, 126.3, 127.2, 128.3, 150.4, 150.7, 152.6, 171.9 ppm. HRMS (MALDI) calcd. for $C_{19}H_{26}O_5Si$ ($[M + H]^+$): 363.1622; found 363.1634.

Preparation of *S*-Pyridinyl Ester 8: 2,2′-Dipyridyl disulfide (68.7 mg, 0.31 mmol) and PPh_3 (81.3 mg, 0.31 mmol) were added successively to a stirred solution of **7** (100.0 mg, 0.26 mmol) in anhydrous CH_3CN (1 mL). The mixture was stirred at 25 °C for 1 h (reaction progress monitored by TLC) and the solvent was then evaporated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, hexanes/EtOAc, 8:2) to afford **8** as a yellow solid (106.6 mg, 90% yield). R_f = 0.60 (hexanes/EtOAc, 7:3); m.p. 92−94 °C. IR (KBr): $\tilde{\nu}$ = 2932, 2858, 1681, 1595, 1507, 1456, 1384, 1282, 918, 834 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 0.23 (s, 6 H, Me_2Si), 1.02 (s, 9 H, tBuSi), 3.83 (s, 3 H, OMe), 3.94 (s, 3 H, OMe), 6.76 (AB_q, J = 8.6 Hz, $\Delta\nu$ = 18.2 Hz, 2 H, CH_{ar}), 7.26−7.33 (m, 1 H, CH_{ar}), 7.36 (d, J = 1.5 Hz, 1 H, CH_{ar}), 7.75 (m, 2 H, CH_{ar}), 8.65 (m, 2 H, CH_{ar}) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 2.7, 18.5, 25.8, 55.8, 105.0, 108.0, 112.9, 116.6, 122.9, 123.4, 128.1, 130.8, 133.5, 137.1, 150.2, 150.4, 150.7, 151.7, 153.0, 189.1 ppm. HRMS (MALDI) calcd. for $C_{24}H_{29}NO_4SSi$ ($[M + H]^+$): 456.1659; found 456.1680.

Preparation of Imidazolide 9: Carbonyldiimidazole (84.3 mg, 0.52 mmol) was added in one portion to a stirred solution of **7** (100.0 mg, 0.26 mmol) in anhydrous THF (4 mL). The mixture was stirred at 25 °C for 10 min (monitored by TLC) and the solvent was then evaporated under reduced pressure. The easily hydrolyzed crude product was purified by small column filtration (silica gel, hexanes/EtOAc, 6:4) to afford **9** as a yellow solid (101.9 mg, 94% yield). R_f = 0.50 (hexanes/EtOAc, 7:3); m.p. 99−101 °C. IR (KBr): $\tilde{\nu}$ = 3117, 2932, 2858, 1718, 1599, 1362, 1236, 1058, 921, 805 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 0.21 (s, 6 H, Me_2Si), 1.01 (s, 9 H, tBuSi), 3.83 (s, 3 H, OMe), 3.88 (s, 3 H, OMe), 6.78 (AB_q, J = 8.6 Hz, $\Delta\nu$ = 19.0 Hz, 2 H, CH_{ar}), 7.14 (s, 1 H, CH_{imid}), 7.18 (s, 1 H, CH_{ar}), 7.58 (s, 1 H, CH_{imid}), 8.14 (s, 1 H, CH_{imid}), 8.28 (s, 1 H, CH_{ar}) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 2.6, 18.4, 25.7, 55.7, 105.2, 107.9, 115.1, 118.1, 118.5, 122.5, 127.8, 128.5, 130.7, 138.3, 149.8, 150.6, 153.3, 165.9 ppm.

Preparation of Weinreb Amide 10: *N*,*O*-Dimethylhydroxylamine hydrochloride (30.4 mg, 0.31 mmol), carbon tetrabromide (103.5 mg, 0.31 mmol), pyridine (25.2 μL, 0.31 mmol), and PPh_3 (81.3 mg, 0.31 mmol) in small portions, were added successively, to a stirred solution of **7** (100.0 mg, 0.26 mmol) in anhydrous CH_2Cl_2 (5 mL). The mixture was stirred at 25 °C until no starting material was observed (monitored by TLC; about 30 min) and the solvent was then evaporated under reduced pressure. The gummy residue was purified by flash column chromatography (silica gel, hexanes/EtOAc, 8:2) to afford **10** as a white solid (91.7 mg, 87% yield). R_f = 0.55 (hexanes/EtOAc, 7:3); m.p. 104−105 °C. IR (KBr): $\tilde{\nu}$ = 2933, 2858, 1651, 1599, 1506, 1463, 1386, 1257, 1101, 1057, 960, 842 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 0.20 (s, 6 H, Me_2Si), 1.02 (s, 9 H, tBuSi), 3.35 (s, 3 H, NMe), 3.52 (s, 3 H, NOMe), 3.83 (s, 3 H, ArO*Me*), 3.90 (s, 3 H, ArO*Me*), 6.70 (s, 2 H, CH_{ar}), 7.14 (s, 1 H, CH_{ar}), 8.21 (s, 1 H, CH_{ar}) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$ 25 °C): δ = 2.7, 18.6, 25.9, 33.9, 55.7, 55.8, 61.0, 104.3, 106.1, 115.7, 116.0, 121.2, 131.2, 149.8, 150.6, 151.8, 169.6 ppm. HRMS (MALDI) calcd. for $C_{21}H_{31}NO_5Si$ ($[M + H]^+$): 406.2044; found 406.2051.

General Procedure for Alkylation: The organometallic reagent (0.11 to 0.22 mmol) was added dropwise to a stirred solution of **8**, **9**, or **10** (0.1 mmol) in the appropriate solvent (concentration was between 0.2−0.3 M) and at the desired temperature. The reaction mixture was stirred at the same temperature until no starting material could be observed by TLC analysis and then quenched with a saturated aqueous solution of NH_4Cl (3−4 mL). The organic layer was separated and washed with brine (7 mL) whereas the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic extracts were dried with Na_2SO_4 and the solvent was evaporated under reduced pressure. The crude mixture was purified by flash column chromatography (silica gel, hexanes/EtOAc, 95:5 to 9:1) to afford **11** and/or **12** as pale yellow solids (for yields see table in Scheme 3).

Compound 11: R_f = 0.85 (hexanes/EtOAc, 95:5); m.p. 82−84 °C. IR (KBr): $\tilde{\nu}$ = 2932, 2858, 1684, 1597, 1508, 1463, 1362, 1257, 1076, 919, 839, 780 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 0.22 (s, 6 H, Me_2Si), 1.03 (s, 9 H, tBuSi), 3.77−3.90 (m, 5 H, OMe and $COCH_2$), 3.94 (s, 3 H, OMe), 5.17−5.28 (m, 2 H, $=CH_2$), 6.02−6.21 (m, 1 H, $CH{=}CH_2$), 6.75 (AB_q, J = 8.6 Hz, $\Delta\nu$ = 17.1 Hz, 2 H, CH_{ar}), 7.40 (d, J = 1.5 Hz, 1 H, CH_{ar}), 8.49 (d, J = 1.5 Hz, 1 H, CH_{ar}) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 2.7, 18.6, 25.9, 43.3, 55.8, 104.6, 107.6, 113.8, 117.2, 118.5, 122.6, 128.2, 131.4, 133.8, 150.2, 150.8, 152.9, 197.8 ppm. HRMS (MALDI) calcd. for $C_{22}H_{30}O_4Si$ ($[M + H]^+$): 387.1986; found 387.1974.

Compound 12: R_f = 0.80 (hexanes/EtOAc, 95:5); m.p. 97−99 °C. IR (KBr): $\tilde{\nu}$ = 3522, 2928, 2860, 1602, 1597, 1507, 1463, 1374,

1262, 1058, 842 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 0.19 (s, 6 H, Me_2Si), 1.04 (s, 9 H, *t*BuSi), 2.28 (s, 1 H, OH), 2.46−2.80 (m, 4 H, $CH_2CH=$), 3.83 (s, 3 H, OMe), 3.91 (s, 3 H, OMe), 4.99−5.15 (m, 4 H, $=CH_2$), 5.49−5.70 (m, 2 H, $CH=CH_2$), 6.64 (AB_q, J = 8.6 Hz, $\Delta\nu$ = 11.5 Hz, 2 H, CH_{ar}), 6.91 (d, J = 1.9 Hz, 1 H, CH_{ar}), 7.88 (d, J = 1.9 Hz, 1 H, CH_{ar}) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 2.7, 18.6, 26.0, 46.8, 55.6, 75.1, 103.8, 104.2, 111.4, 115.0, 119.0, 128.3, 128.6, 133.4, 143.6, 149.3, 150.7, 152.0 ppm. HRMS (MALDI) calcd. for $C_{25}H_{36}O_4Si$ ($[M + H]^+$): 429.2455; found 429.2440.

Preparation of Compound 13: Cs_2CO_3 (94.2 mg, 0.29 mmol), benzyl bromide (37.9 μL, 0.32 mmol), and a catalytic amount of Bu_4NI were added successively to a stirred solution of **20a** (41.0 mg, 0.15 mmol, detailed procedure for the preparation of **20a** is given later in this section) in anhydrous DMF (0.5 mL) at 25 °C. The mixture was stirred at the same temperature for 5 h (monitored by TLC) and then diluted with water (4 mL) and EtOAc (5 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (5 mL). The combined organic extracts were washed with brine (8 mL) and dried with Na_2SO_4, the solvents were evaporated under reduced pressure, and the crude product was purified by flash column chromatography (silica gel, hexanes/EtOAc, 85:15) to afford ethyl 4-benzyloxy-5,8-dimethoxy-2-naphthoate as a white solid (47.8 mg, 87% yield). R_f = 0.70 (hexanes/EtOAc, 8:2); m.p. 98−100 °C. IR (KBr): $\tilde{\nu}$ = 2949, 1714, 1603, 1465, 1365, 1280, 1070, 767 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 1.43 (t, J = 7.1 Hz, 3 H, CH_2CH_3), 3.85 (s, 3 H, OMe), 3.93 (s, 3 H, OMe), 4.43 (q, J = 7.1 Hz, 2 H, CH_2CH_3), 5.24 (s, 2 H, OCH_2Ph), 6.79 (AB_q, J = 8.6 Hz, $\Delta\nu$ = 29.4 Hz, 2 H, CH_{naphth}), 7.26−7.66 (m, 11 H, CH_{ar}), 8.63 (d, J = 1.9 Hz, 1 H, CH_{naphth}) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 14.4, 55.7, 57.2, 61.0, 71.2, 104.9, 107.5, 109.4, 118.0, 127.0, 127.5, 127.9, 128.2, 137.2, 150.3, 150.7, 155.9, 166.8 ppm.

A stirred solution of the above ester (35.2 mg, 0.096 mmol) in anhydrous Et_2O (6 mL) was treated at 0 °C with excess freshly prepared allylmagnesium bromide (1 M in Et_2O, 0.22 mL, 0.22 mmol). The reaction mixture was stirred at the same temperature for 10 min (monitored by TLC) and then quenched with a saturated aqueous solution of NH_4Cl (3 mL). The organic layer was separated and washed with brine (7 mL) whereas the aqueous layer was extracted with EtOAc (2 × 7 mL). The combined organic extracts were dried with Na_2SO_4 and the solvents were evaporated under reduced pressure. The crude mixture was purified by flash column chromatography (silica gel, hexanes/EtOAc, 8:2) to afford **13** as a white solid (36.5 mg, 94% yield). R_f = 0.65 (hexanes/EtOAc, 8:2); m.p. 91−93 °C. IR (KBr): $\tilde{\nu}$ = 3554, 2940, 1606, 1470, 1363, 1277, 1070, 922, cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 2.46−2.80 (m, 4 H, $CH_2CH=$), 3.87 (s, 3 H, OMe), 3.93 (s, 3 H, OMe), 4.96−5.14 (m, 4 H, $=CH_2$), 5.20 (s, 2 H, OCH_2Ph), 5.46−5.68 (m, 2 H, $CH=CH_2$), 6.73 (AB_q, J = 8.6 Hz, $\Delta\nu$ = 11.2 Hz, 2 H, CH_{naphth}), 7.02 (d, J = 1.9 Hz, 1 H, CH_{naphth}), 7.25−7.61 (m, 10 H, CH_{ar}), 7.88 (d, J = 1.9 Hz, 1 H, CH_{naphth}) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 46.7, 55.7, 57.2, 72.0, 75.4, 104.3, 106.4, 108.4, 111.5, 119.2, 127.2, 127.5, 128.4, 133.5, 137.6, 143.6, 149.6, 150.8, 155.6 ppm.

Preparation of Aldehyde 15: Imidazole (62.3 mg, 0.91 mmol), TBSCl (110.3 mg, 0.73 mmol), and a catalytic amount of DMAP were added successively at 0 °C to a stirred solution of **20b** (156.8 mg, 0.37 mmol, detailed procedure for the preparation of **20b** is given later in this section) in anhydrous DMF (1 mL). The ice bath was removed and the reaction mixture was stirred for 2 h at 25 °C (monitored by TLC). The reaction mixture was then quenched with methanol (0.1 mL) and a saturated aqueous solution of NH_4Cl was added (7 mL), followed by addition of EtOAc (8 mL). The organic layer was separated, whereas the aqueous layer was extracted with EtOAc (10 mL). The combined organic extracts were washed with brine (10 mL) and dried with Na_2SO_4, and the solvent was evaporated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, hexanes/EtOAc, 95:5) to afford ethyl 5,8-bisbenzyloxy-4-(*tert*-butyldimethylsilyloxy)-2-naphthoate as a colorless oil (194.8 mg, 97% yield). R_f = 0.75 (hexanes/EtOAc, 9:1). IR (film): $\tilde{\nu}$ = 2929, 1719, 1597, 1456, 1367, 1231, 1052, 830 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 0.20 (s, 6 H, Me_2Si), 0.99 (s, 9 H, *t*BuSi), 1.42 (t, J = 7.1 Hz, 3 H, CH_2CH_3), 4.41 (q, J = 7.1 Hz, 2 H, CH_2CH_3), 5.18 (s, 4 H, OCH_2Ph), 6.69 (AB_q, J = 8.6 Hz, $\Delta\nu$ = 12.7 Hz, 2 H, CH_{naphth}), 7.26−7.55 (m, 11 H, CH_{ar}), 8.73 (d, J = 1.9 Hz, 1 H, CH_{naphth}) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 2.4, 14.3, 18.7, 26.0, 60.9, 70.5, 71.5, 106.3, 109.6, 110.5, 115.4, 118.0, 123.0, 127.1, 127.3, 127.5, 127.8, 128.3, 128.4, 128.5, 137.2, 137.6, 149.5, 149.8, 152.7, 166.6 ppm.

A stirred solution of the above ester (180.1 mg, 0.33 mmol) in anhydrous CH_2Cl_2 (10 mL) was cooled to −78 °C and a solution of DIBAL in CH_2Cl_2 (1 M, 0.76 mL, 0.76 mmol) was added dropwise. The mixture was stirred at the same temperature for 20 min (monitored by TLC) and then quenched with methanol (0.5 mL). The dry ice/acetone bath was removed, allowing the mixture to reach 25 °C, and a saturated aqueous solution of sodium potassium tartrate (10 mL) was then added. Stirring was continued until the cloudy solution became clear (about 2 h), and the mixture was extracted with EtOAc (3 × 10 mL). The organic extracts were washed with brine (15 mL) and dried with Na_2SO_4, the solvents were evaporated under reduced pressure, and the crude product was purified by flash column chromatography (silica gel, hexanes/EtOAc, 7:3) to afford [5,8-bis(benzyloxy)-4-(*tert*-butyldimethylsilyloxy)naphthalen-2-yl]methanol as a white solid (161.9 mg, 98%). R_f = 0.35 (hexanes/EtOAc, 9:1); m.p. 137−139 °C. IR (KBr): $\tilde{\nu}$ = 3414, 2934, 1606, 1461, 1372, 1283, 1061, 836 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 0.17 (s, 6 H, Me_2Si), 0.97 (s, 9 H, *t*BuSi), 1.73 (s, 1 H, OH), 4.74 (s, 2 H, CH_2OH), 5.11 (s, 2 H, OCH_2Ph), 5.18 (s, 2 H, OCH_2Ph), 6.62 (AB_q, J = 8.6 Hz, $\Delta\nu$ = 14.1 Hz, 2 H, CH_{naphth}), 6.95 (d, J = 1.9 Hz, 1 H, CH_{naphth}), 7.26−7.51 (m, 10 H, CH_{ar}), 7.88 (d, J = 1.9 Hz, 1 H, CH_{naphth}) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 2.3, 18.7, 26.1, 65.5, 70.4, 71.3, 105.7, 107.9, 112.8, 115.6, 120.3, 127.3, 127.4, 127.5, 127.8, 128.4, 128.5, 129.2, 137.3, 137.9, 138.6, 148.6, 149.9, 152.8 ppm.

A solution of the above alcohol (150.0 mg, 0.30 mmol) in anhydrous CH_2Cl_2 (15 mL) was treated with 4-methylmorpholine *N*-oxide (86.4 mg, 0.74 mmol) and TPAP (20.7 mg, 0.06 mmol) at 25 °C for 2 h (monitored by TLC). The reaction mixture was then filtered through a pad of silica gel (CH_2Cl_2) and the organic solvent was concentrated under reduced pressure to afford **15** as a yellow oil (146.6 mg, 98% yield). R_f = 0.60 (hexanes/EtOAc, 9:1). IR (film): $\tilde{\nu}$ = 3068, 2928, 1694, 1601, 1512, 1453, 1376, 1252, 1050, 836 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 0.22 (s, 6 H, Me_2Si), 0.99 (s, 9 H, *t*BuSi), 5.16 (s, 2 H, OCH_2Ph), 5.20 (s, 2 H, OCH_2Ph), 6.77 (AB_q, J = 8.6 Hz, $\Delta\nu$ = 17.9 Hz, 2 H, CH_{naphth}), 7.26−7.53 (m, 11 H, CH_{ar}), 8.44 (d, J = 1.5 Hz, 1 H, CH_{naphth}), 10.04 (s, 1 H, CHO) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 2.3, 18.6, 26.0, 70.6, 71.5, 106.6, 111.1, 111.9, 122.7, 123.8, 127.3, 127.4, 127.6, 128.1, 128.5, 128.6, 134.0, 136.8, 137.5, 149.5, 149.9, 153.6, 192.2 ppm.

Preparation of Compound 16: A solution of freshly prepared allylmagnesium bromide (1 M in Et_2O, 0.35 mL, 0.35 mmol) was added

dropwise at 0 °C to a stirred solution of aldehyde **15** (131.4 mg, 0.26 mmol) in anhydrous Et_2O (6 mL). The reaction mixture was stirred at the same temperature for 15 min (monitored by TLC) and then quenched with a saturated aqueous solution of NH_4Cl (6 mL). The organic layer was separated and washed with brine (8 mL) whereas the aqueous layer was extracted with EtOAc (2 × 8 mL). The combined organic extracts were dried with Na_2SO_4 and the solvents were evaporated under reduced pressure. The crude product was dissolved in anhydrous DMF (1 mL) and cooled at 0 °C, followed by addition of imidazole (35.9 mg, 0.53 mmol), TBSCl (66.6 mg, 0.44 mmol), and a catalytic amount of DMAP. The ice bath was removed and the reaction mixture was stirred at 25 °C for 1.5 h (monitored by TLC). The reaction was then quenched with methanol (0.15 mL) and a saturated aqueous solution of NH_4Cl was added (7 mL), followed by EtOAc (10 mL). The organic layer was separated and washed with brine (10 mL), and the solvent was evaporated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, hexanes/EtOAc, 95:5) to afford **16** as a colorless oil (151.6 mg, 89% yield, based on **15**). R_f = 0.85 (hexanes/EtOAc, 9:1). IR (film): $\tilde{\nu}$ = 2930, 2855, 1603, 1457, 1375, 1255, 1083, 1057, 833 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = −0.03 (s, 3 H, MeSi), 0.13 (s, 3 H, MeSi), 0.23 (s, 3 H, MeSi), 0.25 (s, 3 H, MeSi), 0.97 (s, 9 H, *t*BuSi), 1.04 (s, 9 H, *t*BuSi), 2.42−2.64 (m, 2 H, CH_2CH=), 4.86 (t, *J* = 6.0 Hz, 1 H, CHOSi), 5.02−5.14 (m, 2 H, $=CH_2$), 5.18 (s, 2 H, OCH_2Ph), 5.23 (s, 2 H, OCH_2Ph), 5.77−5.98 (m, 1 H, $CH=CH_2$), 6.67 (AB_q, *J* = 8.6 Hz, Δ*v* = 16.0 Hz, 2 H, CH_{naphth}), 7.02 (s, 1 H, CH_{naphth}), 7.30−7.59 (m, 10 H, CH_{ar}), 7.91 (s, 1 H, CH_{naphth}) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 2.1, 2.2, 2.6, 3.1, 18.2, 18.7, 25.9, 26.1, 45.4, 70.5, 71.3, 74.9, 105.5, 107.2, 111.9, 114.8, 116.8, 120.0, 127.3, 127.4, 127.7, 128.3, 128.4, 128.5, 129.1, 135.2, 137.5, 138.0, 142.9, 148.7, 150.1, 152.3 ppm.

Treatment of Compound 16 with CAN: A solution of CAN (0.30−0.90 mmol) in water (4 mL) was added dropwise at 25 °C to a stirred solution of **16** (100 mg, 0.15 mmol) in CH_3CN (10 mL). The mixture was stirred at the same temperature for 10−40 min (monitored by TLC) and then diluted with water (8 mL) and EtOAc (10 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (2 × 8 mL). The combined organic extracts were washed with brine (10 mL) and dried with Na_2SO_4, the solvents were evaporated under reduced pressure, and the residue was purified by flash column chromatography (silica gel, hexanes/EtOAc, 9:1 to 7:3) to afford **17** as a colorless oil and **18** as an orange oil (yields of **17** and **18** vary from 20 to 40%). **17**: R_f = 0.80 (hexanes/EtOAc, 9:1); **18**: R_f = 0.50 (hexanes/EtOAc, 8:2). IR (film): $\tilde{\nu}$ = 2925, 1659, 1577, 1279, 1093, 836 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = −0.02 (s, 3 H, MeSi), 0.07 (s, 3 H, MeSi), 0.89 (s, 9 H, *t*BuSi), 2.24−2.61 (m, 2 H, CH_2CH=), 4.89−5.09 (m, 3 H, $=CH_2$ and CHOSi), 5.17 (s, 2 H, OCH_2Ph), 5.19 (s, 2 H, OCH_2Ph), 5.68−5.91 (m, 1 H, $CH=CH_2$), 6.85 (d, *J* = 1.5 Hz, 1 H, CH_{quin}), 7.22 (s, 2 H, CH_{naphth}), 7.27−7.59 (m, 10 H, CH_{ar}).

Preparation of Juglone Derivative 19: A solution of lithium naphthalenide or lithium 4,4′-di-*tert*-butylbiphenylide (4.5 mmol) in THF was added dropwise at −20 °C to a stirred solution of **16** (200 mg, 0.30 mmol) in anhydrous THF (15 mL). Lithium naphthalenide and lithium 4,4′-di-*tert*-butylbiphenylide were prepared according to literature procedures (see refs.[36−38]). Upon completion of the addition, the temperature was allowed to rise to 0 °C and the mixture was stirred for about 2 h (monitored by TLC). The reaction was quenched with a saturated aqueous solution of NH_4Cl (6 mL) and diluted with EtOAc (10 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (10 mL). The combined organic extracts were washed with brine (15 mL) and dried with Na_2SO_4, the solvents were evaporated under reduced pressure, and the crude product was purified by flash column chromatography (silica gel, hexanes/EtOAc, 95:5 to 9:1) to afford **19** as a orange oil (32.3 mg, 30% yield). R_f = 0.75 (hexanes/EtOAc, 9:1). IR (film): $\tilde{\nu}$ = 2925, 1648, 1591, 1257, 1088, 829 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = −0.01 (s, 3 H, MeSi), 0.03 (s, 3 H, MeSi), 0.87 (s, 9 H, *t*BuSi), 2.39 (t, *J* = 6.3 Hz, 2 H, CH_2CH=), 4.72 (t, *J* = 5.6 Hz, 1 H, CHOSi), 4.89−5.07 (m, 2 H, $=CH_2$), 5.60−5.82 (m, 1 H, $CH=CH_2$), 6.90 (s, 2 H, CH_{quin}), 7.23 (1 H, CH_{ar}), 7.52 (d, *J* = 1.5 Hz, 1 H, CH_{ar}), 11.87 (s, 1 H, OH).

General Procedure for the Preparation of Naphthols 20a and 20b: A catalytic amount of sodium ethoxide was added to a stirred solution of either **3a** or **3b** (4.25 mmol) in absolute ethanol (40 mL). The mixture was heated under reflux for 1 h (monitored by TLC). Upon completion of the reaction, half of the solvent was evaporated under reduced pressure, and saturated aqueous NH_4Cl solution (20 mL) and EtOAc (35 mL) were added. The organic layer was separated, washed with brine (30 mL), and dried with Na_2SO_4. Evaporation of the organic solvents under reduced pressure afforded crude naphthols, which were recrystallized from EtOAc and Et_2O to afford **20a** and **20b**, respectively, as pale yellow, crystalline solids. **20a**: yield 89%, all spectroscopic data were in accordance with those reported; **20b**: yield 93%; R_f = 0.60 (hexanes/EtOAc, 8:2); m.p. 154−156 °C. IR (KBr): $\tilde{\nu}$ = 3384, 2980, 1715, 1619, 1377, 1293, 1226, 1034, 741 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 1.40 (t, *J* = 7.1 Hz, 3 H, CH_2CH_3), 4.39 (q, *J* = 7.1 Hz, 2 H, CH_2CH_3), 5.16 (s, 2 H, OCH_2Ph), 5.19 (s, 2 H, OCH_2Ph), 6.73 (AB_q, *J* = 8.6 Hz, Δ*v* = 25.7 Hz, 2 H, CH_{naphth}), 7.26−7.56 (m, 11 H, CH_{ar}), 8.57 (d, *J* = 1.5 Hz, 1 H, CH_{naphth}), 9.52 (s, 1 H, OH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 14.3, 61.0, 70.4, 72.1, 105.5, 107.3, 110.6, 116.0, 127.1, 127.9, 128.3, 128.6, 128.8, 129.0, 129.1, 135.2, 136.9, 149.0, 150.2, 154.6, 166.6 ppm. HRMS (MALDI) calcd. for $C_{27}H_{24}O_5$ ($[M + Na]^+$): 451.1516; found 451.1501.

Preparation of Naphthol 21: A solution of DIBAL in CH_2Cl_2 (1 M, 6.43 mL, 6.43 mmol) was added dropwise at −78 °C to a stirred solution of **3a** (512.0 mg, 1.61 mmol) in anhydrous CH_2Cl_2 (20 mL). The mixture was stirred at the same temperature for 2 h and then quenched with methanol (1 mL). The dry ice/acetone bath was removed, allowing the mixture to reach 25 °C, and a saturated aqueous solution of sodium potassium tartrate (20 mL) was then added. Stirring was continued until the cloudy solution became clear (about 3 h) and the mixture was extracted with EtOAc (3 × 20 mL). The organic extracts were washed with brine (30 mL) and dried with Na_2SO_4, the solvents were evaporated under reduced pressure, and the crude product was purified by flash column chromatography (silica gel, hexanes/EtOAc, 3:7) to afford 3-hydroxymethyl-5,8-dimethoxynaphthalen-1-ol as a white solid (358.3 mg, 95% yield). R_f = 0.25 (hexanes/EtOAc, 7:3); m.p. 140−142 °C. IR (KBr): $\tilde{\nu}$ = 3334, 2846, 1619, 1446, 1387, 1280, 1248, 1095, 1044, 974 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 1.87 (s, 1 H, CH_2OH), 3.90 (s, 3 H, OMe), 3.97 (s, 3 H, OMe), 4.73 (s, 2 H, CH_2), 6.62 (s, 2 H, CH_{ar}), 6.89 (s, 1 H, CH_{ar}), 7.65 (s, 1 H, CH_{ar}), 9.42 (s,1 H, ArOH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 55.7, 56.2, 65.5, 103.3, 103.4, 110.0, 110.6, 115.0, 128.3, 140.3, 150.0, 150.2, 154.7. HRMS (MALDI) calcd. for $C_{13}H_{14}O_4$ [M^+]: 234.0887; found 234.0883.

This alcohol (300.0 mg, 1.28 mmol) was dissolved in anhydrous DMF (0.5 mL) and cooled to 0 °C, followed by addition of imida-

zole (113.0 mg, 1.66 mmol) and TBSCl (212.5 mg, 1.41 mmol). The ice bath was removed and the reaction mixture was stirred overnight at 25 °C. Upon consumption of the starting material (monitored by TLC), the reaction mixture was quenched with methanol (0.15 mL) and a saturated aqueous solution of NH_4Cl was added (10 mL), followed by EtOAc (15 mL). The organic layer was separated and washed with brine (15 mL), and the solvent was evaporated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, hexanes/EtOAc, 9:1) to afford **21** as a white solid of low melting point (379.2 mg, 85% yield). R_f = 0.70 (hexanes/EtOAc, 8:2). IR (KBr): $\tilde{\nu}$ = 3380, 2929, 2854, 1645, 1620, 1516, 1463, 1386, 1251, 1093, 842, 780 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 0.09 (s, 6 H, Me_2Si), 0.95 (s, 9 H, *t*BuSi), 3.90 (s, 3 H, OMe), 3.97 (s, 3 H, OMe), 4.82 (s, 2 H, CH_2), 6.61 (s, 2 H, CH_{ar}), 6.89 (s, 1 H, CH_{ar}), 7.64 (s, 1 H, CH_{ar}), 9.40 (s, 1 H, OH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 3.8, 18.8, 26.0, 55.8, 56.2, 65.2, 102.7, 102.9, 109.9, 110.0, 114.5, 128.4, 140.9, 150.0, 150.2, 154.2 ppm. HRMS (MALDI) calcd. for $C_{19}H_{28}O_4Si$ ($[M + Na]^+$): 371.1649; found 371.1651.

General Procedure for Salcomine-Catalyzed Oxidation: Salcomine (32.0 mg, 0.09 mmol) was added to a stirred solution of **20a**, **20b**, or **21** (0.47 mmol) in CH_3CN (35 mL), and the mixture was stirred under air at 25 °C for 20−24 h (until no starting material was observed by TLC analysis). The dark red solution was then filtered through a pad of Celite and the solvent was evaporated under reduced pressure to afford **23a**, **23b**, or **23c**, respectively, as shiny dark red crystals.

Compound 23a: Yield 90%; R_f = 0.60 ($CHCl_3$/MeOH, 95:5); m.p. 172−174 °C. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 1.37 (t, *J* = 7.1 Hz, 3 H, CH_2CH_3), 3.92 (s, 3 H, OMe), 3.94 (s, 3 H, OMe), 4.36 (q, *J* = 7.1 Hz, 2 H, CH_2CH_3), 7.19 (AB_q, *J* = 9.5 Hz, Δ*v* = 9.7 Hz, 2 H, CH_{ar}), 8.66 (s, 1 H, CH_{quin}) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 14.8, 56.6, 62.1, 119.5, 121.4, 122.2, 126.1, 143.9, 152.5, 157.3, 163.2, 177.1, 177.2 ppm. HRMS (MALDI) calcd. for $C_{15}H_{14}O_6$ ($[M + Na]^+$): 313.0683; found 313.0682.

Compound 23b: Yield 90%; R_f = 0.60 ($CHCl_3$/MeOH, 95:5); m.p. 179−181 °C. IR (KBr): $\tilde{\nu}$ = 2926, 1730, 1663, 1604, 1452, 1383, 1194, 1006, 726 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 1.30 (t, *J* = 7.1 Hz, 3 H, CH_2CH_3), 4.26 (q, *J* = 7.1 Hz, 2 H, CH_2CH_3), 5.08 (s, 2 H, OCH_2Ph), 5.10 (s, 2 H, OCH_2Ph), 7.11 (AB_q, *J* = 9.5 Hz, Δ*v* = 18.8 Hz, 2 H, CH_{ar}), 7.20−7.57 (m, 10 H, CH_{ar}), 8.66 (s, 1 H, CH_{quin}) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 14.0, 61.4, 70.6, 71.5, 120.6, 122.2, 126.4, 127.2, 127.7, 128.4, 128.5, 128.7, 135.4, 135.7, 143.8, 151.6, 155.9, 163.2, 177.1, 177.2 ppm. HRMS (MALDI) calcd. for $C_{27}H_{22}O_6$ ($[M + Na]^+$): 465.1309; found 465.1322.

Compound 23c: Yield 93%; R_f = 0.30 (hexanes/EtOAc, 7:3); m.p. 137−139 °C. IR (KBr): $\tilde{\nu}$ = 2938, 2858, 1653, 1632, 1485, 1276, 1196, 1079, 845, 782 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 0.06 (s, 6 H, Me_2Si), 0.91 (s, 9 H, *t*BuSi), 3.81 (s, 3 H, OMe), 3.84 (s, 3 H, OMe), 4.48 (s, 2 H, CH_2), 7.01 (AB_q, *J* = 9.3 Hz, Δ*v* = 42.4 Hz, 2 H, CH_{ar}), 7.96 (s, 1 H, CH_{quin}) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 3.7, 18.3, 28.8, 56.4, 56.7, 59.4, 115.8, 118.6, 120.8, 124.2, 133.8, 137.5, 150.7, 157.0, 178.8, 180.1 ppm. HRMS (MALDI) calcd. for $C_{19}H_{26}O_5Si$ ($[M + H]^+$): 363.1622; found 363.1624.

General Procedure for the Oxidation with PIFA: A stirred solution of **20a**, **20b**, or **21** (0.29 mmol) in a 2:1 mixture of CH_3CN/H_2O (15 mL) was cooled to 0 °C and [bis (trifluoroacetoxy)iodo]benzene (PIFA, 311.8 mg, 0.72 mmol) was added (in the case of **21** an equimolar amount of K_2CO_3 was added before the addition of PIFA). The ice bath was then removed and the mixture was stirred for 1 h at 25 °C. The reaction mixture was quenched with a saturated aqueous solution of $NaHCO_3$ (15 mL), followed by extraction with EtOAc (2 × 15 mL). The organic layer was washed with brine (20 mL) and dried with Na_2SO_4, the solvents were evaporated under reduced pressure, and the crude product was purified by flash column chromatography (silica gel, hexanes/EtOAc) to afford **25a**, **25b**, or **22c**, respectively.

Compound 25a: Orange solid, yield 55%; R_f = 0.45 (hexanes/EtOAc, 7:3); m.p. 132−134 °C. IR (KBr): $\tilde{\nu}$ = 3425, 2916, 1715, 1669, 1640, 1583, 1289, 998, 818 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 1.35 (t, *J* = 7.1 Hz, 3 H, CH_2CH_3), 3.52 (d, *J* = 4.5 Hz, 1 H, OH), 3.88 (s, 3 H, OMe), 3.92 (s, 3 H, OMe), 4.34 (q, *J* = 7.1 Hz, 2 H, CH_2CH_3), 5.85 (d, *J* = 4.5 Hz, 1 H, CHOH), 6.99 (s, 1 H, COCH=), 7.06 (AB_q, *J* = 9.1 Hz, Δ*v* = 43.4 Hz, 2 H, CH_{ar}) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 14.1, 56.3, 56.6, 60.1, 61.9, 112.8, 116.9, 120.0, 132.1, 135.4, 142.2, 150.8, 154.3, 165.7, 184.8 ppm. HRMS (MALDI) calcd. for $C_{15}H_{16}O_6$ [M^+]: 292.0941; found 292.0942.

Compound 25b: Orange solid, yield 75%; R_f = 0.45 (hexanes/EtOAc, 7:3); m.p. 101−103 °C. IR (KBr): $\tilde{\nu}$ = 3461, 2932, 1724, 1672, 1590, 1456, 1248, 1105, 1018, 806, 741 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 1.31 (t, *J* = 7.1 Hz, 3 H, CH_2CH_3), 3.54 (s, 1 H, OH), 4.30 (q, *J* = 7.1 Hz, 2 H, CH_2CH_3), 5.08 (s, 2 H, OCH_2Ph), 5.00−5.20 (m, 4 H, OCH_2Ph), 5.86 (s, 1 H, CHOH), 6.96 (s, 1 H, COCH=), 6.98 (AB_q, *J* = 9.1 Hz, Δ*v* = 44.1 Hz, 2 H, CH_{ar}), 7.24−7.54 (m, 10 H, CH_{ar}) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 14.0, 60.1, 61.8, 71.2, 71.4, 115.4, 118.4, 126.8, 127.3, 127.6, 128.3, 128.5, 128.8, 132.4, 135.2, 136.7, 142.3, 150.4, 153.2, 165.7, 184.4 ppm. HRMS (MALDI) calcd. for $C_{27}H_{24}O_6$ ($[M + Na]^+$): 467.1465; found 467.1449.

Compound 22c: Orange-brown oil, yield 53%; R_f = 0.50 (hexanes/EtOAc, 7:3). IR (thin film): $\tilde{\nu}$ = 2956, 2861, 1653, 1569, 1474, 1281, 1108, 1057, 970, 845, 776 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 0.05 (s, 6 H, Me_2Si), 0.87 (s, 9 H, *t*BuSi), 3.87 (s, 3 H, OMe), 3.88 (s, 3 H, OMe), 4.58 (d, *J* = 2.2 Hz, 2 H, CH_2), 6.79 (t, *J* = 2.2 Hz, 1 H, CH_{quin}), 7.23 (AB_q, *J* = 9.7 Hz, Δ*v* = 10.8 Hz, 2 H, CH_{ar}) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 3.8, 18.3, 28.8, 56.7, 56.8, 59.3, 119.9, 120.5, 121.1, 121.2, 132.8, 149.4, 153.5, 153.7, 184.8, 184.9 ppm. HRMS (MALDI) calcd. for $C_{19}H_{26}O_5Si$ ($[M + H]^+$): 363.1622; found 363.1624.

General Procedure for the Oxidation with PIFA/H^+/$FeCl_3$: A stirred solution of either **20a** or **20b** (0.35 mmol) in a 2:1 mixture of CH_3CN/H_2O (17 mL) was cooled to 0 °C, and PIFA (227.9 mg, 0.53 mmol) was added. The ice bath was then removed, the mixture was stirred for 1 h at 25 °C, and a solution of $FeCl_3 \cdot 6H_2O$ (270.3 mg, 1.0 mmol) in HCl (1 N, 2.5 mL) was then added. The reaction mixture was stirred for 6 h at 25 °C and then diluted with water (10 mL) and EtOAc (18 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (12 mL). The combined organic extracts were washed with brine (20 mL) and dried with Na_2SO_4, the solvents were evaporated under reduced pressure, and the crude product was purified by flash column chromatography (silica gel, hexanes/EtOAc, 7:3) to afford **22a** or **22b**, respectively, as orange solids.

Compound 22a: Yield = 48%; R_f = 0.65 ($CHCl_3$/MeOH, 95:5); m.p. 110−112 °C. IR (KBr): $\tilde{\nu}$ = 2923, 2858, 1729, 1659, 1482, 1288, 1115, 1016, 831 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 1.34 (t, *J* = 7.1 Hz, 3 H, CH_2CH_3), 3.92 (s, 3 H, OMe), 3.93 (s, 3 H, OMe), 4.34 (q, *J* = 7.1 Hz, 2 H, CH_2CH_3), 7.02 (s, 1 H, CH_{quin}),

7.30 (AB_q, J = 9.7 Hz, $\Delta\nu$ = 10.4 Hz, 2 H, CH_{ar}) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 14.1, 56.8, 56.9, 62.2, 120.2, 121.1, 137.4, 139.8, 153.5, 153.8, 163.6, 181.0, 184.2 ppm. HRMS (MALDI) calcd. for $C_{15}H_{14}O_6$ ([M + Na]$^+$): 313.0683; found 313.0681.

Compound 22b: Yield = 67%; R_f = 0.65 ($CHCl_3$/MeOH, 95:5); m.p. 117−119 °C. IR (KBr): $\tilde{\nu}$ = 2924, 1740, 1664, 1567, 1448, 1284, 1118, 1021, 742 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 1.35 (t, J = 7.1 Hz, 3 H, CH_2CH_3), 4.36 (q, J = 7.1 Hz, 2 H, CH_2CH_3), 5.17 (s, 4 H, OCH_2Ph), 7.02 (s, 1 H, CH_{quin}), 7.20−7.57 (m, 12 H, CH_{ar}) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 14.1, 62.2, 71.6, 71.7, 122.3, 123.1, 126.8, 127.0, 127.9, 128.0, 128.6, 136.1, 136.2, 137.3, 139.8, 152.6, 152.9, 163.6, 180.6, 183.9 ppm. HRMS (MALDI) calcd. for $C_{27}H_{22}O_6$ ([M + Na]$^+$): 465.1309; found 465.1310.

Preparation of Aldehyde 29: A saturated aqueous solution of $Na_2S_2O_4$ (1 mL) was added at 25 °C to a stirred solution of **22a** (72.6 mg, 0.25 mmol) in $CHCl_3$ (5 mL) and the mixture was vigorous stirred for 15 min (disappearance of the orange color of the quinone moiety). It was then diluted with water (5 mL) and the organic layer was separated. The aqueous layer was extracted with $CHCl_3$ (2 × 5 mL), and the combined organic extracts were washed with brine (10 mL), dried with Na_2SO_4, and concentrated under reduced pressure to afford the crude hydroquinone, which was used in the next step without further purification.

A solution of the crude product in anhydrous DMF (0.5 mL) was treated at 0 °C with imidazole (51.1 mg, 0.75 mmol), TBSCl (95.0 mg, 0.63 mmol), and a catalytic amount of DMAP. The ice bath was removed and the reaction mixture was stirred overnight. The reaction mixture was then quenched with MeOH (0.3 mL) and a saturated aqueous solution of NH_4Cl (5 mL) was added, followed by extraction with EtOAc (2 × 7 mL). The organic layer was washed with brine (10 mL), dried with Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, hexanes/Et_2O, 9:1) to afford **27** as a white solid of low melting point (115.9 mg, 89% yield based on **22a**). R_f = 0.75 (hexanes/Et_2O, 8:2). IR (thin film): $\tilde{\nu}$ = 2951, 2857, 1739, 1608, 1576, 1384, 1366, 1264 1138, 1061, 930 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 0.00 (s, 6 H, Me_2Si), 0.20 (s, 6 H, Me_2Si), 1.03 (s, 9 H, *t*BuSi), 1.07 (s, 9 H, *t*BuSi), 1.39 (t, J = 7.1 Hz, 3 H, CH_2CH_3), 3.82 (s, 3 H, OMe), 3.84 (s, 3 H, OMe), 4.39 (q, J = 7.1 Hz, 2 H, CH_2CH_3), 6.73 (AB_q, J = 8.5 Hz, $\Delta\nu$ = 39.0 Hz, 2 H, CH_{ar}), 7.18 (s, 1 H, CH_{ar}) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$, 25 °C): δ = −5.1, −4.5, 14.3, 18.0, 18.2, 20.2, 25.9, 26.0, 55.3, 55.7, 61.2, 105.7, 107.5, 116.8, 119.9, 123.2, 123.9, 146.0, 146.8, 150.2, 152.0, 167.7 ppm.

A solution of DIBAL in CH_2Cl_2 (1.0 M, 0.44 mL, 0.44 mmol) was added dropwise at −78 °C to a stirred solution of **27** (104.2 mg, 0.20 mmol) in CH_2Cl_2 (7 mL). The reaction mixture was stirred at the same temperature for 1 h (monitored by TLC) and then quenched with MeOH (0.4 mL), followed by addition of a saturated aqueous solution of sodium potassium tartrate (8 mL) and EtOAc (5 mL). The resulting mixture was vigorously stirred for 2 h, whereupon the organic layer was separated and the aqueous layer was extracted with EtOAc (2 × 8 mL). The combined organic extracts were washed with brine (10 mL), dried with Na_2SO_4, and concentrated under reduced pressure, and the crude product was purified by flash column chromatography (silica gel, hexanes/EtOAc, 8:2) to afford [1,4-bis(*tert*-butyldimethylsilyloxy)-5,8-dimethoxynaphthalen-2-yl]methanol as a colorless oil (89.0 mg, 93% yield). R_f = 0.35 (hexanes/Et_2O, 7:3). IR (neat): $\tilde{\nu}$ = 3445, 2929, 2856, 1602, 1373, 1258, 1062, 926, 839 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 0.00 (s, 6 H, Me_2Si), 0.18 (s, 6 H, Me_2Si), 1.03 (s, 9 H, *t*BuSi), 1.05 (s, 9 H, *t*BuSi), 3.79 (s, 3 H, OMe), 3.83 (s, 3 H, OMe), 4.76 (d, J = 3.5 Hz, 2 H, CH_2OH), 6.63 (s, 2 H, CH_{ar}), 6.95 (s, 1 H, CH_{ar}) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$, 25 °C): δ = −4.4, −4.5, 18.3, 18.5, 25.8, 25.9, 55.2, 55.5, 60.8, 104.7, 105.0, 116.8, 121.5, 122.5, 128.7, 141.9, 146.5, 150.3, 150.6 ppm. HRMS (FAB) calcd. for $C_{25}H_{42}O_5Si_2$ ([M + H]$^+$): 479.2649; found 479.2662.

A solution of the above alcohol (160.4 mg, 0.34 mmol) in anhydrous CH_2Cl_2 (15 mL) was treated with 4-methylmorpholine *N*-oxide (98.1 mg, 0.84 mmol) and TPAP (23.5 mg, 0.07 mmol) at 25 °C for 3 h (the reaction progress was monitored by TLC). The reaction mixture was then filtered through a pad of silica gel (CH_2Cl_2) and the organic solvent was concentrated under reduced pressure to afford **29** as a yellow oil (154.9 mg, 97% yield). R_f = 0.70 (hexanes/Et_2O, 7:3). IR (thin film): $\tilde{\nu}$ = 2955, 2858, 1678, 1605, 1574, 1516, 1392, 1372, 1259, 1074, 1059, 925 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.00 (s, 6 H, Me_2Si), 0.20 (s, 6 H, Me_2Si), 1.01 (s, 9 H, *t*BuSi), 1.07 (s, 9 H, *t*BuSi), 3.83 (s, 3 H, OMe), 3.84 (s, 3 H, OMe), 6.78 (AB_q, J = 8.7 Hz, $\Delta\nu$ = 44.4 Hz, 2 H, CH_{ar}), 7.15 (s, 1 H, CH_{ar}), 10.40 (s, 1 H, CHO) ppm. ^{13}C NMR (100.5 MHz, $CDCl_3$, 25 °C): δ = −4.8, −4.4, 18.5, 25.8, 25.9, 55.4, 55.9, 106.3, 109.2, 111.4, 124.6, 128.8, 130.9, 146.9, 150.8, 151.8, 152.2, 189.6 ppm. HRMS (FAB) calcd. for $C_{25}H_{40}O_5Si_2$ ([M + H]$^+$): 477.2493; found 477.2478.

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