conducted at ambient temperature (24 °C).

1. Neutralization of the THF Nonextractable Component of Illinois No. 6 Coal. A 100-mL single-necked, round-bottomed flask was equipped with a magnetic stirring bar and charged with 4.00 g of THF-insoluble Illinois No. 6 coal. The solid coal was stirred and 55.0 mL of 0.26 M KOH (1 equiv assuming 3.5 mequiv of acidic hydrogens per gram of coal) in methanol was added in one portion rapidly. When addition of the base solution was completed, a timer was started and the kinetics run begun. During the course of the neutralization, the solution was maintained under a positive pressure of nitrogen. Periodically, the slurry was sampled by using a large bore calibrated glass tube and a Glasfirn "Pi-Pump" pipetting aid. A 2-mL aliquot was removed. Control experiments showed that the slurry was well agitated and that equal portions of coal and solution were removed regardless of the sampling depth of the pipette. The removed aliquot was filtered by using a sintered glass, medium frit filtration funnel. The coal was washed with 2 mL of methanol and the filtrate was diluted with 20 mL of deionized, degassed water. The aqueous methanol solution was then titrated with 0.020 M HCl to a pH of 7.0. Blank titrations, without coal, were done to determine the initial base concentration. Final base concentrations in the reaction mixture were determined after 24 h.

2. Base Capacity Measurements. Equilibrium base capacities were measured after 2 weeks by titration of a known volume aliquot removed from the supernatant of the centrifuged swelling samples. The titration was conducted at room temperature with standard acid solution (0.020 M HCl) using a Beckman Potentiograph (E 536) and a Metrohm (655) Dosimat.

Acknowledgment. We extend special thanks to Professor J. W. Larsen for insightful discussions and his instrumental contributions to the progress of our work. Appreciation is also given to M. L. Gorbaty, P. S. Hagan, J. S. Gethner, and D. Brenner for valuable suggestions.

Conjugate Addition of Acylate-Nickel Complexes to Quinone Monoketals: Formal Synthesis of the Naphthoquinone Antibiotics Nanaomycin A and Deoxyfrenolicin

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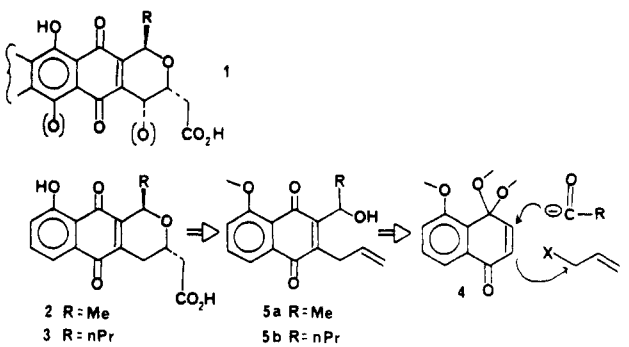
A direct approach to the synthesis of isochromanone antibiotics such as nanaomycin A (2) and deoxyfrenolicin (3) is the conjugate addition of a carbonyl anion equivalent to the appropriate naphthoquinone monoketal followed by trapping with an allylic halide. This provides a naphthoquinone nucleus with two side chains which are appropriate for the palladium-promoted heterocyclization developed earlier to complete the fused pyrano ring system. As previously observed in related systems, conjugate addition of carbonyl anion equivalents to benzoquinone and naphthoquinone monoketals leads to reductive cleavage as a major pathway, especially with the benzoquinone monoketals. The most general solution to the problem is the Corey-Hegedus procedure for preparation and reaction of acylate-nickel complexes. In the first tests with quinone monoketals, efficient conjugate addition is observed with naphthoquinone monoketals, and the intermediate enolate anions can be trapped with high efficiency by using allyl iodide. Manipulation of the quinone and acyl functionality allows the formation of the α-(hydroxyalkyl)naphthoquinone system, and the palladium(II)-catalyzed ring closure gives the desired isochromanone ring system. Use of the acyl-nickel complex from methyllithium and nickel carbonyl provides nanaomycin A (2), while the combination of *n*-propyllithium and nickel carbonyl leads to deoxyfrenolicin (3) by the same route.

Introduction

There is a set of natural products that have as common structural features a pyran ring with an alkyl substituent at C-2 and an acetic acid unit at C-6, usually trans, and fused to a naphthoquinone unit at C-3/C-4, as represented by structure 1. Examples are nanaomycin A (2)[3] and deoxyfrenolicin (3),[3,4] and more complex members exist. We have been interested in this set of compounds as a testing ground for synthesis methodology, and earlier papers give a more complete introduction.[5]

Scheme I



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(2) (a) Omura, S.; Tanaka, J.; Koyana, Y.; Oiwa, R.; Katagiri, M. *J. Antibiot.* **1974**, *25*, 363. (b) Tanaka, H.; Koyama, Y.; Marumo, H.; Oiwa, R.; Katagiri, M.; Nagai, T.; Omura, S. *Ibid.* **1975**, *28*, 860. (c) Tanaka, H.; Koyama, Y.; Nagai, T.; Marumo, H.; Omura, S. *Ibid.* **1975**, *78*, 868.

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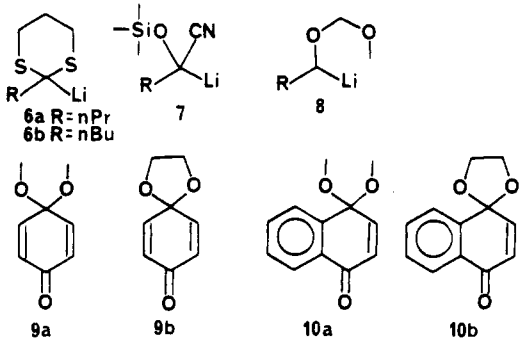
In this paper we report a study of the Corey–Hegedus procedure for conjugate addition of acylate–nickel complexes,[6] extending the reaction to quinone monoketals (e.g., **4**) and including the first trapping procedures for the intermediate enolate using carbon electrophiles.[7] The process allows particularly direct syntheses of nanaomycin A (**2**) and deoxyfrenolicin (**3**) through the key intermediates **5a** and **5b** (Scheme I). The pyran ring would be formed by palladium-promoted alkoxycarbonylation, on the basis of our successful procedure with a closely related system.[5a]

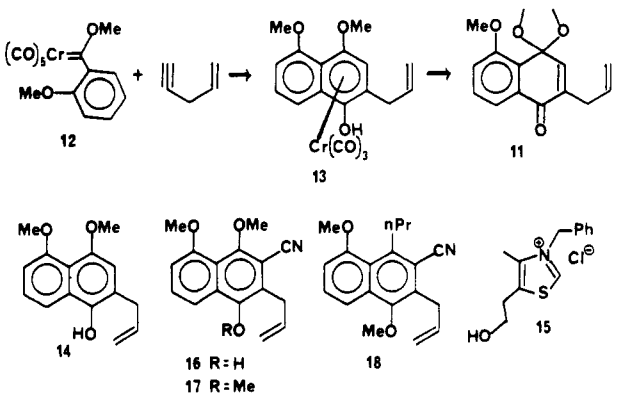
Conjugate addition of carbonyl anion equivalents to α,β-unsaturated carbonyl compounds is generally possible, of course,[8] with especially simple examples such as Stetter's thiazolium-catalyzed addition of aldehyde acyl units to acyclic enones.[9] The convenient but highly reactive carbon nucleophiles such as the 2-alkyl-1,3-dithianyl system (e.g., **6**),[10] cyanohydrin acetal anion (e.g., **7**),[11] and



1-lithio-1-[(methoxymethyl)oxy]butane (**8**)[12] typically favor 1,2-addition over 1,4-addition. However, the special effect of hexamethylphosphoric triamide (HMPA) in promoting 1,4-addition to simple enones looked promising with these species.[13]

Quinone monoketals (**9**, **10**) do not behave exactly as simple cyclohexenones; cyanide anion[14] and active methylene compounds (malonate,[15] cyanoacetate,[15] β-keto ester,[15] dimethyloxosulfonium methylide[16]) give efficient conjugate addition at least with simple substrates such as **9** and **10**, but lithiodimethylcuprate gives exclusively reductive cleavage to the hydroquinones monoether (e.g., *p*-methoxyphenol from **9a**).[17]

Survey of Acylate–Nickel Additions to Quinone Monoketals. Our initial studies were carried out on the quinone ketal **11**, from which simple protonation of the



expected enolate would produce a useful intermediate related to **5**. The quinone ketal **11** was prepared in four steps (40% overall) from *o*-bromoanisole and allylacetylene via the carbene complex **12** and naphthol complex **13**.[7,18] Reaction of 2-lithio-2-propyl-1,3-dithiane (**6a**) with **11** in THF–HMPA produced primarily the reduction product **14** (46% isolated yield) along with a product tentatively identified as a coupling product of 2-propyl-1,3-dithiane. Heating a methyl alcohol solution of **11** with the thiazolium salt **15** and triethylamine[9] again gave the naphthol **14**, in 90% yield. The α-alkoxy anion **8** gave a complex mixture of products, with no carbonyl-containing species in significant amount. Reaction of the cyanohydrin acetal anion **7** gave a product from conjugate addition to **11**, but it was identified as **16** (43% yield), in which cyanide anion has added. Apparently the cyanide liberated during the usual hydrolysis sequence[11a] on the cyano hydrin acetal was sufficient to produce **16**.

The deliberate addition of cyanide anion (KCN, methyl alcohol at reflux) followed by treatment with dilute acid to induce elimination of methyl alcohol gave cyanophenol **16** in 74% yield. Methylation of the free phenolic hydroxyl produced the trimethoxy derivative **17** (75–85% yield overall from **11**). Obvious routes lead from **17** to key intermediate **5a**, but none have been sufficiently successful to give a practical pathway. For example, addition of *n*-propyllithium (ether, 25 °C) gave a product (49% yield) from substitution for a methoxy group, tentatively identified as **18**.[19] Similar results were obtained (77% yield of **18**) with *n*-propylmagnesium bromide. Hydride reduction was also unsatisfactory. The cyano group was resistant to reduction (with diisobutylaluminum hydride, L-Selectride, and lithium triethylborohydride; days at 25 °C); lithium aluminum hydride produced the desired aldehyde but in only 16% yield and again accompanied by a product where one methoxyl was replaced by hydride (14%).

In our studies, the only other successful conjugate additions to **11** by a carbon nucleophile involved the lithium and potassium salts of nitromethane and the potassium salt of nitroethane. Both soluble lithionitromethane and the insoluble potassium analogue added to **11** in THF–HMPA at 23 °C to give a stereoisomeric mixture of adducts **19** in 95% yield. Loss of methyl alcohol proceeded smoothly upon addition of 2–3 mol equiv of magnesium

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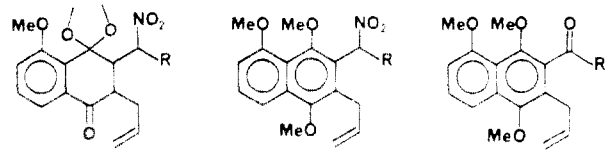
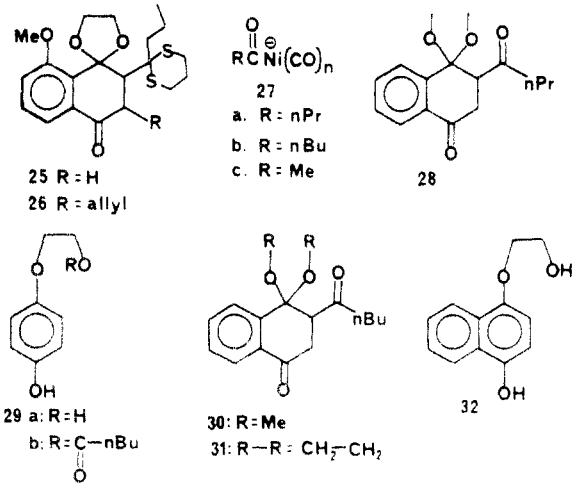


19 R = H
22 R = Me
20 R = H
23 R = Me
21 R = H
24 R = Me

bromide etherate. The easily oxidized naphthol was converted to the methyl ether **20** only with difficulty, the optimum procedure involving a mixture of methyl iodide and potassium carbonate in acetone (40% yield). Unfortunately Nef-type reaction of the nitromethyl unit to give an aldehyde **21** was not successful using a variety of old and new procedures.[20] The corresponding intermediates from nitroethane (**22**, **23**) were obtained in better yields but also could not be converted to the acetyl derivative **24** in useful efficiency.

With the general failure of the intermediates from direct addition to **11** and an expectation that the substituent at C-2 (allyl) was at least partly responsible for hindering 1,4-addition, we considered conjugate addition and enolate trapping with carbon electrophiles starting from the simpler quinone ketals **9** and **10**. The use of HMPA, tetramethylethylenediamine, or Dabco in reaction of *n*-butyllithium with **9** and **10** was not promising although reductive cleavage of a ketal oxygen was much less prevelant. The primary competing pathway is 1,2-addition. For example, addition of **10b** to a solution of *n*-butyllithium in THF containing 2 mol equiv of HMPA gave a mixture of about equal amounts of 1,2- and 1,4-addition products.[21] Reaction of 2-lithio-2-propyl-1,3-dithiane (**6a**) with **44** in THF containing 2 mol equiv of HMPA was much more selective; protonation of the intermediate gave the 1,4-addition product **25** in 86% yield while quenching with

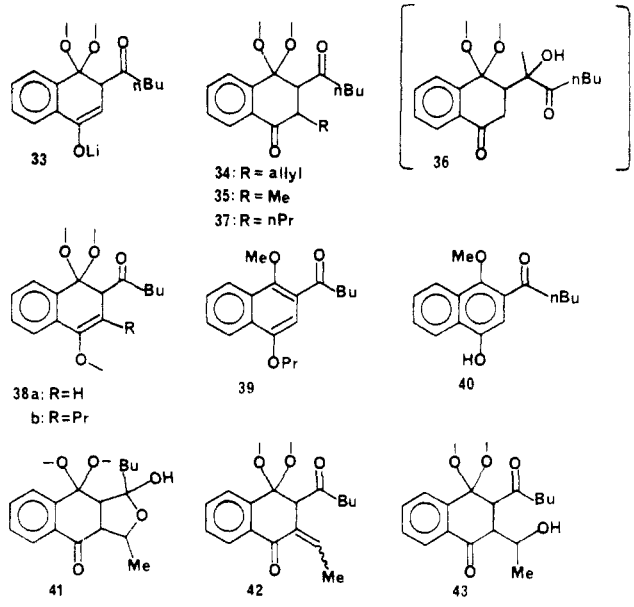


25 R = H
26 R = allyl
27
a. R = nPr
b. R = nBu
c. R = Me
28
29 a: R = H
b: R = C—nBu
30: R = Me
31: R—R = CH_2—CH_2
32

excess allyl bromide produced the fully assembled intermediate **26** in 60% yield. Parallel with this success, a still more efficient process was worked out based on acylate–nickel complexes as carbonyl anion equivalents.

The acylate–nickel complexes **27** are prepared from an organolithium reagent and nickel tetracarbonyl at low temperature but are not easily isolated and are easily decomposed by heat (25 °C) and oxygen.[6] Reaction with simple enones is selective for 1,4-addition; proton quench gives a 1,4-diketone product.[6] Cyclic enones give only moderate yields in the few reported examples; no quinone or quinone ketal examples have been reported nor any attempt to trap the presumed enolate anion intermediate with electrophiles other than protons. The acylate–nickel complex **27a** from *n*-propyllithium reacted with **11** (−50 °C, 1.5 h) to give only the product from reductive cleavage, **14** (67% yield). However, reaction of **27a** with the unsubstituted quinone ketal **10a** (−50 °C) followed by protonation gave the acylated product **28** in 91% yield. The efficiency and simplicity of this *direct* nucleophilic acylation led us to study the process in related systems.

A limited survey was carried out on reactions of the acylate–nickel complex **27b** from *n*-butyllithium, with **9** and **10** as substrates, and final quenching with aqueous ammonium chloride. Addition of **27b** to benzoquinone dimethyl monoketal (**9a**) led to a fast reaction at −50 °C and produced the reductive-cleavage product (hydroquinone monomethyl ether) in 94% yield. The ethylene ketal analogue **9b** was equally unsuccessful, giving a mixture of ketal cleavage products **29a** and **29b**. In the naphthalene series, reductive cleavage is much less favorable; the dimethyl ketal **10a** gives only 1,4-addition (**30**, 91%) while the ethylene ketal **10b** at −50 °C gives both addition (**31**, 67%) and cleavage (**32**, 12% yield; identified tentatively by spectroscopic data on the diacetate). At −78 °C, the yield from **10b** is a bit higher but the ratio is the same (83:17). Trapping experiments with carbon electrophiles involved the intermediate enolate **33** (not isolated) from addition of anion **27b** to quinone ketal **10a**. Acylate anion **27b** was prepared at −50 °C in THF (10-fold molar excess) and a solution of **10a** was slowly added at −50 °C. After the mixture had been stirred at −78 °C for a few minutes allyl iodide (50 mol equiv) and HMPA (50 mol equiv) were added. The mixture was warmed slowly to 21 °C, and adduct **34** was isolated in 85% yield (single



33
34: R = allyl
35: R = Me
37: R = nPr
36
38a: R = H
b: R = Pr
39
40
41
42
43

isomer; assigned as trans on the basis of related alkylations of cyclohexanone enolates[22]). An identical reaction but using methyl iodide produced the parallel product **35** in 43% yield, but it was accompanied by a second product (22% yield) tentatively assigned structure **36** on the basis of spectral data. A similar reaction with *n*-propyl iodide as the trapping agent was still more complicated. In addition to the expected adduct (**37**; 21% yield) and the simple adduct from proton quenching (**30**; 22%), products

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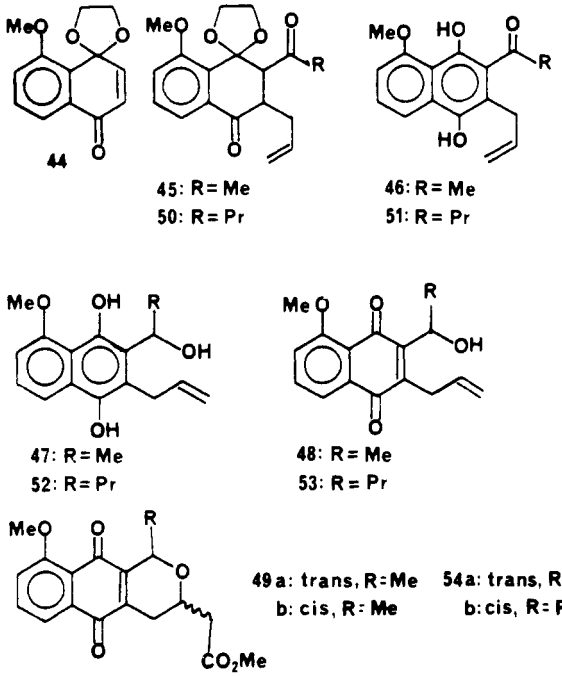
(38a, 10% tentatively identified by ^{1}H NMR spectral analysis; 39, 8%) from O-alkylation of the enolate appeared, as well as the product from dialkylation (38b; 34%). Clearly, with relatively slow alkylation, additional processes can become important including proton transfer to generate the enolate anion of 37. With *n*-propyl bromide, the only products were 39 (75%) and 40 (13%), from methyl alcohol elimination and O-alkylation of the phenol.

Quenching of the intermediate enolate 33 with carbonyl group electrophiles was also only partially successful. For example, reaction with acetaldehyde gave two major adducts 41 (40%) and 42 (31%), in addition to the product (30, 7%) from simple protonation. Both adducts obviously derive from the expected first product 43, suggesting an efficient trapping procedure. Unfortunately, both acetyl chloride and ethyl acetate gave exclusively the product (30) from simple proton transfer.

Nanaomycin A (2) and Deoxyfrenolicin (3). (a) Formal Synthesis of Nanaomycin A (2). As before, reaction of methyllithium with nickel tetracarbonyl at −50 °C in ether gave acylate anion 27c. Addition of quinone ketal 44[23] followed by excess allyl iodide (HMPA added)



led to the adduct 45 which was isolated by flash chromatography, 54% yield, mp 126–127 °C. The ketal unit was hydrolyzed under argon with a mixture of 6 M hydrochloric acid and dioxane, to produce the hydroquinone 46 (100%). The ketone unit was reduced with sodium borohydride to give the triol 47, mp 139.5–142 °C, in 95% yield. Then reoxidation with DDQ (0 °C, 1 h) lead to the key intermediate 48, 66% yield after chromatographic purification. Treatment of 48 with 0.1 mol equiv of palladium dichloride, excess cupric chloride, and carbon monoxide at 1.1 atm in methyl alcohol led directly to the pyran ester isomer 49a and 49b in the ratio 3:2, 66% yield together. Recrystallization gave a pure sample of the major isomer (trans), with mp 144.5–145 °C. Previous work[3a,e] had demonstrated the equilibration of 49a and 49b and the deprotection of the phenol and carboxylic acid to produce (+)-nanaomycin A (2).

(b) Deoxyfrenolicin (3). In a parallel set of experiments, adduct 50 was prepared in 82% yield from addition of acylate anion 27a to 44, with trapping by allyl iodide. The diketo ketal 50 was converted to keto hydroquinone 51 by acid hydrolysis under argon (97% yield), and sodium borohydride reduction produced the triol 52 (98% yield). Oxidation of the hydroquinone with DDQ gave the key intermediate 53 (45%) and palladium-promoted cyclization as before gave the pyrano ester 54 (3:1 trans:cis, 70%). In the presence of BBr_3 at 0 °C, the cis/trans mixture was converted nearly quantitatively to the trans isomer; the phenol ether was cleaved,[5b] and finally the methyl ester was hydrolyzed to produce (±)-deoxyfrenolicin (3).[5b]

Summary. The conjugate addition of acylate–nickel complexes to 2,3-unsubstituted naphthoquinone monoketals is particularly efficient. Benzoquinone monoketals and a 3-substituted naphthoquinone monoketal are not effective substrates due to preferential reductive cleavage of a ketal alkoxy group, presumably via electron transfer. Successful conjugate addition produces an enolate anion which can be trapped with allyl iodide, methyl iodide, and acetaldehyde. Simple alkyl halides, esters, and acyl halides are not efficient trapping agents. Combined with the palladium-promoted alkoxy carbonylation procedure for pyran ring synthesis, the acylate–nickel conjugate addition reaction provides a particularly simple approach to the isochroman naphthoquinone antibiotics.

Experimental Section

Spectra. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded with a Perkin-Elmer R 24B spectrometer operating at 60 MHz or a JEOL FX-90Q Fourier transform spectrometer operating at 90 MHz. Peak positions are reported in parts per million relative to tetramethylsilane internal standard. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded with a JEOL FX-90Q Fourier transform spectrometer operating at 22.5 MHz. Peak positions are reported in parts per million relative to deuteriochloroform (δ 77.00). Spectra which were recorded with off-resonance decoupling have peaks reported as singlet (s), doublet (d), triplet (t), or quartet (q). Infrared (IR) spectra were recorded on a Perkin-Elmer Model 299 spectrometer. Peak intensities were recorded as strong (s), medium (m), or weak (w). The 1606-cm^{-1} signal of polystyrene was used for calibration. Mass spectra were recorded on an AEI MS-902 instrument or a Hewlett-Packard 5487 GC-MS with electron-impact ionization.

Chromatography. Medium-pressure liquid chromatography (MPLC) was done by using Lobar prepacked silica gel columns at pressures up to 50 psi applied by a Fluid Metering Inc. Model RP lab pump. UV-active fractions were detected with an ISCO Model UA-5 Absorbance monitor. Column chromatography was done with E. Merck silica gel 60 (0.040–0.063 mm). Analytical thin-layer chromatography (TLC) was done with E. Merck Reagents silica gel 60 F-254 aluminum-backed plates with a 0.2-mm thickness. Developed plates were visualized under UV light and by charring with 25% aqueous sulfuric acid.

Reagents and Solvents. Diethyl ether (ether), tetrahydrofuran (THF), and *p*-dioxane were distilled under argon from benzophenone ketyl immediately before use. Benzene, chlorotrimethylsilane, dimethylformamide, hexamethylphosphoramide (HMPA), and diisopropylamine were distilled from calcium hydride (under reduced pressure as necessary) and stored under argon. *tert*-Butyl alcohol was distilled from calcium oxide, under argon. Dichloromethane was distilled from phosphorus pentoxide, under argon. Methanol was distilled from magnetsium under argon. Commercial cuprous iodide (Alfa) was further purified according to a literature procedure.[24] Anhydrous cupric chloride was heated at 100 °C under vacuum (0.01 mm) for 15 h and then stored under argon. Triethylamine was filtered through a short plug of alumina immediately before use. *n*-Butyllithium and methyllithium were used as solutions in hexane and their concentrations were determined by using a literature procedure.[25]

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(25) Kofron, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1879.

General Information. The term "concentration" refers to removal of solvent at water aspirator pressure with a Büchi Rotovapor-R. The term "under argon" implies that the apparatus was evacuated (aspirator or oil pump) and then filled with argon 3 times. Melting points and boiling points were uncorrected. Elemental analyses were carried out by Scandinavian Microanalytical Labs, Herlev, Denmark. Lithium diisopropylamide prepared by treating a solution of the amine (1.1 mol equiv) in THF or ether at −78 °C, under argon, with *n*-butyllithium (1.0 mol equiv). The solution was warmed to 0 °C for 15 min and then cooled to −78 °C.

Reaction of 2-Lithio-2-*n*-propyl-1,3-dithiane (6a) with 1,1,5-Trimethoxy-2-allyl-4-oxo-1,4-dihydronaphthalene (11). A solution of the carbanion was prepared by addition of 0.20 mmol of 2-*n*-propyl-1,3-dithiane in 0.5 mL of THF at −78 °C followed by warming to −20 °C for 1 h.[10] Hexamethylphosphoramide (0.36 mmol) was added to the solution at −78 °C, and, after the mixture became homogeneous, a solution of 50 mg (0.18 mmol) of **11** in 0.3 mL of THF was added. After 10 min, the reaction mixure was quenched with aqueous ammonium chloride and allowed to warm to 25 °C. The organic layer was washed sequentially with 1% aqueous sulfuric acid, water, and saturated aqueous sodium chloride before drying ($MgSO_4$). Analytical TLC indicated that starting material was gone and that two products had formed. These were separated by preparative TLC with a 1:1:4 mixture of ether, dichloromethane, and hexane as eluent. The first product to be eluted (14 mg, R_f 0.32) showed no aryl proton signals in the ^1H NMR spectrum, and appears to be a byproduct derived from *n*-propyl-1,3-dithiane. The second component (20 mg, 46% yield, R_f 0.20) was identified as naphthol **14**: ^1H NMR ($CDCl_3$) δ 2.50 (br d, 2 H), 3.87 (s, 3 H), 3.92 (s, 3 H), 4.9–5.4 (m, 2 H), 5.7–6.2 (m, 1 H), 6.55 (s, 1 H), 6.75 (d, 1 H, J = 8.0 Hz), 7.27 (t, 1 H, J = 8.0 Hz), 7.60 (d, 1 H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$) 35.4, 56.4, 57.6, 106.3, 110.2, 114.2, 116.6, 117.5, 119.1, 125.9, 125.5, 135.9, 143.3, 150.8, 156.4; IR ($CHCl_3$) 3520 (w), 2930 (w), 1623 (w), 1598 (s), 1582 (s), 1380 (s), 1275 (s), 1060 (s) cm^{-1}; mass spectrum, m/e 244 (M^+, 100), 229 (12), 188 (9), 187 (8), 135 (9), 128 (9), 115 (11).

Attempted Conjugate Acylation of 11 Using Stetter's Reaction with Thiazolium Salt 15. A solution of 14.4 mg (0.053 mmol) of naphthoquinone monoketal **11**, *n*-butyraldehyde (0.050 mL), triethylamine (0.020 mL), and thiazolium salt **15** (4.0 mg) in methyl alcohol (1.0 ml) was prepared under argon by careful freeze–pump–thaw cycles. The mixture was heated in a sealed tube at 100 °C for 6 days. Analytical TLC indicated complete conversion of **11** and one predominant product (ether on silica gel; R_f 0.47). The solution was diluted to 25 mL with ether and washed sequentially with 1 N sulfuric acid, water, and brine. The ether solution was dried ($MgSO_4$) and concentrated to give 16.6 mg of an amber oil. Chromatography on 0.5 g of silica gel provided pure dimethoxynaphthol **14** (^1H NMR, IR, TLC; 90% yield).

Attempted Conjugate Addition of Cyanohydrin Acetal Anion 7 with Naphthoquinone Monoketal 11. The ethoxyethyl ether of the cyanohydrin of butyraldehyde (32 mg, 0.189 mmol)[11a] was added to a solution of lithium diisopropylamide at 25 °C and stirred for 0.5 h. The resulting solution of **7** was added to a solution of **11** (47 mg, 0.172 mmol) in ether (2 mL) at −78 °C. The mixture was warmed to 25 °C and a second equivalent of **7** was added, because analytical TLC indicated no reaction. Upon addition of HMPA (0.8 mL), the mixture became dark and reaction was complete after 1 h at 25 °C. The mixture was concentrated and then stirred in THF with 6 M aqueous HCl at 25 °C for 1 h. The solution was diluted with ether and shaken with 15% aqueous sodium hydroxide for 5 min. The ether solution was washed with brine, dried ($MgSO_4$), and concentrated to leave a residue which was purified by preparative TLC (silica gel, eluting with 1:1:1 ether/dichloromethane/hexane) to provide the cyanide addition product **16** (20 mg, 43%). The compound was prepared more efficiently by direct reaction with KCN and is fully characterized below.

Preparation of 2-Allyl-3-cyano-1-hydroxy-4,5-dimethoxynaphthalene (16). A solution of 117 mg (0.427 mmol) of **11** and 34 mg (0.513 mmol) of potassium cyanide in 2 mL of methanol was heated at reflux under argon for 24 h. After it was diluted with ether, the reaction mixture was washed sequentially with 1% aqueous sulfuric acid and saturated aqueous sodium chloride before drying. Concentration by rotary evaporation gave a residue which was chromatographed on silica gel with a mixture of ether/dichloromethane/hexane as eluent. The major band (R_f 0.34 with 1:1:1 solvent mixture) was collected to give 85 mg (74%) of **16** as a tan amorphous solid. ^1H NMR ($CDCl_3$) δ 3.73 (br, d, 2 H, J = 5.9 Hz), 3.98 (s, 3 H), 4.01 (s, 3 H), 5.0–6.2 (m, 3 H), 5.95 (br s, 1 H), 6.91 (br d, 1 H, J = 8.4 Hz), 7.49 (t, 1 H, J = 8.4 Hz), 7.79 (br d, 1 H, J = 8.4 Hz); IR ($CHCl_3$) 3100–3600 (m), 2935 (m), 2230 (m), 1655 (m), 1580 (s), 1390 (s), 1290 (s), 1265 (s), 1070 (s), 1027 (s) cm^{-1}; mass spectral mol wt 257.

Preparation of 2-Allyl-3-cyano-1,4,5-trimethoxynaphthalene (17). To a solution of 392 mg of **16** (1.46 mmol) in 3 mL of THF was added 60 mg of sodium hydride (2.5 mmol) and 680 mg of dimethyl sulfate (5.4 mmol). After it was stirred for 30 min, the reaction mixture was diluted with there, washed with water, and stirred with saturated aqueous sodium carbonate for 1 h before being dried over potassium carbonate. Chromatography (silica; 1:1:4 mixture of ether/dichloromethane/hexane as eluent) gave 381 mg (92%) of a colorless solid (mp 95–96.5 °C, R_f 0.26) which was identified as **17** on the basis of the following spectral data: ^1H NMR ($CDCl_3$) δ 3.70 (br d, 2 H, J = 6.2 Hz), 3.88 (s, 3 H), 4.01 (s, 3 H), 4.02 (s, 3 H), 4.9–6.3 (m, 3 H), 6.93 (dd, 1 H, J = 1.7, 7.2 Hz), 7.4–7.8 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 32.5, 56.2, 58.4, 62.2, 63.2, 105.5, 106.9, 114.8, 115.7, 116.5, 119.4, 128.9, 129.7, 133.5, 134.9, 150.1, 156.7, 158.8; IR ($CHCl_3$) 2925 (w), 2225 (w), 1613 (w), 1572 (m), 1370 (s), 1267 (m), 1065 (s), 1040 (s) cm^{-1}; mass spectrum, m/e 283 (M^+, 100), 268 (37), 253 (14), 237 (18), 236 (17), 225 (12), 193 (8), 167 (19), 149 (37).

Reaction of 17 with *n*-Propyllithium. A solution of 41 mg (0.145 mmol) of **17** in 3 mL of ether was treated with 0.146 mmol of *n*-propyl lithium[26] (0.87 mL of a 0.15 M solution in ether) at 25 °C. Analytical TLC indicated the immediate disappearance of starting material and the formation of one major product. The reaction mixture was hydrolyzed with 15% aqueous hydrochloric acid, washed sequentially with water and saturated aqueous sodium chloride, and dried ($MgSO_4$). Concentration gave a residue which was chromatographed (silica gel; 1:1:4 mixture of ether/dichloromethane/hexane as eluent). Collection of the band at R_f 0.32 gave 21 mg (49%) of an oil which was identified as 2-allyl-3-cyano-1,5-dimethoxy-4-*n*-propylnaphthalene (**18**) on the basis of the following spectral data: ^1H NMR ($CDCl_3$) δ 0.7–1.9 (m, 5 H), 3.53 (t, 2 H), 3.76 (d, 2 H), 3.88 (s, 3 H), 3.98 (s, 3 H), 4.9–6.3 (m, 3 H), 6.94 (d, 1 H), 7.53 (t, 1 H), 7.74 (d, 1 H); IR ($CHCl_3$) 2950 (m), 2210 (w), 1610 (w), 1560 (m), 1455 (m), 1370 (s), 1260 (s), 1060 (s) cm^{-1}; mass spectrum, m/e 295 (M^+), 85.7, 280 (6), 267 (64), 251 (100); mass spectral mol wt calcd for $C_{19}H_{21}O_2N$ m/e 295.1572, found 295.1570. The same reaction was carried out with *n*-propylmagnesium bromide (THF, 55 °C, 0.5 h). The reaction was quenched with saturated aqueous ammonium chloride and dried over potassium carbonate. The major product was again **18** (77% yield).

Conjugate Addition of Lithionitromethane to Quinone–Ketal 11. A solution of nitromethane (0.030 mL, 0.55 mmol) in 1 mL of THF was prepared under argon and treated, with stirring, with 0.17 mL (0.36 mmol) of a solution of *n*-butyllithium (2.1 M) in hexane. The resulting white gel was diluted with 2 mL of HMPA to give a colorless solution, which was treated with a solution of 49.0 (0.18 mmol) of naphthoquinone **11** in 2 mL of THF. The opaque, red-black reaction mixture was stirred at 25 °C for 3 h until complete conversion was indicated by analytical TLC. [Et_2O; R_f product ≅0.49 (elongated spot, two isomers).] The reaction mixture was acidified with 0.03 mL of glacial acetic acid, swirled for a few minutes, and then partitioned between 50 mL of ether and 10 mL of half-saturated aqueous lithium chloride. The organic layer was washed successively with 3-mL portions of saturated aqueous lithium chloride (3×), water (3×), and brine. Drying ($MgSO_4$), filtration, and concentration gave an amber oil (70 mg) which was dissolved in benzene and filtered through 500 mg of silica. Elution with 7:5 petroleum ether/ether gave adduct **19** as a pale yellow oil, about a 3:2 mixture of isomers by NMR spectral analysis (signals for -OMe at δ 2.89, 2.85). This sample was used directly below. ^1H NMR ($CDCl_3$) δ 7.8–7.6 (m, 1 H), 7.41 (br, t, 1 H, J = 8.0 Hz), 7.2–7.0 (m, 1 H), 6.1–5.5 (m, 1 H), 5.2–4.95 (m, 2 H), 4.8–3.9 (m, 2 H), 2.89 and 2.85 (two s, 3 H total,

(26) Jones, R. G.; Gilman, H. *Org. React.* **1959**, *6*, 352.

OCH_3), 3.8–2.7 (m) overlapping 3.40 (s), 3.31 (s), 3.27 (s), 3.17 (s) (total area 3.8–2.7 is 9 H), 2.2–1.9 (m, 1 H); IR (neat), 3090 (w), 2960 (m), 2855 (m), 1695 (s), 1645 (w), 1596 (s), 1555 (vs), 1475 (s), 1445 (m), 1280 (vs) cm^{-1}; mass spectral mol wt 335. Note that the isomeric composition of the product varied from run to run and varied with the counterion. Careful analytical TLC showed marginal separation of the isomers (ΔR_f 0.05), and in one run a small amount of each was obtained pure by flash chromatography. Infrared and mass spectral data of the pure isomers were identical with each other and with those of the mixture.

Conversion of Nitro Ketal 19 into 2-Allyl-3-(nitromethyl)-1,4,5-trimethoxynaphthalene (20). (a) Preparation of 2-Allyl-3-(nitromethyl)-1-hydroxy-4,5-dimethoxynaphthalene. A side-armed flask fitted with an oven-dried condenser and a stir bar was charged with 16 mg of magnesium powder (0.66 mmol) and 109 mg (0.30 mmol) of mercuric bromide under argon. A mixture of benzene (1 mL) and ether (3 mL) was added, the vessel was stoppered, and the suspension was heated at 45 °C for 1 h. In a separate vessel, a solution of 19.1 mg (0.057 mmol) of nitro ketal **19** in benzene (1 mL) was prepared under argon. The solution of magnesium bromide etherate was allowed to cool and settle, and the supernatant liquid was withdrawn via syringe and added rapidly to the stirred solution of the nitro ketal **19**. After addition, the pale amber reaction mixture was stirred for 2.5 h. Analytical TLC of the reaction mixture was ambiguous as the product was later shown to have the same R_f as the slower reacting of the nitro ketal isomers. Following the reaction period, the solution was diluted to a volume of 30 mL with ether and washed with two 3-mL portions of water and one 3-mL portion of brine. Drying ($MgSO_4$), filtration, and concentration of the solution provided the naphthol as an amber, partially crystalline oil (15.0 mg, 87% yield). The product contained traces of solvent and starting material and was used directly owing to its oxidative lability.

(b) Methylation To Give 20. A round-bottomed flask charged with the crude naphthol and potassium carbonate (15 mg, 0.11 mmol) under argon was fitted with a reflux condenser and a stir bar. A solution of methyl iodide (0.10 mL) in 2 mL of degassed acetone was introduced and the resulting pale yellow reaction mixture was heated under argon at 50 °C for 1 day. A second portion of methyl iodide (0.10 mL) was introduced and heating was continued for an additional 1 day. Analytical TLC (2:1 petroleum ether–ether) showed partial conversion of the naphthol (R_f 0.33) to the trimethoxynaphthalene **20** (R_f 0.42). On other runs, it was found that neither higher temperatures nor longer reaction times improved the yield of **20**.

The reaction mixture was acidified with 10 drops of glacial acetic acid, then diluted to 40 mL with ether, and washed with brine (3×). Drying ($MgSO_4$), filtration, and concentration gave the crude product (10 mg) as an amber oil that was directly chromatographed on 500 mg of silica gel. Elution with 2:1 petroleum ether–ether separated 7.3 mg (36%) of product **20** from 3.5 mg (18%) of starting naphthol. **20**: ^1H NMR (CCl_4) δ 7.68 (d, 1 H, J = 8.5 Hz), 7.40 (t, 1 H, J = 8.5 Hz), 6.84 (d, 1 H, J = 8.5 Hz), 6.2–5.75 (m, 1 H), 5.69 (s, 2 H), 5.1–4.8 (m, CH=CH_2, 2 H), 4.01 (s, 3 H), 3.89 (s, 3 H), 3.81 (s, 3 H), 3.63 (dt, 2 H, J = 5.5, 1.0 Hz, CH_2CH=); IR (neat) 3080 (w), 3010 (w), 2945 (m), 3850 (m), 1640 (w), 1620 (w), 1595 (m), 1580 (s), 1555 (vs), 1380 (vs), 1345 (s), 1210 (s), 1065 (s) cm^{-1}; mass spectral mol wt 317.

Conjugate Addition of 1-Potassio-1-nitroethane to Quinone Ketal 11. The reaction vessel was charged with a stir bar and potassium hydride (253 mg of a 24.9% dispersion in oil, 1.6 mmol) under argon. The hydride was washed with dry pentane (2 mL), then suspended in HMPA (2 mL), and treated with nitrobenzene (0.13 mL, 1.8 mmol). The mixture was stirred until gas evolution ceased (ca. 5 min) and the formation of the white precipitate of 1-potassio-1-nitroethane was complete. A solution of naphthoquinone monoketal **11** (91 mg, 0.33 mmol) in 0.5 mL of THF and 1 mL of HMPA was added to give an orange-red suspension and then stirred at 23 °C for 5 days. The reaction mixture was treated with about 0.15 mL of acetic acid, stirred at 15 °C for 5 min, and partitioned between 10 mL of half-saturated aqueous lithium chloride and 75 mL of ether. The aqueous layer was further extracted with 10 mL of ether and the combined organic layers were washed successively with 6-mL portions of saturated aqueous lithium chloride (4×), water (2×), and brine. The solution was dried ($MgSO_4$), filtered, and concentrated to give a dark brown oil. Flash chromatography on silica gel, 5 g, eluting with 60 mL of 7:5 petroleum ether–ether provided **22** (98.3 mg, 85%), as a pale yellow oil, a mixture of all four diastereoisomers. ^1H NMR (CCl_4) δ 7.73 (m, 1 H), 7.6–7.33 (m, 1 H), 7.25–7.05 (m, 1 H), 6.0–5.4 (m, 1 H), 5.3–4.9 (m, 2 H), 4.8–4.2 (m, 1 H), 3.88 (s, 3 H), 3.50–1.80 (series of eight s overlapping other m, total 10 H), 1.40 (br d, 3 H, J = 7.5 Hz); IR (neat) 3080 (w), 2950 (s), 2840 (m) 1690 (d, vs), 1640 (w), 1590 (vs), 1555 (vs), 1470 (vs), 1270 (vs), 1060 (s) cm^{-1}; mass spectral mol wt 349. The four adduct isomers were marginally separable by careful TLC (2:1 ether–petroleum ether; R_f values of 0.45, 0.41, 0.37, and 0.34). In one run, the less polar pair was separated from the more polar pair. Mass spectral and IR analysis of the two mixtures were identical with each other and with that of the mixture.

Conversion of Quinone Ketal 22 into 2-Allyl-3-(1-nitroethyl)-1,4,5-trimethoxynaphthalene (23). (a) Preparation of 2-Allyl-3-(1-nitroethyl)-1-hydroxy-4,5-dimethoxynaphthalene. A solution of dry *p*-toluenesulfonic acid was prepared by slowly distilling benzene–water azeotrope (5 mL) from a solution of *p*-toluenesulfonic acid monohydrate (6.2 mg) and benzene (15 mL). After the mixture had been cooled at 25 °C, a solution of **22** (98.3 mg) in 5 mL of dry benzene was introduced and 6 mL of benzene was slowly distilled over 15 min. The yellow mixture was cooled, treated with a few drops of saturated aqueous sodium bicarbonate, and then diluted to 40 mL with degassed ether. The solution was washed twice with 5-mL portions of degassed brine, dried ($MgSO_4$), filtered, and concentrated. The amber oil obtained was used directly.

(b) Methylation To Give 23. Exactly as above for **19**, the crude naphthol was converted nearly completely to **23**. Flash chromatography of 5 g of silica gel (3:2 petroleum ether–ether) gave a yellow viscous oil, 68.6 mg (75% from **22**). ^1H NMR (CCl_4) δ 7.61 (dd, 1 H, J = 7.1, 1 Hz), 7.30 (t, 1 H, J = 8.0 Hz), 6.75 (dd, 1 H, J = 7.1, 1 Hz), 6.2–5.8 (m, 1 H), 5.53 (q, 1 H, J = 6.5 Hz), 5.2–4.0 (m, 2 H, CH=CH_2), 3.94 and 3.84 (two s, 3 H together), 3.60 (s) overlapping 3.7 (m) with area 5 H total, 1.89 (d, 3 H, J = 6.5 Hz); IR (neat) 3090 (w), 2950 (s), 2850 (m), 1645 (w), 1620 (m), 1595 (m), 1580 (vs), 1505 (w), 1460 (s), 1380 (vs), 1070 (vs) cm^{-1}; mass spectra mol wt 331.1419, calcd 331.1419.

Reaction of Spiro[1,3-dioxolane-2,1′-8′-methoxy-4′(1′*H*)-naphthalenone)] (44) with 2-Lithio-2-*n*-propyl-1,3-dithiane (6a) (Proton Quench). *n*-Butyllithium (0.170 mL of a 2.36 M solution in hexane, 0.40 mmol) was added dropwise under argon at −20 °C to a solution of 2-*n*-propyl-1,3-dithiane[27] (65 mg, 0.40 mmol) in 5 mL of dry THF. After it was stirred at −20 °C for 1 h, the reaction mixture was cooled to −78 °C; HMPA (143 mg, 0.139 mL, 0.80 mmol) was added followed by a solution of monoketal **44** (80 mg, 0.37 mmol) in 2 mL of dry THF. After the mixture was stirred at −78 °C for 5 min, aqueous ammonium chloride solution 2 mL) was added, and the reaction mixture was warmed to 23 °C. The reaction mixture was diluted with ether, washed once with water and once with saturated brine, dried ($MgSO_4$), and concentrated to afford 138 mg of an oil. Preparative TLC (2:3 ether/hexane) gave 40 mg (86%) of spiro[1,3-dioxolane-2,1′-(8′-methoxy-2′-[2-(2-*n*-propyl-1,3-dithianyl)]-2′,3′-dihydro-4′(1′*H*)-naphthalenone)] (**25**); R_f 0.3; ^1H NMR ($CDCl_3$) δ 0.99 (t, 3 H, J = 7 Hz, $CH_2CH_2CH_3$), 1.30–2.97 (m, 13 H, (CH_2)$_2$CH_3, S(CH_2)$_3$S, O=CCH_2CH), 3.89 (s, 3 H, OCH_3), 4.20 (s, 4 H, OCH_2CH_2O), 7.03–7.62 (m, 3 H, Ar); IR ($CHCl_3$) 2960, 2900, 1680 (s, C=O), 1590 (m), 1581 (m), 1470 (m), 1294 (s), 1270 (s) cm^{-1}; mass spectral mol wt 394.

Spiro[1,3-dioxolane-2,1′-(8′-methoxy-3′-allyl-2′-2-(2-*n*-propyl-1,3-dithianyl)]-2′,3′-dihydro-4′(1′*H*)-naphthalenone)] (26). *n*-Butyllithium (0.137 mL of a 2.56 M solution in hexane, 0.35 mmol) was added dropwise under argon at −25 °C to a solution of 2-*n*-propyl-1,3-dithiane (60 mg, 0.37 mmol) in 5 mL of dry THF. After it was stirred at −25 °C for 5 h, the solution was cooled to −78 °C, HMPA (0.129 mL, 132, mg, 0.74 mmol) was added followed by a solution of monoketal **44** (80 mg, 0.34 mmol) in 2 mL of dry THF. After the mixture had been stirred at −78 °C for 5 min, allyl bromide (0.161 mL, 224 mg, 1.85 mmol) was added, and the reaction mixture was allowed to warm to 23 °C.

(27) Corey, E. J.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 1075.

After 30 min at 23 °C, the mixture was diluted with 100 mL of ether, washed twice with water and once with saturated brine, dried ($MgSO_4$), and concentrated to afford 190 mg of crude product. Preparative TLC (1:1 ether/hexane) gave a major band with R_f 0.40 (89 mg, 60%) of spiro[1,3-dioxolane-2,1'-(8'-methoxy-3'-allyl-2'-[2-(2-*n*-propyl-1,3-dithianyl)]-2',3'-dihydro-4'-(1'*H*)-naphthalenone)] (**26**) as a crystalline solid: ^{1}H NMR ($CDCl_3$) δ 0.84 (t, 3 H, J = 7.5 Hz, $(CH_2)_2CH_2)_2CH_3$), 1.19–2.92 (m, 14 H, $(CH_2)_2CH_3$, $S(CH_2)_3S$, O=C-$CHCH$, $CH_2CH{=}CH_2$), 3.86 (s, 3 H, OCH_3), 4.09 (m, 4 H, OCH_2CH_2O), 4.95–5.14 (m, 2 H, $CH_2CH{=}CH_2$), 5.88 (m, 1 H, $CH_2CH{=}CH_2$), 6.97–7.60 (m, 3 H, Ar); IR ($CHCl_3$) 2945 (m), 1675 (s, C=O), 1580 (s), 1463 (m), 1309 (m), 1259 (vs, C—O), 885 (s, C=C) cm^{-1}; mass spectral mol wt 434.

General Procedure for Reaction of Acylate–Nickel Complex 27b with Quinone Monoketals 9 and 11. To 12 mL of dry THF in a 100-mL flask under argon was added all at once nickel tetracarbonyl[28] (1.30 mL, 10.0 mmol) at −50 °C. With vigorous stirring, *n*-butyllithium (5.10 mL of a 2.0 M solution in *n*-hexane, 10.0 mmol) was added over 10 min. The mixture was stirred for 1.5 h at −50 °C to give a dark red-brown solution. Naphthoquinone monoketal (**9a**, **9b**, **10a**, or **10b**; typically 1.00 mmol) was added dropwise with a syringe pump over 4.5 h. The mixture was stirred for 4.5 h at −50 °C and then cooled to −78 °C. HMPA (9 mL, 51.7 mmol) was added all at once into the mixture followed by the quenching agent (excess 10% aqueous ammonium chloride, methyl iodide, allyl iodide, *n*-propyl iodide, *n*-propyl bromide; typically 50 mmol of the halides). After addition, the mixture was allowed to warm gradually to 25 °C and then stirred for 15 h. The excess nickel carbonyl was decomposed by careful addition of iodine in ether until the brown iodine color persisted. The mixture was partitioned between ether and aqueous ammonium chloride, and the ether layer was washed with saturated sodium chloride solution containing sodium sulfite until it was colorless, then dried ($MgSO_4$), filtered, and concentrated to leave an orange liquid. The moderately volatile components (HMPA and byproducts derived from excess acylate nickel complex) were removed by short-path distillation (66–70 °C air bath, 0.004 mmHg), and the residual oil was chromatographed on silica gel (15 g; eluent was *n*-hexane/benzene) to afford the addition product or reduction product.

(a) With **9a** and proton quench, the only product detected was hydroquinone monomethyl ether, 113 mg, 94% yield.

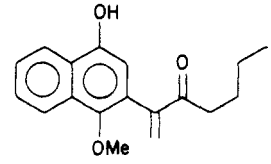
(b) With **9b** and proton quench (0.66-mmol scale), chromatography gave the products of reductive cleavage, **29b** (61 mg, 40%) and **29a** (44 mg, 43%). **29a**: ^{1}H NMR (acetone-d_6) δ 3.90 (m, 4 H), 6.76 (s, 4 H); IR (Nujol) 3460, 3250, 1603, 1500, 1220, 1037, 830 cm^{-1}; mass spectral mol wt 154.0629, calcd for $C_8H_{10}O_3$ 154.0631; mp 93–95 °C (CCl_4). **29b**: colorless oil; ^{1}H NMR ($CDCl_3$) δ 0.91 (br t, 3 H, J = 7.0 Hz), 1.1–1.8 (m, 4 H), 2.36 (t, 2 H, J = 7.2 Hz), 4.12 (m, 2 H, $AA'BB'$), 4.40 (m, 2 H, $AA'BB'$), 6.80 (s, 4 H); ^{13}C NMR ($CDCl_3$) δ 13.6, 22.2, 26.9, 33.9, 62.8, 66.9, 116.1, 150.2, 152.6, 174.0; IR (neat) 3400, 1730, 1520 cm^{-1}; mass spectral mol wt 238.1209, calcd for $C_{13}H_{18}O_4$ 238.1206.

(c) With **10a** (0.88 mmol) and proton quench, chromatography produced 232 mg (91%) of **30** as a colorless semisolid. ^{1}H NMR ($CDCl_3$) δ 0.80 (br t, 3 H, J = 7.0 Hz), 0.9–1.6 (m, 4 H), 2.44 (m, 2 H), 2.80 (dd, 1 H, J = 18.0, 2.9 Hz), 2.92 (s, 3 H), 3.04 (dd, 1 H, J = 18.0, 5.4 Hz), 3.83 (dd, 1 H, J = 5.4, 2.9 Hz), 7.38–7.77 (m, 3 H), 8.05 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.67, 22.01, 25.21, 37.73, 42.11, 48.88, 49.48, 52.40, 98.34, 126.35, 126.78, 129.12, 132.2, 132.4, 137.8, 195.53, 208.48; IR (neat) 1715, 1700 cm^{-1}; mass spectral mol wt 290.1509, calcd 290.1519.

(d) With **10b** (0.79 mmol) and proton quench, chromatography produced adduct **31** (colorless oil, 153, mg 67%) and reduction product **32** (19 mg, 12%). Spectral data for **31**: ^{1}H NMR ($CDCl_3$) δ 0.84 (t, 3 H, J = 7.2 Hz), 1.00–1.65 (m, 4 H), 2.28–2.86 (m, 2 H), 2.95 (m, 2 H), 3.57 (t, 1 H, J = 5.1 Hz), 4.0–4.44 (m, 4 H), 7.32–7.70 (m, 1 H), 8.02 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.7, 22.1, 25.4, 38.2, 43.9, 54.8, 65.1, 66.1, 106.4, 124.3, 126.6, 129.3, 132.2, 133.5, 140.2, 193.0, 208.5; IR (neat) 1715 (s), 1700 (m) cm^{-1}; mass spectral mol wt 288.1343, calcd for $C_{17}H_{20}O_4$ 288.1363. The reduction product **32** was converted to the diacetate (acetic anhydride/pyridine) for spectral characterization. ^{1}H NMR ($CDCl_3$) δ 2.11 (s, 3 H), 2.44 (s, 3 H), 4.33 (m, 2 H, $AA'BB'$), 4.60 (m, H, $AA'BB'$), 6.78 (d, 1 H, J = 7.9 Hz), 7.13 (d, 1 H, J = 7.9 Hz), 7.54 (m, 2 H), 7.80 (m, 1 H), 8.28 (m, 1 H); IR ($CHCl_3$) 1740, 1587, 1370 cm^{-1}; mass spectrum (70 eV, EI), m/e 228 (M^+, 11%), 2.39 (4), 160 (6), 149 (10), 111 (15), 97 (25), 87 (100), 85 (28), 83 (29), 71 (41), 70 (24), 69 (35).

(e) With **10a** (1.03 mmol) and quenching with excess allyl iodide, chromatography produced **34** as a colorless oil (288 mg, 85%): ^{1}H NMR ($CDCl_3$) δ 0.84 (br t, 3 H, J = 7 Hz), 1.0–1.6 (m, 4 H), 2.46 (t, 2 H, J = 7.0 Hz), 2.6–3.0 (m, 3 H), 2.91 (s, 3 H), 3.40 (s, 3 H), 3.74 (d, 1 H, J = 3.6 Hz), 5.0–5.3 (m, 5.3 (m, 2 H), 5.8 (m, 1 H), 7.3–7.8 (m, 3 H), 7.96 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.67, 22.1, 25.4, 36.1, 42.2, 46.7, 49.2, 49.4, 55.0, 99.0, 117.7, 125.9, 127.2, 129.1, 132.4, 132.6, 136.2, 138.9, 197.9, 208.5; IR (neat) 1713, 1695, 1608 cm^{-1}; mass spectral mol wt 330.1817, calcd for $C_{20}H_{26}O_4$ 330.1833.

(f) With **10a** (1.03 mmol) and quenching with excess methyl iodide, chromatography produced **35** (colorless oil, 95 mg, 43%) and **36** (colorless oil, 55 mg, 22%). Spectral data for **35**: ^{1}H NMR ($CDCl_3$) δ 0.86 (br t, 3 H, J = 7 Hz), 1.0–1.7 (m, 4 H), 1.36 (d, 3 H, J = 7.2 Hz), 2.51 (t, 2 H, J = 7.2 Hz), 3.03 (br quintet, 1 H, J = 7 Hz), 3.08 (s, 3 H), 3.32 (s, 3 H), 3.47 (d, 1 H, J = 6.3 Hz), 7.4–7.7 (m, 3 H), 8.00 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.8, 17.2, 22.2, 25.5, 41.9, 49.5, 50.1, 60.4, 99.0, 126.1, 127.5, 129.2, 132.4, 138.9, 198.8, 208.6; IR (neat) 2960, 1693, 1240, 1047 cm^{-1}; mass spectral mol wt 304.1646, calcd 304.1676. Byproduct **36** showed the following data: ^{1}H NMR ($CDCl_3$) δ 0.96 (t, 3 H, J = 7.0 Hz), 1.2–1.9 (m, 4 H), 1.32 (s, 3 H), 2.40 (d, 1 H, J = 12.5 Hz), 2.6–2.9 (m, 2 H), 2.74 (d, 1 H, J = 5.4 Hz), 3.00 (s, 3 H), 3.48 (s, 3 H), 3.57 (dd, 1 H, J = 12.5, 5.4 Hz), 7.44 (td, 1 H, J = 7.2, 1.8 Hz), 7.62 (td, 1 H, J = 7.0, 1.8 Hz), 7.78 (m, 1 H), 7.97 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.9 (q), 22.5 (t), 23.53 (q), 26.0 (t), 31.9 (t), 35.5 (t), 48.6 (d), 49.5 (q), 51.8 (q), 78.84 (s), 97.5 (s), 126.4 (d), 127.6 (d), 129.0 (d), 133.1 (d), 140 (s), 197.6 (s), 212.8 (s); IR (neat) 3450, 1712, 1690, 1605 cm^{-1}; mass spectrum (20 eV, EI), m/e 316 (M − 18). Treatment of **36** with *p*-toluenesulfonic acid in ether at 25 °C for 2 h induced elination of water to give a product tentatively identified as i on the basis of spectral data. ^{1}H NMR



i

($CDCl_3$) δ 0.88 (br t, 3 H, J = 6 Hz), 1.1–1.7 (m, 4 H), 2.30 (s, 3 H), 2.60(t, 1 H, J = 7.2 Hz), 4.01 (s, 3 H), 5.75 (d, 1 H, J = 1.8 Hz), 6.25 (d, 1 H, J = 1.8 Hz), 6.65 (s, 1 H), 7.40–7.80 (m, 3 H), 8.28 (m, 1 H); IR ($CHCl_3$) 1773, 1704, 1604, 1378 cm^{-1}; mass spectral mol wt 284.

(g) With **10a** (0.86 mmol) and quenching with *n*-propyl iodide, chromatography produced **37** (colorless oil, 61 mg, 21.4%), **30** (54 mg, 22%), **38a** (26 mg, 10%), **38b** (22 mg, 8%), and **39** (108 mg, 34%). Data for **37**: ^{1}H NMR ($CDCl_3$) δ 0.84 (t, 3 H, J = 7.0 Hz), 0.95 (t, 3 H, J = 7.0 Hz), 1–2 (m, 8 H), 2.42 (t, 2 H, J = 7.2 Hz), 2.78 (m, 1 H), 2.94 (s, 3 H), 3.39 (s, 3 H), 3.60 (d, 1 H, J = 4.1 Hz), 7.4–7.8 (m, 3 H), 7.98 (m, 1 H); IR (CCl_4) 2980, 1710 (sh), 1693 cm^{-1}; mass spectral mol wt 332.1958, calcd for 332.1989. Data for **38b**: ^{1}H NMR ($CDCl_3$) δ 0.66 (br t, 3 H, J = 7 Hz), 0.96 (br t, 3 H, J = 7.0 Hz), 1.08 (br t, 3 H, J = 7.0 Hz), 1–2.2 (m, 10 H), 2.3–2.7 (m, 2 H), 2.85 (s, 3 H), 3.39 (m, 3 H), 3.60 (m, 1 H, ABC_2), 3.68 (s, 1 H), 3.82 (m, 1 H, ABC_2), 7.2–7.6 (m, 3 H), 7.68 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 10.64 (q), 13.62 (q), 14.21 (q), 21.20 (t), 21.96 (t), 23.42 (t), 25.37 (t), 31.06 (t), 37.35 (t), 48.88 (q), 49.10 (q), 61.72 (d), 73.80 (t), 98.18 (s), 122.40 (d), 122.56 (s), 126.68 (d), 12.89 (d), 128.90 (d), 131.99 (s), 133.67 (s), 148.08 (s), 207.72 (s); mass spectral mol wt 374.2428, found 374.2459. Data for **39**: ^{1}H

(28) Nickel carbonyl is toxic and volatile and does not have a strong odor; therefore, it is well-known as a reagent to be used after obtaining full information on its properties. A useful discussion can be found in a brochure from the Matheson Co., entitled "Nickel Carbonyl is Dangerous".

NMR ($CDCl_3$) δ 0.95 (br t, 3 H, J = 7.0 Hz), 1.12 (t, 3 H, J = 7.0 Hz), 1.28–2.05 (m, 6 H), 3.15 (t, 2 H, J = 7.0 Hz), 3.93 (s, 3 H), 4.12 (t, 2 H, J = 7.0 Hz), 6.96 (s, 1 H), 7.58 (m, 2 H, $AA'BB'$), 8.23 (m, 2 H, $AA'BB'$); IR (CCl_4) 2980, 2960, 2900, 1680, 1603, 1373 cm^{-1}; mass spectrum (70 eV) m/e 300 (M^+, 100%), 258 (6.5), 257 (5.0), 243 (40), 201 (55), 186 (16), 173 (7.0), 143 (5.0), 115 (8.0). Data for **38a**: ^1H NMR ($CDCl_3$) δ 0.68 (br t, 3 H, J = 7.0 Hz), 0.8–1915 (m, 8 H), 2.01 (m, 2 H), 2.88 (s, 3 H), 3.38 (s, 3 H), 3.78 (m, 2 H), 3.80 (d, 1 H, J = 7.2 Hz), 4.86 (d, 1 H, J = 7.2 Hz), 7.25–7.80 (m, 4 H).

(h) With **10a** (0.59 mmol) and quenching with *n*-propyl bromide, chromatgraph produced **39** (133 mg, 75%) and **40** (20 mg, 13%). Data for **40**: ^1H NMR ($CDCl_3$) δ 0.96 (br t, 3 H, J = 7.0 Hz), 1.2–1.9 (m, 4 H), 3.18 (t, 2 H, J = 7.2 Hz), 3.96 (s, 3 H), 7.19 (s, 1 H), 7.62 (m, 2 H, $AA'BB'$), 8.20 (m, 2 H, $AA'BB'$); IR (CCl_4) 3420, 2980, 1665, 1605, 1390 cm^{-1}; mass spectral mol wt 258.1243, found 258.1257.

(i) With **10a** (1.00 mmol) quenching with acetaldehyde and chromatography produced **41** (130 mg, 40%) and **42** (105 mg, 31%). Data for **41**: ^1H NMR ($CDCl_3$) δ 0.66 (br t, 3 H, J = 7.0 Hz), 0.8–1.5 (m, 4 H), 1.10 (t, 3 H, J = 7.2 Hz), 1.90 (m, 2 H), 2.30 (m, 2 H), 2.81 (s, 3 H), 3.52 (s, 3 H), 4.55 (d, 1 H, J = 0.9 Hz), 7.20 (td, 1 H, J = 7.6, 0.9), 7.56 (m, 2 H), 7.76 (m, 1 H), 8.10 (m, 1 H); ^{13}C NMR ($CDCl_3$) 12.7, 13.5, 21.8, 25.2, 39.9, 48.8, 49.0, 58.1, 97.2, 106.5, 126.4, 127.9, 129.3, 132.5, 133.0, 139.2, 146.7, 185.1, 205.7; IR (CCl_4) 2980, 1710, 1690, 1610, 1465, 1255, 1060 cm^{-1}; mass spectral mol wt 330.1823, calcd 330.1833. Data for **42**: ^1H NMR (C_6D_6) δ 0.84 (br t, 3 H, J = 7.0 Hz), 1.02 (br t, 3 H, J = 7.0 Hz), J = 7.6, 1.8 Hz), 7.26 (td, 1 H, J = 7.6, 1.8 Hz), 7.78 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 9.0, 14.0, 22.9, 25.6, 28.7, 39.1, 48.9, 49.2, 49.4, 53.5, 80.5, 97.9, 105.1, 125.6, 126.9, 128.4, 132.1, 132.5, 141.3, 198.0; IR (CCl_4) 3620, 3480, 1690, 1610, 1470, 1054 cm^{-1}; mass spectral mol wt 348.1914, calcd 348.1938.

Preparation of Diketo Ketal 45. A solution of 2.1 mL (16 mmol) of nickel tetracarbonyl in 30 mL of ether was stirred under argon at −50 °C as 6.4 mL (13 mmol) of methyllithium–lithium bromide solution, 2.05 M in ether (Aldrich), was added over 5 min. After the dark red solution had been stirred at −50 °C for 1 h, a solution of 756 mg (3.26 mmol) of monoketal **44** in 25 mL of THF was added dropwise over 10 min. The red reaction mixture was further stirred at −50 °C for 1.5 h and then diluted with 10 mL of HMPA. Allyl iodide (3.0 mL, 33.0 mmol) was added rapidly, and then the reaction mixture was warmed slowly to 23 °C and stirred for 14 h. The mixture was concentrated to ca. 20 mL by allowing argon to bubble slowly through at 35 °C for 2 h. The resulting slurry was poured into 300 mL of dilute aqueous ammonium chloride and extracted twice with 50-mL portions of ether and once with 50 mL of 2:1 ether–dichloromethane. The combined extracts were washed with water (4×) and with brine (2×), then dried (Na_2SO_4), filtered, and concentrated in vacuo to give an oily residue still containing HMPA and allyl iodide. Analytical TLC showed three components (ether; R_f 0.29, 0.52, 0.58), the most polar of which was desired diketo ketal **44**. The mixture was flashed chromatographed as a solution in benzene on 40 g of silica. Elution with 5:2 ether–petroleum ether separated **45** from the less polar contaminants, as a pale tan powder (559 mg, 54%). Two recrystallizations of a 30-mg sample (hexane–ethyl acetate, 2:1) gave 20 mg of colorless plates, mp 126–127 °C, showing spectra identical with that of the chromatographed material. ^1H NMR ($CDCl_3$) δ 7.65 (d, 1 H, J = 9.0 Hz), 7.38 (t, 1 H, J = 9.0 Hz), 7.08 (d, 1 H, J = 9.0 Hz), 6.0–5.4 (m, 1 H), 5.0–4.85 (m, 2 H), 4.4–4.0 (m, 4 H), 3.88 (s, 3 H), 3.55 (d, J = 9.0 Hz), overlapping with 3.4–2.25 (m, 4.3 H together), 2.25 (s, 3 H); IR ($CHCl_3$) 3080 (s), 3000 (m), 2900 (m), 2840 (w), 1710 (s), 1690 (s), 1640 (w), 1585 (s), 1470 (s), 1440 (m), 1290 (s) cm^{-1}. Anal. C, H.

Preparation of Keto Hydroquinone 46. A solution of diketo ketal **45** (99.9 mg, 0.32 mmol) in 4 mL of dioxane was prepared under argon, cooled briefly, and stirred as 2 mL of degassed 6 N HCl was added quickly. The reaction mixture was stirred as 23 °C for 3 days, during which time the color changed from pale yellow to cherry red. Analytical TLC showed clean conversion to the hydroquinone **46** (ether; R_f 0.38). The solution was poured into 20 mL of brine and extracted with one 40-mL and one 10-mL portion of 2:1 ether–dichloromethane. The combined extracts were washed twice with brine, then dried (Na_2SO_4), filtered, and concentrated in vacuo. Keto hydroquinone **46** was obtained as a dark, viscous oil, yield 88.3 mg (102%), contaminated with dioxane but otherwise pure by NMR and IR spectral analysis. This sample was used directly. ^1H NMR ($CDCl_3$) δ 9.12 (s, 1 H), 7.70 (d, 1 H, J = 9.0 Hz), 7.27 (t, 1 H, J = 9.0 Hz), 6.71 (d, 1 H, J = 9.0 Hz), 6.2–5.7 (m, 1 H), 5.6–5.3 (br s, 1 H), 5.2–4.95 (2 H, allyl C=CH_2), 4.00 (s, 3 H), 3.43 (dt, 2 H, J = 5.5, 1.5 Hz), 2.59 (3 H, s); IR (neat) 3400 (br, s), 3080 (w), 3020 (w), 2980 (m), 2950 (m), 2860 (w), 1685 (s), 1630 (s), 1610 (s), 1590 (m), 1500 (w), 1450 (s), 1400 (s); mass spectral mol wt 272.1029, calcd 272.1049.

Preparation of Triol 47. To a solution of crude acetylnaphthohydroquinone **46** (88.3 mg, 0.32 mmol) in 5 mL of THF stirring under argon was added all at once 25 mg (0.66 mmol) of solid sodium borohydride. The mixture was stirred at 23 °C for 14 h, then cooled to 0 °C, and quenched by the dropwise addition of 0.3 mL of acetic acid. The resulting mixture was stirred at 0 °C for 15 min, diluted with 1 mL of water, and cautiously saturated with potassium carbonate. The mixture was partitioned between 10 mL of degassed brine and 30 mL of degassed 2:1 ether–dichloromethane. The aqueous layer was further extracted with one 10-mL portion of solvent. The combined organic layers were washed with degassed brine, then dried (Na_2SO_4), filtered, and concentrated in vacuo. Triol **47** (82.0 mg, 95%) was obtained as an amber solid. The solid was swirled with ether to give a white powder (mp 139.2–142 °C), but the crude product was used without further purification. ^1H NMR ($CDCl_3$) δ 9.60 (s, 1 H), 7.73 (d, 1 H, J = 8.0 Hz), 7.28 (t, 1 H, J = 8.0 Hz), 6.78 (d, 1 H, J = 8.0 Hz), 5.75–6.25 (m, 1 H), 5.3–4.95 (m, 4 H), 4.47 (br d, 1 H, J = 11 Hz), 4.05 (s, 3 H), 3.56 (br d, 2 H, J = 5.0 Hz), 1.63 (d, 3 H, J = 6.5 Hz); IR (neat) 3350 (br, s), 3080 (w), 2990 (s), 2920 (m), 1630 (m), 1600 (m) 1580 (m), 1400 (vs), 1260 (vs); mass spectral mol wt 274.1198, calcd 274.1205.

Preparation of Hydroxy Quinone 48. To a solution of triol **47** (487 mg, 1.88 mmol, from 1.71 mmol of **45**) in 10 mL of dry, degassed methanol stirred under argon at 0 °C was added DDQ (403 mg, 1.78 mmol), followed by solid potassium bicarbonate (188 mg, 1.88 mmol). The deep red reaction mixture was stirred at 0 °C for 1 h, then diluted with 20 mL of dichloromethane, and stirred for an additional 5 min. The resulting mixture was filtered through a short column of activity I alumina. Elution with dichloromethane and collection of all colored eluants gave on concentration crude quinone **48** (407 mg). Flash chromatography on 15 g of silica (twice; eluting with 4:1 ether–petroleum ether) gave **48** (321 mg, 69% from **45**) as a dark orange oil. Two recrystallization from ether–petroleum ether gave orange crystals: mp 76–78 °C; ^1H NMR ($CDCl_3$) δ 7.63–7.4 (m, 2 H), 7.13 (dd, 1 H, J = 8.5, 2.5 Hz), 6.0–5.58 (m, 1 H), 5.2–4.65 (m, 3 H), including apparent dq at δ 4.78 (1 H, J = 11, 7 Hz); irradiation at δ 1.50 gives δ 4.8 (d, 1 H, J = 1 Hz), 3.92 (s, 3 H), 3.63 (d, 1 H, J = 11 Hz; collapses to s with irradiation at δ 4.7), 3.36 (dt, 2 H, J = 6, 1.5 Hz), 1.51 (s, 2 H, J = 7.0 Hz); IR ($CHCl_3$) 3500 (br), 3080 (w), 3000 (m), 2930 (s), 2840 (w), 1650 (s), 1630 (s), 1570 (s) cm^{-1}. Anal. C, H.

Cyclization of 48 to the Pyrano Esters 49a and 49b. The reaction vessel was charged with 25.1 mg (0.092 mmol) of 2-allyl-3-[(1-hydroxy)ethyl]-5-methoxy-1,4-naphthoquinone (**48**), 2.2 mg (0.009 mmol) of palladium chloride bis(acetonitrile)8 and 28.7 mg (0.214 mmol) of copper(II) chloride, and a stir bar was evacuated and vented to a carbon monoxide filled balloon, 5 times. Methyl alcohol (0.5 mL) was added, and the reaction mixture was stirred at 23 °C for 6 h. The reaction mixture was cooled to 0 °C and all volatile material was removed in vacuo. The dark red residue was triturated thoroughly with two 1-mL portions of benzene, and the triturates were filtered through a pipette of silica. Elution with ether and collection of all colored eluant gave on concentration the crude product as a dark red oil, yield 34 mg (112%). The crude product was flash chromatographed on 4 g of silica, loaded as a solution in benzene. Elution with 5:1 ether–petroleum ether separated **49** as an orange foam, yield 26.9 mg (89%), a 3:2 mixture of trans/cis epimers. A similar preparation starting with **48** (152 mg, 0.56 mmol) gave **45** (3:2 mixture; 66% yield). Recrystallization from hot 2:1 hexane–ethyl acetate gave **49a** orange prisms of mp 144.5–145 °C. Anal. C, H. Spectral data match the published data (no melting point value given).[3a]

Preparation of Diketo Ketal 50. The procedure to prepare diketo ketal **50** was identical with that used for **45**. Thus mo-

noketal **44** (892 mg, 3.84 mmol) was allowed to react with the acyl nickel complex from 2.5 mL (19 mmol) of nickel tetracarbonyl and 15.4 mL (15.4 mmol) of propyllithium solution (1.0 M) in ether, in a mixture of ether (60 mL) and THF (25 mL), at −50 °C for 1 h. Dilution with 10 mL of HMPA and addition of 2.8 mL (31 mmol) of allyl iodide, followed by stirring at 23 °C for 14 h, gave conversion to three products (TLC (ether) R_f 0.43, 0.48, 0.30). Isolation as before followed by flash chromatography (40 g of silica, eluting with 2:1 ether–petroleum ether) provided the major component **50** as a yellow solid, yield 1.086 g (82%). Two recrystallizations from ethyl acetate–hexane (1:1) gave colorless prisms, mp 113.5–114 °C, identical with the chromatographed material by NMR and IR spectral analysis. ^{1}H NMR ($CDCl_3$) δ 7.70 (dd, 1 H, J = 7, 2 Hz), 7.13 (dd, 1 H, J = 8.0, 1.5 Hz), 7.40 (t, 1 H, J = 7.0 Hz), 6.0–5.55 (m, 1 H), 5.2–4.9 (m, 2 H), 4.5–4.0 (m, 4 H), 3.88 (s, 3 H), 3.65 (d, 1 H, J = 6.5 Hz), 3.15–2.25 (m, 5 H), 1.7–1.35 (m, 2 H), 0.90 (t, 3 H, J = 7.0 Hz); IR ($CHCl_3$) 3080 (w), 3000 (m), 2970 (s), 2840 (w), 1710 (s), 1690 (s), 1640 (w), 1590 (s), 1480 (s), 1270 (s) cm^{-1}. Anal. C, H.

Preparation of Keto Hydroquinone 51. Diketo ketal **50** was hydrolyzed exactly as described for **46**. Thus a solution of 444 mg (1.29 mmol) of **50** in 12 mL of dioxane and 6 mL of 6 N HCl was stirred at 23 °C for 2 days. Analytical TLC showed two components (2:1 ether–petroleum ether; R_f 0.58 and 0.32), the more polar of which was desired hydroquinone **51**. On a smaller scale, using recrystallized material, the less polar component was not observed. Isolation as before gave a labile, amber oil, yield 376 mg (97%), contaminated with a trace of dioxane but otherwise homogeneous by NMR spectral analysis. ^{1}H NMR ($CDCl_3$) δ 0.99 (t, 3 H, J = 6 Hz, CH_3), 1.48–1.81 (m, 2 H, $CH_2CH_2CH_3$), 2.82 (t, 2 H, J = 6 Hz), 2.33 (dt, 2 H, J = 5, 1 Hz, $CH_2C{=}C$), 3.96 (s, 3 H, OCH_3), 4.95–5.25 (m, 2 H, allyl $C{=}CH_2$), 5.72–6.15 (m, 1 H, allyl), 6.72 (dd, J = 6, 1 Hz, Ar), 7.30 (t, 1 H, J = 7 Hz, Ar), 7.70 (dd, 1 H, J = 6, 1 Hz, Ar); IR (CCl_4) 3400 (m, OH), 2960 (m), 2930 (m), 1690 (m), 1450 (m), 1400 (s), 1260 (s), 1060 (s) cm^{-1}; mass spectral mol wt 300.1365, calcd for $C_{18}H_{20}O_4$ 300.1361.

Preparation of Triol 52. To a solution of ketohydroquinone **51** (376 mg, 1.25 mmol) in THF (10 mL) under argon was added solid sodium borohydride (110 mg, 2.9 mmol) at 23 °C. The mixture was allowed to stir for 15 h, then diluted with 1.0 mL of water, and carefully saturated with potassium carbonate. The mixture was partioned between 10 mL of degassed brine and 30 mL of degassed 2:1 ether/dichloromethane. The aqueous layer was further extracted with one 10-mL portion of 2:1 ether/dichloromethane. The combined organic solutions were washed with degassed brine, dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude triol **52** was obtained as an amber oil, 369 mg, 98%. ^{1}H NMR ($CDCl_3$) δ 9.5 (s, 2 H), 7.7 (br d, 1 H, J = 8.0 Hz), 7.25 (br t, 1 H, J = 8.0 Hz), 6.73 (br d, 1 H, J = 8.0 Hz), 6.2–5.7 (br m, 1 H), 5.3–4.8 (m, 3 H), 4.03 (s, 3 H), 4.2–3.8 (m, 2 H), 3.54 (br d, 1 H, J = 7.0 Hz), 2.30–0.8 (m, 7 H); IR (neat) 3350 (br, s), 3080 (w), 2970 (s), 2870 (m), 1630 (w), 1610 (m), 1580 (m), 1450 (s), 1380 (vs), 1250 (vs).

Preparation of Hydroxy Quinone 53. The crude triol **52** (312 mg, 1.03 mmol) was stirred in a mixture of DDQ (224 mg, 0.99 mmol) and potassium bicarbonate (117 mg, 1.17 mmol) in 10 mL of methyl alcohol under argon at 0 °C for 1.0 h. Dilution with dichloromethane and filtration through alumina gave crude naphthoquinone **53** as an orange oil, 242 mg. Flash chromatography on silica gel (15 g; elution with 4:1 ether–petroleum ether) gave pure **53** as an orange oil, 134 mg, 45% yield overall from **50**. ^{1}H NMR ($CDCl_3$) δ 7.8–7.5 (m, 2 H), 7.25 (dd, 1 H, J = 8.0, 2.5 Hz), 6.1–5.6 (m, 1 H), 5.3–5.0 (m, 2 H), 4.9–4.6 (m, 1 H), 4.00 (s, 3 H), 3.72 (d, 1 H, J = 11 Hz), 3.38 (br d, 2 H, J = 3.5 Hz), 2.2–1.3 (m, 4 H), 0.95 (t, 3 H, J = 6.0 Hz); IR (neat) 3500 (br, s), 3080 (w), 2960 (s), 2880 (m), 2840 (m), 1650 (d, vs), 1620 (s), 1590 (vs), 1470 (vs), 1450 (vs), 1280 (vs) cm^{-1}; mass spectrum, m/e 300 (M^+, 58%), 282 (30), 271 (28), 257 (100), 239 (33), 229 (19), 214 (12).

Preparation of Pyrano Ester 54a,b. The hydroxynaphthoquinone **53** (174 mg, 0.58 mmol) was stirred with a mixture of bis(acetonitrile)palladium dichloride (14 mg, 0.058 mmol), anhydrous cupric chloride (171 mg, 1.27 mmol), and methyl alcohol (3 mL) under carbon monoxide (1.0 atm) for 3.3 h and gave essentially one component detected by analytical TLC (ether on silica gel, R_f 0.35). The mixture was concentrated at oil pump pressure, triturated with benzene (5 mL), and purified by flash chromatography on silica gel (5 g). Elution with 7:2 ether–petroleum ether gave as the main component an orange viscous oil, 144 mg (70%). Analysis by HPLC (Poracil column, 8:1 hexane–ethyl acetate, 5 mL/min; R_v trans 8.85 mL, R_v cis 10.3 mL) indicated a mixture of isomers in the ratio 75:25 later identified as the trans/cis mixture **54a,b**. The chromatographed material was crystallized from 3 mL of warm 3:1 hexane–ethyl acetate to provide pure **54a** as dark orange needles, mp 128–133 °C. Recrystallization gave the analytical sample, mp 134–136 °C. ^{1}H NMR ($CDCl_3$) δ 7.7–7.4 (m, 2 H), 7.13 (dd, 1 H, J = 7.5, 2.5 Hz), 4.80 (br t, 1 H, J = 5.0 Hz), 4.4–4.1 (m, 1 H), 3.97 (s, 3 H), 3.70 (s, 3 H), 2.85–2.58 (m, 3 H), 2.22 (ddd, 1 H, J = 17.0, 10.0, 1.0 Hz), 1.9–1.2 (m, 4 H), 0.95 (t, 3 H, J = 6.5 Hz); IR ($CHCl_3$) 3030 (m), 2960 (m), 2880 (m), 2840 (m), 1735 (s), 1660 (vs), 1590 (s), 1470 (m), 1440 (s), 1280 (vs) cm^{-1}. Anal. C, H. The cis isomer **54b** was previously characterized.[5a]

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Structural Effects in Solvolytic Reactions. 51. Examination of the Differences in the Behavior of Secondary and Tertiary U-Shaped Bicyclic Derivatives toward Solvolysis

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The solvolyses (acetolysis) of secondary bicyclic tosylates such as *cis*-bicyclo[3.3.0]oct-2-yl and 5,6-*endo*-trimethylene-8-norbornyl and -9-norbornyl proceed with low exo/endo rate ratios (<10), unlike secondary 2-norbornyl (280) and the analogous tertiary derivatives wherein the exo/endo rate ratios increase progressively with increasing U-shaped character. The possible factors responsible for this difference in behavior are discussed. One possible factor can be nucleophilic solvent participation in the secondary systems, absent both in secondary 2-norbornyl and in tertiary solvolyses. An examination of the products of acetolysis of a number of bicyclic secondary tosylates reveals predominant inversion during acetolysis, suggesting solvent participation.

Winstein and Trifan[2] proposed that the large exo/endo rate ratio observed in the acetolysis of 2-norbornyl tosylate (280) arises from nonclassical stabilization of the exo transition state by σ-participation of the C_1–C_6 electron

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