Oxidative Coupling of the Enolate Anion of (1*R*)-(+)-Verbenone with Fe(III) and Cu(II) Salts. Two Modes of Conjoining This Bicyclic Ketone across a Benzene Ring†

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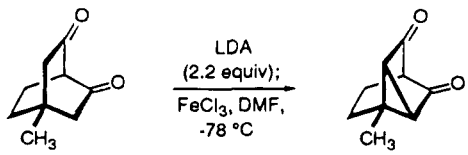
The regioselectivity of the oxidative coupling of the enolate anion of (1*R*)-(+)-verbenone (97% ee) has been examined with $CuCl_2$ and $FeCl_3$ as catalysts. With Cu(II), selective formation of the γ,γ-product is observed. An increase in temperature above −40 °C results in further oxidation of the intra-ring ethano bridge to a trans double bond, provided that excess LDA has been added. In the presence of Fe(III), the coupling is partially diverted to the α,γ-product, which has proven amenable to direct conversion to that C_2-symmetric "dimer" having the carbonyl groups in a para relationship. The second C_2 "dimer" featuring meta orientation of the ketone functionalities has been conveniently prepared from the trienedione or its derived diol by thermal or photochemical trans → cis equilibration, thermal 6π electrocyclization with concurrent aromatization, and PCC oxidation. Some potential applications of this conformationally rigid benzenoid system to enantioselective synthesis are outlined.

The formation of 1,4-diketones by the oxidative coupling of enolate anions with cupric and ferric ions[2] has served as an important synthetic tool for 2 decades. The process has serviced several synthetic objectives in both its intermolecular[2-5] and intramolecular[3,6-8] modes. Perhaps most notable is the ability of these transition metal salts to effect cyclopropane construction as in **1**.[8] In our view, the intermolecular variant should represent a powerful first step in the construction of structurally complex polycyclic ring systems starting with inexpensive, commercially available materials. Optically active α,β-unsaturated ketones hold particular fascination.



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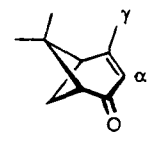
This paper presents a detailed account of our initial studies involving (1*R*)-(+)-verbenone (**2**), which is readily available in high optical purity.[9] Little precedent exists with which to gauge the potential response of **2** to oxidative dimerization. Products resulting from α,α-, α,γ-, and γ,γ-coupling are all possible, and no mechanistic insight is available with which to venture a prediction regarding product distribution. Is it reasonable to entertain the idea that the regiochemical outcome will exhibit a dependency on the particular metal salt employed? One operating assumption that we adopted was that γ,γ-coupling might well be kinetically favored under certain circumstances, since steric effects would be maximally reduced when the methyl substituent from each anionic partner was the reaction center. Our long-range goal was to determine the feasibility of preparing from **2** the structurally unusual benzo-linked C_2-symmetric "dimers" **3** and **4**.



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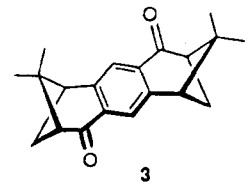

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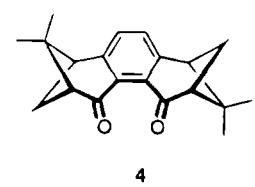

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Results and Discussion

(1*R*)-(+)-Verbenone (97% ee)[9] was deprotonated with lithium diisopropylamide (LDA) in a THF/HMPA solvent system (7.5:1) at −78 °C. After 3 h, slightly more than 2 equiv of copper(II) chloride dissolved in DMF was introduced dropwise, and the reaction temperature was allowed to rise to ca. −40 °C during an additional 3 h. Quenching of the reaction with aqueous NH_4OH solution and chromatographic purification afforded **5** in 29% yield (Scheme 1). Trace quantities of products subsequently identified as **6** and **8** were also seen in addition to polymer. A second coupling reaction, performed under comparable conditions except for warming to room tem-

† Atomic coordinates for the structure have been deposited with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.

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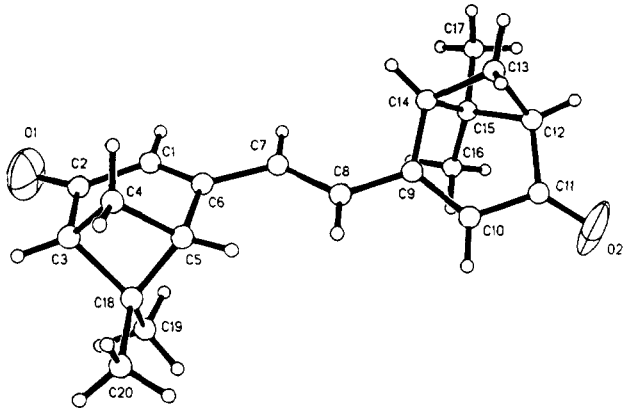
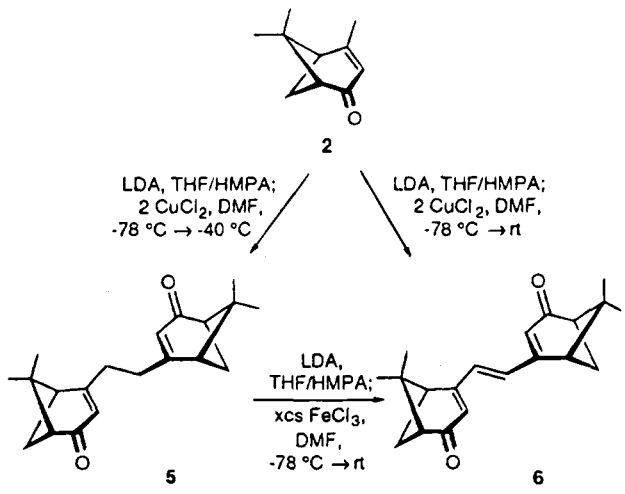


Figure 1. Crystallographically determined molecular structure of **6** as drawn with 50% probability ellipsoids.

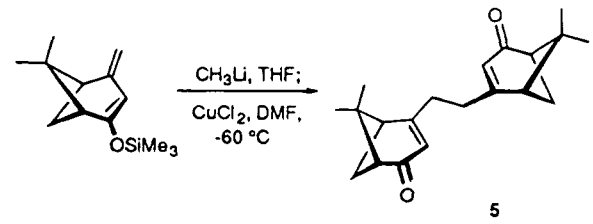
Scheme 1



perature, produced **6** with the same efficiency. Although the high-field ^1H and ^{13}C NMR spectra of **6** clearly revealed that an additional center of unsaturation had been introduced, these data did not satisfactorily establish the geometry of the interconnective olefinic linkage. Recourse was therefore made to X-ray crystallographic analysis, which confirmed the trans intra-ring stereochemical relationship (Figure 1). The closely related structural features shared by **5** and **6** were unequivocally ascertained by treatment of the dienedione with a 4-fold excess of LDA followed by a solution of anhydrous ferric chloride in DMF. The near-quantitative nature of this conversion (70% isolated) suggests that the modest yield accompanying the direct formation of **6** arises from the inefficiency of the initial formation of **5**. The use of $CuBr_2$, $Cu(BF_4)_2$, and $Cu(OTf)_2$ did not improve matters significantly.

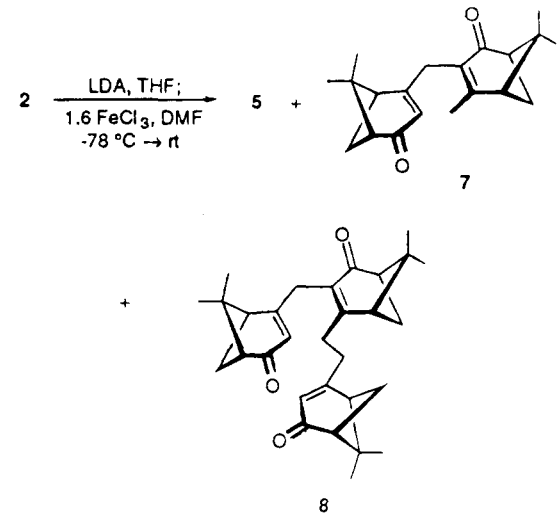
These developments prompted generation of the silyl enol ether of **2**. Following its purification, the enolate anion was regenerated with methyllithium in THF. In this way, the solution was free of excess LDA and diisopropylamine. Inverse addition of the enolate to a cold (−60 °C) solution of $CuCl_2$ in DMF gave rise to **5** in 44% yield. Significantly, little if any polymerization was evident, and no trimers or other dimers were detected. Some verbenone was recovered, thereby improving the yield to 78%.

The formation of **5** correlates with γ,γ-coupling of the delocalized verbenone enolate anion. Several mechanistic rationalizations can be advanced in explanation of this



regioselectivity. One possibility involves the covalent linking of *metal-free* carbon-centered radicals formed by electron transfer to Cu(II). This assumption would appear to lack cogency when considered in light of results obtained with ferric chloride as the catalyst (Scheme 2).

Scheme 2

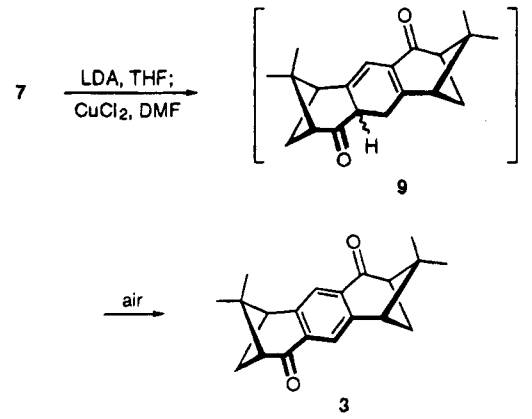


Under these circumstances, **2** is transformed into a mixture of **5** (19%), **7** (13%), and **8** (4%). A modest amount of unreacted **2** (16%) was recovered. It is noteworthy that **7** did not appear on TLC analysis until after chromatographic separation had been undertaken, suggesting that the initial β,γ-unsaturated tautomer formed by α,γ-coupling has reasonable stability. Unlike **5**, whose symmetry halves the number of observable ^{13}C NMR peaks, **7** exhibits 20 distinct signals. Only one of its four olefinic carbons (120.1 ppm) is bonded to a hydrogen atom. Of the five methyl groups appearing in the 300 MHz ^1H NMR spectrum, only one (δ 1.95) is seen to be allylic. Compound **8** is the only trimer to be uncovered in this study. Its spectral properties are a composite of those exhibited by **5** and **7**. Arrival at **8** can be realized by the γ,γ-coupling of **7** or the α,γ-coupling of **5** to verbenone.

The significantly different product distribution realized with Fe(III) establishes that a close interdependency involving the metallic species does exist. Although the actual regiocontrol factors remain elusive and require further study, it might reasonably be supposed that structural features should be capable of overriding the quite subtle partitioning of reaction pathways. Diketone **7** was viewed to be a reasonable test case. Intramolecular oxidative coupling within **7** should proceed in an α,γ-selective manner irrespective of the transition metal ion promoter, since this regioselectivity is accompanied by favorable six-membered ring formation. Indeed, the use of $CuCl_2$ for this purpose proved successful (Scheme 3).

The conversion of **7** into **3** was observed by TLC not to proceed directly. The major initial products, which were

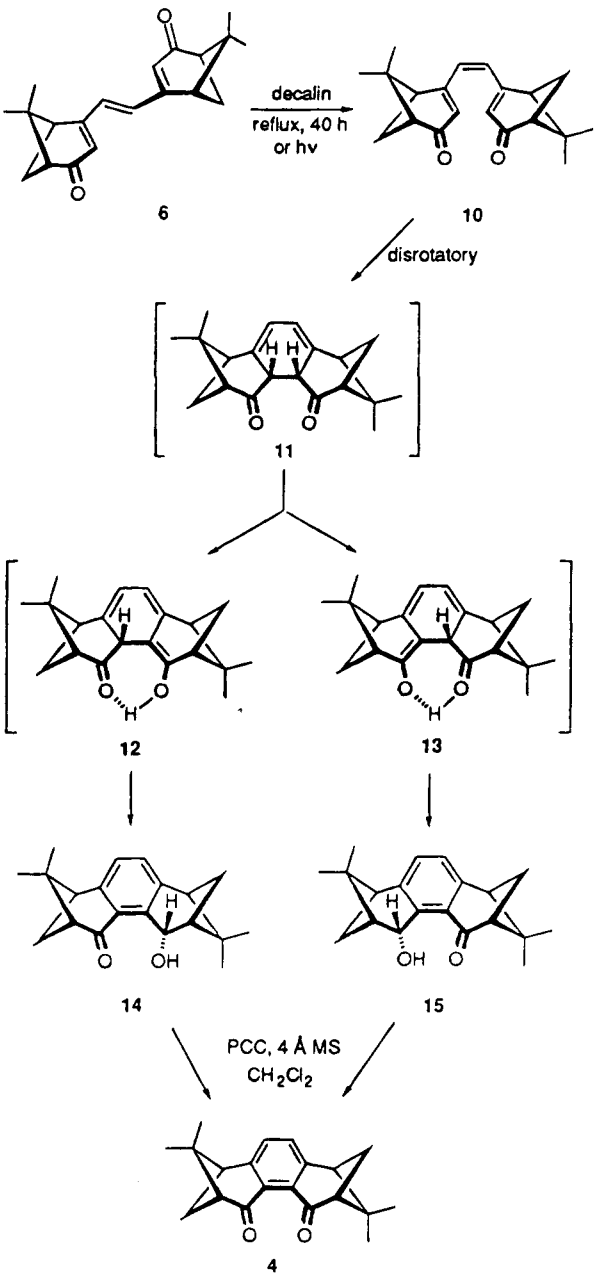
Scheme 3



somewhat less polar than **3**, were completely aromatized only after being stirred open to the air in ethyl acetate solution to which a small amount of silica gel had been added. These intermediates are considered to be **9**. The 300 MHz ^{1}H NMR spectrum of **3** is notable in that the chemical shift of the two methyl groups syn to the benzene ring (δ 0.75) are subject to shielding by the ring current. This anisotropy contribution results in an upfield displacement of ca. 0.22 ppm. As a consequence of the inherent symmetry of **3**, its ^{1}H and ^{13}C NMR spectra exhibit one-half the number of carbons and hydrogens. A unique feature of this diketone is the appearance of its aryl protons at δ 7.76 (in $CDCl_3$ solution). These protons are ortho to one carbonyl and meta to a second. Since an ortho arrangement is known to exert the greater deshielding effect,[10] the two aromatic protons in **3** should appear downfield of those in **4**.

A projected synthesis of **4** offered the opportunity to evaluate the feasibility of effecting trans–cis isomerization of the interlinking double bond in **6** and subsequent 6π electrocyclization of the isomerized trienedione. Attempts to effect concurrent photoequilibration and photocyclization in the presence of an oxidant, a process that operates so effectively with stilbene,[11] were singularly unsuccessful. Thermal activation of neat samples did not produce detectable quantities of an aromatized compound. These results stand in sharp contrast to the response of **6** when heated in refluxing decalin (190 °C) (Scheme 4). After 40 h, no **6** remained and a 2.6:1 mixture of **14** and **15** was isolated in 47% yield. This pair of epimeric hydroxy ketones is presumably formed as the result of initial disrotatory cyclization to give **11**, an intermediate capable of enolization in two stereochemically distinctive directions. Enolization toward the right carbonyl in **11** (as drawn) leaves behind a highly labile hydrogen atom that is uniquely syn-oriented to a dimethyl-substituted apical carbon as in **12**. When enolization occurs to the left, the resident angular hydrogen finds itself disposed syn to an unsubstituted one-carbon bridge (see **13**). Both of these unobserved intermediates are ideally constituted for suprafacial 1,3- or 1,7-hydrogen migration. In the event, **12** would serve as the precursor to **14**, and **13** would lead with comparably complete stereocontrol to **15**. The substantial rigidity of these π networks would appear to make antarafacial 1,7-hydrogen shifts impossible.

Scheme 4



Following their chromatographic separation, inspection of the ^{13}C NMR spectra of these products established that only one carbonyl group remained. For **14**, this signal was present at 205.9 ppm. In addition, six peaks due to the benzenoid carbons were evident at 149.3, 145.8, 140.5, 130.3, 127.8, and 124.7 ppm. The appearance of two doublets at δ 6.81 and 6.69 in the ^{1}H NMR spectrum argues convincingly for the fact that only two protons are bonded to the sp^2-hybridized carbon. A doublet at δ 5.53, which disappeared following a D_2O wash, was identified as being due to the hydroxyl proton. An analogous, though distinctively different group of signals was exhibited by **15**, whose three-dimensional structural features were defined by X-ray crystallographic analysis (Figure 2).

Treatment of either **14** or **15** with pyridinium chlorochromate provided **4** in >90% yield. Interestingly, **15** underwent oxidation much more slowly than **14**. Evidently, the more crowded environment of the C*H*–OH proton in **15** exerts a significant rate-retarding effect on

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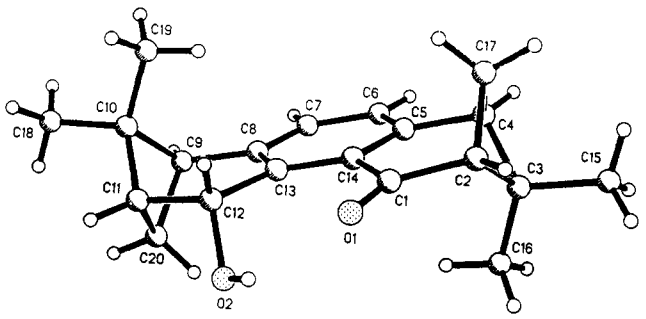


Figure 2. Crystallographically determined molecular structure of **15** as drawn with 50% probability ellipsoids.

the conversion of the chromate ester to product. Like **3**, **4** is characterized by greatly simplified NMR spectra. The aryl proton absorption appears at δ 7.18, almost 0.6 ppm upfield of that in **3**, in line with the expectations advanced above.

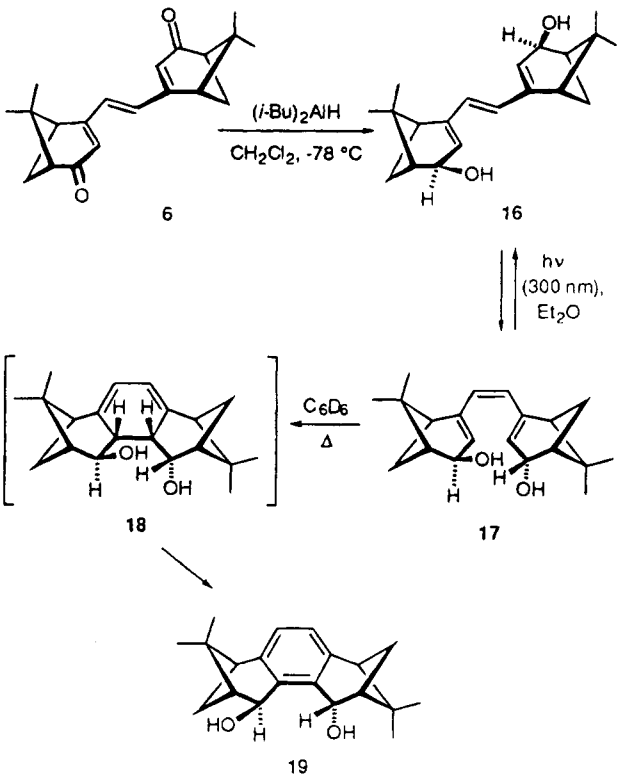
With these successes in hand, further consideration was given to the photoisomerization of **6**. Irradiation of benzene solutions at several wavelengths (254, 300, and 350 nm) only returned unchanged trienedione. In contrast, photoexcitation of **6** dissolved in ether with a 450 W Hanovia lamp housed in a uranium filter resulted in smooth isomerization to **10**. In a representative, carefully monitored run, the extent of conversion was determined to be 38% after 25.5 h, 71% after 44 h, and 67% after 66 h. The onset of decomposition becomes significant only after prolonged irradiation. Clean separation of **10** from **6** was not possible owing to their near-identical R_f values. However, **10** proved to be entirely stable to standard laboratory conditions.

Heating of the **6/10** mixture in benzene did not result in cyclization. However, in toluene at somewhat higher temperatures, **10** was smoothly converted to **14** and **15** in ratios which varied widely. For example, only **14** was obtained in one experiment, while a 4:1 mixture of **14** and **15** resulted in an otherwise identical cyclization. The reasons underlying these changes in product composition have not been elucidated.

Exhaustive reduction of **6** with Dibal-H proceeded smoothly and with complete stereoselectivity to deliver trienediol **16** in 59% yield (Scheme 5). Irradiation of 10^{-3} M etheral solutions of this more photochemically reactive intermediate with 300 nm light resulted in establishment of a photoequilibrium with its cis isomer **17**. At the apparent photostationary state, the **16:17** ratio is 77:23 on the basis of ^{1}H NMR integration. The proportion of **17** could be improved by utilizing a triplet sensitizer. Thus, irradiation in the presence of 2-fluorenone resulted in 57% conversion, while the use of benzanthrone afforded **17** at the 60% level.

Both diols are unstable to storage at room temperature, decomposing significantly within several days. Their lability extends to chromatography on silica gel, such that their separation by this means is not possible. Direct treatment of the mixture with manganese dioxide afforded **14/15** and **6** as expected. When a sample enriched in **17** was heated in C_6D_6 and the progress of reaction was monitored by ^{1}H NMR spectroscopy, the signals attributable to **17** were seen to disappear, being replaced in turn by a singlet at δ 6.69 and a doublet at δ 5.21. These signals are attributed to the aromatic and carbinol protons, respectively, in **19**. As in the carbonyl example,

Scheme 5



disrotatory closure to **18** and subsequent oxidative aromatization are expected to be operative.

Conclusion

The route to the "dimeric" ketones **3** and **4** developed herein begins in both cases with oxidative coupling of the enolate anion of (1*R*)-(+)-verbenone. With ferric chloride as the promoter, dimerization occurs in that regioselective direction which delivers a modest amount of the α,γ-isomer **7**. The dianion of this dienedione undergoes smooth ring closure under cupric chloride catalysis to make **3** available after air oxidation.

Extension of the oxidative coupling to the involvement of $CuCl_2$ resulted in C–C bond formation across the γ-position with good regiocontrol. At low temperatures, dienedione **5** was routinely isolated. However, for obvious synthetic advantages, the reaction mixture was allowed to warm to room temperature in order to induce more advanced oxidation of the tether. Under these circumstances, **6** was conveniently produced. A subsequent regimen of thermal isomerization of the intra-ring double bond, 6π electrocyclization, and oxidation gave rise to **14** and **15**, from which **4** was easily obtained.

In contemplating potentially important uses for **4** in organic synthesis, we hope to take advantage of its high structural rigidity, C_2 symmetry, and unique geometry in order to produce ligands having significant potential in enantioselective processes. For example, it is planned to examine those chiral titanium complexes derived from diol **19** as catalysts for the addition of dialkylzinc[12] and alkyltitanium reagents[13–15] to achiral carbonyl compounds. Other studies aimed at the asymmetric steering

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(14) Waldmann, H.; Weigerding, M.; Dreisbach, C.; Wandrey, C. *Helv. Chim. Acta* **1994**, *77*, 2111.

of Diels–Alder cycloadditions,[16] ene reactions,[17] and Claisen rearrangements[18] are also planned. Finally, applications of the diols to other enantiocontrolled transformations[19] and of derived diamines and diphosphines[20] as serviceable chiral ligands are to be probed.

Experimental Section

Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded at the indicated field strengths. High-resolution mass spectra were recorded at The Ohio State University Chemical Instrumentation Center. Elemental analyses were performed at the Scandinavian Microanalytical Laboratory, Herlev, Denmark. All reactions were carried out under a nitrogen atmosphere, and the ensuing separations were effected under flash chromatography conditions on Merck silica gel HG_{254}. The organic extracts were dried over anhydrous magnesium sulfate. Solvents were reagent grade and in many cases dried before use.

(1*R*,1′*R*,5*S*,5′*S*)-4,4′-Ethylenebis[6,6-dimethylbicyclo-[3.1.1]hept-3-en-2-one] (5). Lithium diisopropylamide was generated in the usual fashion from diisopropylamine (71.7 mL, 0.513 mol) and *n*-butyllithium (306 mL of 1.6 M in hexanes, 0.489 mmol) in dry THF (450 mL) containing distilled HMPA (60 mL, 0.35 mol). (1*R*)-(+)-Verbenone (97% ee, 35.0 g, 0.233 mol) was introduced dropwise at −78 °C over a period of 25 min. After 3 h, a solution of copper(II) chloride (65.7 g, 0.489 mol) in dry DMF (600 mL) was added during 25 min, during which time the temperature was not allowed to rise more than 20 °C. After an additional 3 h, the reaction mixture was allowed to warm to −40 °C, quenched with concentrated NH_4OH solution, stirred overnight at rt, and extracted with ethyl acetate (2 × 500 mL). The combined organic layers were washed with dilute HCl until the washings were acidic and then with saturated $NaHCO_3$ solution and brine prior to drying and solvent evaporation. Chromatography of the residual oil on silica gel (gradient elution with 10–35% ethyl acetate in hexanes) afforded 9.95 g (29%) of **5** as a colorless, crystalline solid: mp 97–98.5 °C (from ethyl acetate–hexanes, 1:4); IR (film, cm^{-1}) 1670, 1610, 1280, 1235, 1195, 725; ^1H NMR (300 MHz, $CDCl_3$) δ 5.66 (s, 2 H), 2.77 (dt, J = 9.2, 5.5 Hz, 2 H), 2.62–2.58 (m, 2 H), 2.45–2.37 (m, 6 H), 2.00 (d, J = 9.2 Hz, 2 H), 1.45 (s, 6 H), 0.94 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.2, 170.9, 120.4, 57.7, 53.7, 48.5, 40.7, 33.3, 26.4, 22.2; MS m/z (M^+) calcd 298.1933, obsd 298.1901; $[\alpha]^{20}_D$ +308.3 (*c* 1.45, CH_2Cl_2). Anal. Calcd for $C_{20}H_{26}O_2$: C, 80.50; H, 8.78. Found: C, 80.26; H, 8.78.

(1*R*,1′*R*,5*S*,5′*S*)-4,4′-(*E*)-Vinylenebis[6,6-dimethylbicyclo[3.1.1]-hept-3-en-2-one] (6). Lithium diisopropylamide was prepared from diisopropylamine (2.94 mL, 21 mmol), *n*-butyllithium (12.5 mL of 1.6 M in hexanes, 20 mmol), and HMPA (3 mL) in dry THF (30 mL). Verbenone (1.23 mL, 8.0 mmol) was introduced into this solution via syringe at −78 °C. After 1.5 h, a solution of copper(II) chloride (4.47 g, 20 mmol) in DMF (35 mL) was added over a period of 15 min. The reaction mixture turned violet to dark blue and subsequently to dark green-black. After an additional 2 h, the cooling bath was removed and stirring was maintained at rt for 7 h. The now dark red-brown mixture was quenched by the addition of concentrated ammonium hydroxide solution and extracted with ether (3 × 75 mL). The combined ethereal extracts were washed successively with dilute HCl, water, and saturated $NaHCO_3$ solution. After drying and solvent evaporation, the residual dark oil was purified by chromatography on silica gel (elution with 25% ethyl acetate in hexanes) furnishing **6** (327 mg, 27%) as bright yellow plates: mp 180.5–181.5 °C (from hexanes–ethanol); IR (film, cm^{-1}) 1670, 1585, 1380, 1295, 1045, 975; $\lambda^{CH_2Cl_2}_{max}$ 238 nm (ϵ 41 500); ^1H NMR (300 MHz, $CDCl_3$) δ 6.72 (s, 2 H), 5.96 (t, J = 1.6 Hz, 2 H), 3.04 (dt, J = 5.8, 1.1 Hz, 2 H), 2.91 (ddt, J = 9.4, 5.6, 5.6 Hz, 2 H), 2.74 (dt, J = 5.7, 1.6 Hz, 2 H), 2.07 (d, J = 9.4 Hz, 2 H), 1.58 (s, 6 H), 0.99 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.5, 162.6, 132.9, 125.2, 58.2, 52.7, 43.6, 39.9, 26.6, 22.1; MS m/z (M^+) calcd 296.1776, obsd 296.1782; $[\alpha]^{20}_D$ +310.9 (*c* 1.3, C_2H_5OH). Anal. Calcd for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16. Found: C, 81.10; H, 8.30.

Oxidation of 5 with Ferric Chloride. To a cold (−78 °C), magnetically stirred solution of lithium diisopropylamide [from 136 μL (0.97 mmol) of diisopropylamine and 590 μL (0.95 mmol) of *n*-butyllithium in hexanes] in anhydrous THF (3 mL) containing HMPA (174 μL, 1 mmol) was added a solution of **5** (69 mg, 0.23 mmol) in THF (2.5 mL) via cannula. The resulting deep yellow-orange solution was stirred at −78 °C for 2 h before a solution of 1 M ferric chloride in DMF (3.88 mmol) was introduced via syringe. Two hours later, the cooling bath was removed, and once rt was reached (1 h), dilute HCl was added and the product was extracted into ether. The combined organic layers were washed with saturated $NaHCO_3$ solution, dried, and concentrated. ^1H NMR analysis of the residue (71 mg) indicated it to be **6**. After chromatography of this material on silica gel (elution with 25% ethyl acetate in hexanes), there was isolated 48 mg (71%) of pure **6**, spectroscopically identical with the material described above.

Coupling of Verbenone via Its Silyl Enol Ether. A sample of verbenone (10 mL, 64.8 mmol) was added neat to a cold (−78 °C), magnetically stirred solution of LDA (110 mmol) in anhydrous THF (200 mL). After 3 h, chlorotrimethylsilane (25 mL, 1.97 mmol) was introduced dropwise, and the reaction mixture was stirred overnight, filtered twice through neutral alumina, and evaporated. The remaining orange oil was purified by Kugelrohr distillation as required.

A solution of the colorless silyl enol ether (4.31 g, 19.38 mmol) in THF (40 mL) was treated with methyllithium (15.2 mL, 19.38 mmol) at −78 °C, stirred for 4 h, and added dropwise to a cold (−60 °C) solution of $CuCl_2$ (3.91 g, 29.1 mmol) in DMF (30 mL) dropwise during 20 min. The reaction mixture was allowed to warm to ambient temperature overnight and worked up in the predescribed fashion. Purification of the residue by chromatography on silica gel (elution with 25% ethyl acetate in hexanes) provided 1.26 g (44%) of **5** and returned 730 mg of unreacted verbenone. The adjusted yield of **5** is therefore 78%.

Coupling of 2 with Ferric Chloride. A solution of *n*-butyllithium in hexanes (23.0 mL of 1.6 M, 36.8 mmol) was added via syringe to a solution of dry diisopropylamine (5.40 mL, 38.6 mmol) in anhydrous THF (45 mL) at −78 °C. This solution was stirred for 15 min before being treated with a solution of **2** (2.63 g, 17.5 mmol) in dry THF (5 mL). After being stirred for 15 min, the reaction mixture was treated with a solution of $FeCl_3$ in DMF (135 mL of 0.21 M, 28 mmol) via cannula, allowed to warm to rt over 2 h, poured into ether, filtered through a pad of Celite, and concentrated. Removal of the DMF under reduced pressure in a Kugelrohr apparatus left a dark residue that was triturated with ether. The ethereal extracts were evaporated, and the resulting dark oil was chromatographed on silica gel. Gradient elution with 10–20% ethyl acetate in hexanes furnished in order of elution 431 mg (61%) of unreacted **2**, 327 mg (13%) of **7**, 487 mg (19%) of **5**, and 98 mg (4%) of **8**.

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7: colorless oil; IR (neat, cm^{-1}) 1680, 1470, 1370, 1345, 1285, 1245, 1205; ^1H NMR (300 MHz, $CDCl_3$) δ 5.60 (t, J = 1.6 Hz, 1 H), 3.43 (dd, J = 16.7, 1.0 Hz, 1 H), 3.07 (dd, J = 16.8, 1.2 Hz, 1 H), 2.82–2.68 (m, 3 H), 2.62–2.58 (m, 1 H), 2.46–2.42 (m, 2 H), 2.03 (d, J = 9.2 Hz, 2 H), 1.95 (s, 3 H), 1.46 (s, 3 H), 1.45 (s, 3 H), 0.97 (s, 3 H), 0.94 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.8, 202.2, 171.4, 165.5, 125.8, 120.1, 57.9, 57.3, 54.1, 53.7, 50.7, 48.6, 41.1, 40.6, 30.5, 26.6, 26.5, 22.1 (2 C), 20.7; MS m/z (M^+) calcd 298.1933, obsd 298.1930. Anal. Calcd for $C_{20}H_{26}O_2$: C, 80.50; H, 8.79. Found: C, 80.26; H, 8.78.

8: colorless oil; IR (neat, cm^{-1}) 1670, 1615, 1470, 1375, 1350, 1285, 1245, 1205, 735; ^1H NMR (300 MHz, $CDCl_3$) δ 5.69 (d, J = 1.3 Hz, 1 H), 5.56 (d, J = 1.6 Hz, 1 H), 3.47 (dd, J = 17.3, 1.6 Hz, 1 H), 3.06 (dd, J = 17.3, 1.7 Hz, 1 H), 2.87–2.74 (m, 4 H), 2.69–2.55 (m, 3 H), 2.51–2.30 (m, 7 H), 2.06 (d, J = 8.9 Hz, 2 H), 1.51 (s, 3 H), 1.50 (s, 3 H), 1.48 (s, 3 H), 1.00 (s, 3 H), 0.97 (s, 3 H), 0.96 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.4, 203.2, 202.0, 171.3, 170.6, 165.9, 126.3, 120.4, 119.9, 57.9, 57.8, 57.4, 54.0, 53.9, 53.7, 49.0, 48.7 (2 C), 48.4, 41.1 40.9, 40.8, 33.9, 30.9, 30.4, 26.6, 26.5, 22.6, 22.3, 22.2; MS m/z (M^+) calcd 447.2899, obsd 447.2868. Anal. Calcd for $C_{30}H_{38}O_3$: C, 80.68; H, 8.58. Found: C, 81.07; H, 8.92.

(1*S*,3*R*,5*S*,7*R*)-1,2,3,5,6,7-Hexahydro-2,2,6,6-tetramethyl-1,3:5,7-dimethanoanthracene-4,8-dione (3). A solution of *n*-butyllithium in hexanes (0.45 mL of 1.6 M, 0.72 mmol) was added via syringe to a solution of dry diisopropylamine (0.10 mL, 0.73 mmol) in anhydrous THF (2 mL) at −78 °C. After 15 min, diketone **7** (43 mg, 0.14 mmol) dissolved in dry THF (1 mL) was introduced, and stirring was maintained for 15 min before a solution of $CuCl_2$ (135 mg, 1.01 mmol) in dry DMF (2.5 mL) was added via cannula. The reaction mixture was stirred for 10 min at −78 °C, allowed to warm to rt during 1 h, poured into ether (100 mL), filtered through a pad of Celite, and concentrated. The DMF was removed under reduced pressure in a Kugelrohr apparatus, and the residue was triturated with ether. The extracts were evaporated, and the residual oil was chromatographed on silica gel (elution with 30% ethyl acetate in petroleum ether) to furnish a small amount of **3** followed by a mixture of coeluting compounds. This mixture was dissolved in ethyl acetate and stirred open to the air for 48 h with a small amount of silica gel present. Chromatography as before gave 7 mg (32%) of **3** as a white solid: mp 188–189 °C (from 10% ethanol in hexane); IR ($CHCl_3$, cm^{-1}) 1690, 1440, 1330, 1270, 1200, 1100, 980; ^1H NMR (300 MHz, $CDCl_3$) δ 7.76 (s, 2 H), 3.12 (t, J = 5.7 Hz, 2 H), 3.05 (dt, J = 9.8, 5.8 Hz, 2 H), 2.93 (t, J = 5.8 Hz, 2 H), 2.09 (d, J = 9.8 Hz, 2 H), 1.58 (s, 6 H), 0.75 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.0, 148.5, 133.9, 123.3, 57.9, 52.5, 48.3, 39.4, 26.7, 22.7; MS m/z (M^+) calcd 294.1620, obsd 294.1617; $[\alpha]^{20}_D$ +203.1 (*c* 10.13, C_2H_5OH). Anal. Calcd for $C_{20}H_{22}O_2$: C, 81.60; H, 7.53. Found: C, 81.97; H, 7.61.

Thermally Induced Electrocyclization of 6. A solution of **6** (90 mg, 0.304 mmol) in dry decalin (25 mL) was refluxed under an atmosphere of argon for 40 h while monitoring the progress of reaction by TLC. The cooled solution was passed through a column of silica gel to remove the decalins (hexane elution). Subsequent use of 8% ethyl acetate in hexanes afforded 42 mg (47%) of a 2.6:1 mixture of **14** and **15** as a white crystalline solid. Careful rechromatography of this material on silica gel afforded pure samples of **14** and **15**.

14: colorless solid; mp 152 °C; ^1H NMR (300 MHz, C_6D_6) δ 6.81 (d, J = 7.4 Hz, 1 H), 6.69 (d, J = 7.4 Hz, 1 H), 5.58 (br t, J = 3.7 Hz, 1 H), 5.53 (br d, J = 4.0 Hz, 1 H), 2.80 (t, J = 6.0 Hz, 1 H), 2.71 (td, J = 6.1, 3.3 Hz, 1 H), 2.56 (dd, J = 5.5, 6.1 Hz, 2 H), 2.49–2.38 (m, 2 H), 1.76 (d, J = 9.8 Hz, 1 H), 1.35 (s, 3 H), 1.15 (m, 1 H), 1.13 (s, 3 H), 1.10 (s, 3 H), 0.59 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) δ 205.9, 149.3, 145.8, 140.5, 130.3, 127.8, 124.7, 71.8, 59.4, 51.8, 49.2, 49.1, 47.1, 40.0, 39.2, 34.5, 26.5, 26.3, 23.4, 22.7; MS m/z (M^+) calcd 296.1776, obsd 296.1749. Anal. Calcd for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16. Found: C, 80.90; H, 8.46.

15: colorless solid; mp 155–156 °C; ^1H NMR (300 MHz, C_6D_6) δ 6.80 (ABq, J = 7.4 Hz, 2 H), 6.05 (d, J = 3.3 Hz, 1 H), 5.45 (t, J = 3.2 Hz, 1 H), 2.80 (t, J = 6.0 Hz, 1 H), 2.67–2.56 (m, 3 H), 2.50–2.39 (m, 2 H), 2.05 (d, J = 9.5 Hz, 1 H), 1.64 (d, J = 9.7 Hz, 1 H), 1.25 (s, 3 H), 1.11 (s, 3 H), 0.66 (s, 3 H), 0.54 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) δ 205.5, 149.4, 146.1, 141.0, 130.6, 128.8, 124.8, 68.9, 59.0, 52.8, 49.5, 49.3, 46.9, 44.5, 39.2, 29.6, 26.3 (2 C), 22.5, 21.0; MS m/z (M^+) calcd 296.1776, obsd 296.1776; $[\alpha]^{25}_D$ +114.9 (*c* 1.29, C_2H_5OH). Anal. Calcd for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16. Found: C, 82.36; H, 8.22.

Photoisomerization of 6 and Electrocyclization of 10. A solution of **6** (578 mg, 1.95 mmol) in dry ether (350 mL) contained in a Pyrex well was irradiated with a 450 W Hanovia lamp housed in a uranium filter for 44 h with cooling from tap water. ^1H NMR analysis of an aliquot at this point in time revealed 71% conversion to **10**. After 66 h, the level of **10** was determined to be 67%. The solvent was removed in vacuo, the residue was dissolved in dry toluene (125 mL), and the solution was refluxed for 3 h. After evaporation of the solvent, the residue was chromatographed on silica gel (elution with 25% ethyl acetate in hexanes) to give 110 mg (31% based upon the proportion of **10**) of a 4:1 mixture of **14** and **15**.

(1*S*,3*R*,6*R*,8*S*)-1,2,3,6,7,8-Hexahydro-2,2,7,7-tetramethyl-1,3:6,8-dimethanophenanthrene-4,5-dione (4). The mixture of **14** and **15** (or each isomer separately) (91 mg, 0.307 mmol) was dissolved in dry CH_2Cl_2 (5 mL) and treated sequentially with 4 Å molecular sieves (200 mg) and pyridinium chlorochromate (200 mg, 0.92 mmol). The mixture was stirred at rt until no hydroxy ketone remained (usually within 3 days if both isomers were initially present), diluted with ether, filtered through silica gel, and concentrated. Purification by chromatography (silica gel, elution with 30% ethyl acetate in hexanes) afforded pure **4** (84 mg, 93%) as light yellow crystals: mp 201–202 °C (from hexanes–ethyl acetate); ^1H NMR (300 MHz, $CDCl_3$) δ 7.18 (s, 2 H), 3.04–2.92 (m, 6 H), 2.15 (d, J = 9.2 Hz, 2 H), 1.55 (s, 6 H), 0.70 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.3, 150.3, 131.9, 129.5, 58.7, 54.4, 49.3, 37.2, 26.8, 22.6; MS m/z (M^+) calcd 294.1620, obsd 294.1624; $[\alpha]^{25}_D$ +1479 (*c* 0.55, $CHCl_3$). Anal. Calcd for $C_{20}H_{22}O_2$: C, 81.60; H, 7.53. Found: C, 81.45; H, 7.57.

(1*R*,1′*R*,2*R*,2′*R*,5*S*,5′*S*)-4,4′-(*E*)-Vinylenebis[6,6-dimethylbicyclo[3.1.1]hept-3-en-2-ol] (16). A cold (−78 °C), magnetically stirred solution of **6** (305 mg, 1.03 mmol) in dry CH_2Cl_2 (12 mL) was blanketed with N_2 and treated dropwise with Dibal-H (2.3 mL of 1 M in toluene, 2.3 mmol) during 10 min. The reaction mixture was allowed to warm slowly to −25 °C during 3 h, at which point Rochelle's salt was introduced to quench the reduction. The product was extracted into ether, and the combined organic layers were dried and concentrated. Rapid passage of the resulting white solid through silica gel (elution with 25% ethyl acetate in hexanes) afforded **16** (180 mg, 59%) as unstable colorless crystals: mp 150–151 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 6.24 (s, 2 H), 5.66 (br s, 2 H), 4.56 (br s, 2 H), 2.64–2.61 (m, 2 H), 2.51–2.49 (m, 2 H), 2.34 (br, 2 H), 1.41 (s, 6 H), 1.38–1.21 (m, 2 H), 1.03 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.6, 128.3, 125.7, 73.5, 48.5, 41.9, 38.5, 35.1, 26.9, 22.7; MS m/z (M^+) calcd 300.2089, obsd 300.2984; $[\alpha]^{25}_D$ −176.0 (*c* 0.36, C_2H_5OH).

Photolysis–Cyclization of 16. A. A solution of **16** (240 mg, 0.80 mmol) in dry, deoxygenated ether (110 mL) was irradiated at 300 nm in a Rayonet apparatus for 5 h. The solvent was removed in vacuo to leave a yellow solid, ^1H NMR analysis of which indicated a trans/cis ratio of 3.3:1. This material was dissolved in a minimum amount of 20% ethyl acetate in hexanes and passed through a silica gel column. Although significant decomposition occurred, it was possible to obtain 13 mg of **17** and 45 mg of **16**. This sample was immediately dissolved in C_6D_6, sealed in an NMR tube, and placed in a probe heated to 330 K. Spectra were recorded for 1 h at 15 min intervals during which time the vinyl and carbinol signals of **17** (δ 5.83, 5.59, 4.41) were replaced by the aromatic and carbinol protons of **19** (δ 6.69, 5.55).

B. Irradiation of a 315 mg sample of **16** dissolved in ether (50 mL) was performed in the manner described above and the photolysate was directly stirred with manganese dioxide (4.0 g) for 12 h. After filtration and solvent evaporation, the residue was subjected to chromatography on silica gel. Elution with 10% ethyl acetate in hexanes afforded 28 mg (17%) of **14/15** mixture. An increase in solvent polarity to 40% ethyl acetate resulted in the recovery of **6** (152 mg).

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Supporting Information Available: Copies of the ^{1}H NMR spectra of those compounds for which analytical data are not provided and the ^{13}C NMR spectrum of **16** (5 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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