**Cytotoxicity Tests.** For cytotoxicity tests the compounds were dissolved in DMSO (1 mg/mL stock solution) and the solutions diluted in 20% DMSO/phosphate buffered saline just prior to addition to cultures of HL 60 cells. Control cells received equal amounts of the DMSO/phosphate buffered saline. After incubation for 48 h the cells were washed, trypan blue was added, and the cells were counted.[20]

**Acknowledgment.** This investigation was supported in part by grant 1-KT-02 from the Tobacco-related Disease Research Program of the University of California. X-ray crystallographic analysis was carried out by Dr Peter Gantzel, Department of Chemistry, University of California, San Diego.

**Registry No.** 1, 1149-99-1; 1 monoacetate, 144156-55-8; 1 diacetate, 1099-42-9; 1 mono(3,5-dinitrobenzoate), 3677-16-5; 1 mono(fluorosulfonylbenzoate), 144156-56-9; 1 bis(fluorosulfonylbenzoate), 144156-57-0; 2, 1146-04-9; 3, 87625-62-5; 4, 112953-13-6; 5, 112953-12-5; 6, 25532-76-7; 7, 34338-99-3; 8, 30950-46-0; 10, 35938-45-5; 10 alcohol, 93525-52-1; 11, 125392-73-6; 12, 125472-36-8; 13, 35938-43-3; 14, 137247-02-0; 15, 34175-96-7; 18, 28282-65-7; 19, 144156-45-6; 20, 144156-46-7; 21, 144156-47-8; 22, 144156-48-9; 23, 144156-49-0; 24, 144156-50-3; 25, 144156-51-4; 26, 144156-52-5; 27, 144156-53-6; 28, 144156-54-7; $HSCH_2COOCH_3$, 2365-48-2.

**Supplementary Material Available:** Experimental details of the X-ray structure determination of 22, tables of atomic coordinates and equivalent isotropic displacement coefficients, bond lengths, bond angles, and anisotropic displacement coefficients, and $^1H$ NMR spectra for compounds 5, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, and 28 (21 pages). This material is contained in many 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.

# Reductive Cyclization of Quinone Methides

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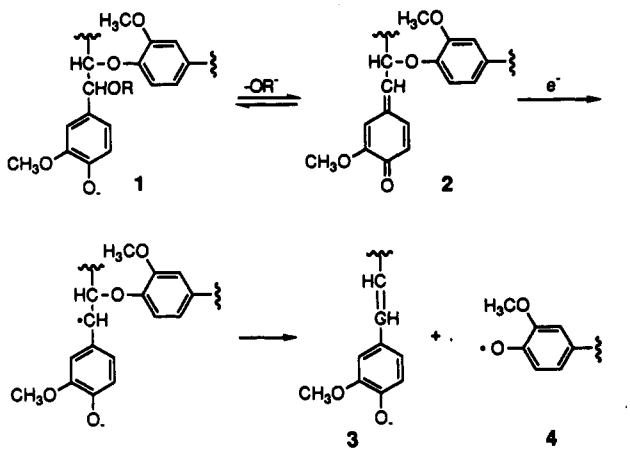
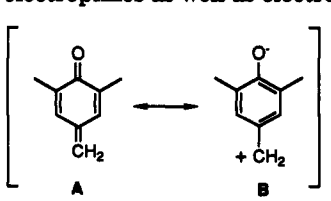
The first use of reduced quinone methides for the formation of carbon–carbon bonds in cyclization reactions is described. Treatment of quinone methides with $SmI_2$ resulted in intramolecular reaction with internal activated multiple bonds to afford 5- and 6-membered carbocycles in good yields. The activated multiple bonds used are aldehydes and $\alpha,\beta$-unsaturated esters and nitriles.

## Introduction

Simple *p*-quinone methides such as *p*-benzoquinone methide **A** are highly reactive compounds that readily undergo 1,6-addition of nucleophiles.[1,2] Aromatization of quinone methide **A** produces resonance structure **B** which illustrates the dipolar character of *p*-quinone methides. Upon O-protonation, or complexation with a Lewis Acid, the electrophilicity of the exocyclic alkylidene is enhanced to the point that even simple alkenes can act as nucleophiles toward quinone methides.[1,2] Quinone methides have been proposed as intermediates in a number of biological transformations and synthetic reactions.[1-4] Thus far, the synthesis applications of *p*-quinone methides have exploited their electrophilic character in reactions with nucleophiles, whereas the biological processes where quinone methides have been proposed as intermediates call for them to act as electrophiles as well as electron acceptors.[3]

**Scheme I. Proposed Mechanism of Lignan Fragmentation[3]**




Lignin fragmentation in pulping processes is proposed to involve the reduction of transient quinone methide intermediates.[4] In support of this notion, anthraquinone has been observed to accelerate fragmentation of lignans containing $\beta$-aryl ether linkages such as **1**. The acceleration

(1) (a) Angle, S. R.; Turnbull, K. D. *J. Am. Chem. Soc.* **1990**, *112*, 3698. (b) Angle, S. R.; Turnbull, K. D. *J. Am. Chem. Soc.* **1989**, *111*, 1136. (c) Angle, S. R.; Louie, M. S.; Mattson, H. L.; Yang, W. *Tetrahedron Lett.* **1989**, *30*, 1193. (d) Angle, S. R.; Arnaiz, D. O. *J. Org. Chem.* **1990**, *55*, 3708.

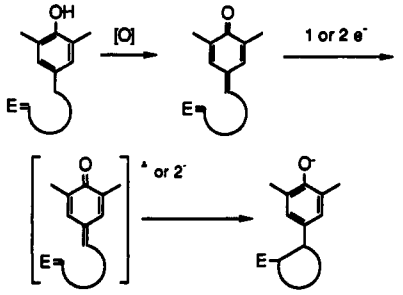
(2) For reviews on quinone methides see: (a) Turner, A. B. *Quart. Rev.* **1964**, *18*, 347. (b) Wagner, H. U.; Gompper, R. In *The Chemistry of Quinonoid Compounds*; Patai, S., Ed.; John Wiley and Sons: New York, 1974; Vol. 1, pp 1145–1178. (c) Gruenanger, P. In *Houben-Weyl Methoden der Organischen Chemie*; Mueller, E., Bayer, O., Eds.; G. Thieme Verlag: Stuttgart, 1979; Vol. VII/36, pp 395–521. (d) Peter, M. G. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 555. (e) Volod'kin, A. A.; Ershov, V. V. *Russ. Chem. Rev.* **1988**, *57*, 336.

(3) For recent reviews and leading references to lignans and neolignans see: (a) Macrae, W. D.; Towers, G. H. N. *Phytochemistry* **1984**, *23*, 1207. (b) Whiting, D. A. *Nat. Prod. Rep.* **1990**, *7*, 349. (c) Whiting, D. A. *Nat. Prod. Rep.* **1987**, *4*, 499.

(4) (a) Smith, D. A.; Dimmel, D. R. *J. Org. Chem.* **1988**, *53*, 5428 and references cited therein. (b) Pardini, V. L.; Smith, C. Z.; Utley, J. H. P.; Vargas, R. R.; Viertler, H. *J. Org. Chem.* **1991**, *56*, 7305.

0022-3263/92/1957-6883$03.00/0 

**Scheme II. Proposed Reductive Cyclization of Quinone Methides**

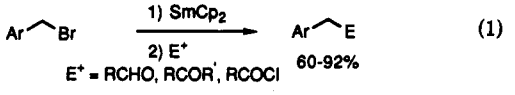


is thought to result from electron transfer to an intermediate quinone methide **2** to afford a radical anion which then fragments to styrene **3** and phenoxy radical **4** (Scheme I).[4a] The presence of radicals is supported by the observation that stable β-aryl ether quinone methides can be cleaved in the presence of electrochemically generated anthraquinone radical anions.[4] In addition, Smith and Dimmel subjected phenols with pendant alkenes to pulping conditions (NaOH, 135 °C, anthraquinone or glucose) and observed small amounts of cyclized products. These authors provided evidence that the cyclized products resulted from the addition of a benzylic radical to the alkene.[4a]

Utley and co-workers have shown that highly substituted, sterically hindered quinone methides could be electrochemically reduced to radical anions and dianions which could then be used as bases in Wittig reactions.[5] Quinone methides lacking significant steric hindrance were not well behaved and prone to polymerization upon reduction.

We felt that it might be possible to exploit quinone methides as electron acceptors and employ the resulting intermediates in the formation of carbon–carbon bonds. Addition of an electron(s) to a preformed quinone methide followed by reaction of the resulting benzylic radical and/or anion with a pendant activated multiple bond would result in the net coupling of two electrophilic moieties. Among the many electron donors capable of chemically reducing quinone methides, we felt that reductive coupling using $SmI_2$ would be successful. $SmI_2$ has a high reduction potential and has been used in a number of one- and two-electron reduction processes.[6]

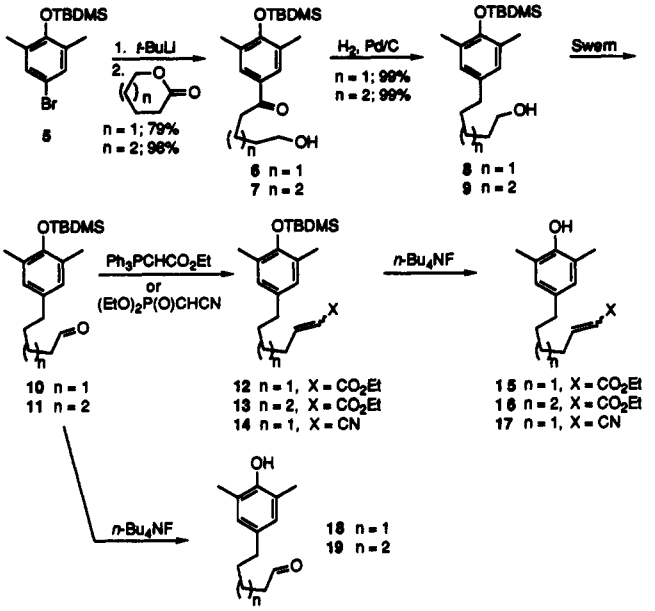
Kagan has shown that 2 equiv of $SmI_2$ effectively reduced benzylic bromides to benzylic samarium compounds which could be trapped with electrophiles in intermolecular reactions (eq 1).[7] The conventional methods for coupling benzylic carbons to carbon electrophiles involves the synthesis of labile benzylic halides.[8]



(1)

Quinone methides which could be derived from the corresponding phenols via oxidation might serve as precursors to benzylic radicals and/or anions upon reduction with $SmI_2$ (Scheme II). Either species might undergo cyclization by addition to an activated multiple bond. This approach would avoid preparation and handling of reactive benzylic halides.

**Scheme III. Synthesis of the Cyclization Substrates**



If successful, the oxidation/reduction sequence described above would be an important method for the synthesis of oxygenated aromatic compounds. In addition, it complements the present synthesis methods that we[1] and others[2] have developed to exploit quinone methides as electrophiles. This study might also provide further insight into the lignin degradation processes where quinone methides have been postulated as intermediates.[4] To our knowledge, this is the first reported use of quinone methides as synthons for benzylic radicals/anions in carbon–carbon bond-forming reactions.

## Results and Discussion

Cyclization precursors **15–19** containing aldehydes, α,β-unsaturated esters, and an α,β-unsaturated nitrile were synthesized as shown in Scheme III. Aldehydes **10** and **11** served as versatile intermediates that were elaborated into the cyclization substrates. Particularly noteworthy was the high yield in the reaction of the aryllithium derived from **5** with both caprolactone and valerolactone.

Oxidation of the phenolic cyclization precursors was accomplished with $Ag_2O$ (15 equiv, benzene-$d_6$).[9] The resulting quinone methides were characterized by $^1H$ NMR spectroscopy and were generally reduced immediately but were stable enough to be stored in solution if desired. The reaction of the quinone methides and $SmI_2$ afforded several products depending upon the reaction conditions (Table I). Optimized conditions afforded cyclized material in good yield and called for addition of a dilute solution of quinone methide (≤5 mM) to a solution of $SmI_2$ at 65 °C for the activated alkenes or at 35 °C for the aldehydes. Excess $SmI_2$ must be present during the reaction to avoid $Sm^{3+}$-catalyzed formation of styrene byproducts.

Treatment of cyclization precursor **20** with $SmI_2$ afforded *trans*-arylcyclopentanol **21** as a >5:1 ratio of diastereomers (Table I, entry 1). All other cyclizations afforded 1:1 mixtures of cyclized products. The relative stereochemistry of the aryl and hydroxyl substituents of

(5) Goulart, M. O. F.; Ling-Chung, S. K.; Utley, J. H. P. *Tetrahedron Lett.* **1987**, *28*, 6081.

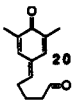
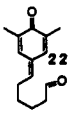
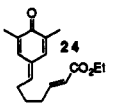
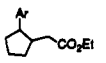
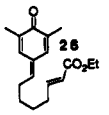
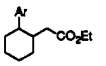
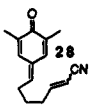
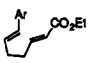
(6) For reviews on the use of $SmI_2$ in organic chemistry see: (a) Molander, G. A. *Chem. Rev.* **1992**, *92*, 29. (b) Soderquist, J. A. *Aldrichim. Acta* **1991**, *24*, 15.

(7) Collin, J.; Namy, J. L.; Bied, C.; Kagan, H. B. *Inorg. Chim. Acta* **1987**, *140*, 29.

(8) Benzylic halides are especially labile when the aromatic ring is highly oxygenated: cf. Angle, S. R.; Louie, M. S. *J. Org. Chem.* **1991**, *56*, 2853.

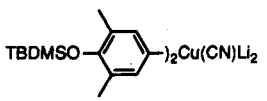
(9) A solvent effect on the oxidation was observed. For example, the oxidation of quinone methide **24** in benzene-$d_6$ required 1–2 h at rt while the same oxidation in THF required 9–10 h at 65 °C.

**Table I. Quinone Methide-$SmI_2$ Cyclizations**

| entry | phenol | quinone methide | reaction conds[a] | product[b] | yield[c] |
|---|---|---|---|---|---|
| 1 | 18 |  20 | A |  21 | 67% |
| 2 | 19 |  22 | A |  23 | 30-50% |
| 3 | 15 |  24 | B |  25 | 87% |
| 4 | 15 | 24 | D | 25 | 40% |
| 5 | 16 |  26 | C |  27 | 70% |
| 6 | 17 |  28 | B |  29 | 78% |
| 7 | 15 | 24 | E |  30 | 64% |

[a] Reaction conditions: A = quinone methide (5 mM for **20**, 1 mM for **22**) was added to $SmI_2$ (0.03 M) at 35 °C; B = quinone methide (5 mM) was added to $SmI_2$ (0.05 M) at 65 °C; C = quinone methide (1 mM) was added to $SmI_2$ (0.05 M) at 65 °C; D = quinone methide (5 mM) was added to $SmI_2$ (0.05 M) at 40 °C; E = $SmI_2$ (0.05 M) was added to quinone methide (5 mM) at 65 °C. [b] Ar = 3,5-dimethyl-4-hydroxyphenyl. [c] Yield for 1:1 mixture of diastereomers except for **21** which is a >5:1 mixture of diastereomers by $^1H$ NMR analysis.

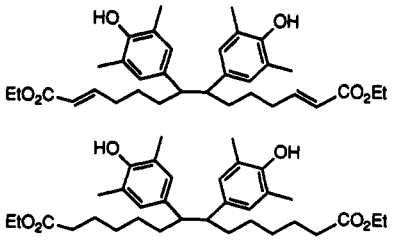
**21** (major isomer) was assigned as trans based upon comparison of the spectral data with an authentic sample obtained from addition of arylcuprate **31** (derived from **5**) to cyclopentene oxide followed by desilylation.[10]




**31**

Addition of α,β-unsaturated ester quinone methide **24** to a solution of $SmI_2$ at lower temperatures (<40 °C) gave a lower yield of the desired product **25** and significant amounts of a compound that is believed to be a dimer resulting from bond formation between the two benzylic carbons (Table I, entry 4). Dimeric products retaining the α,β-unsaturated ester functionality and those with the alkene reduced were isolated as mixtures of diastereomers and characterized by $^1H$ NMR (structures below).[11] The formation of these dimers under mild conditions illustrates the ease of reduction of the quinone methide.

Cyclization to form cyclohexane **27** required that a more dilute solution (1 mM) of quinone methide **26** be added







to $SmI_2$ than the corresponding cyclopentane precursor **24** to avoid the formation of significant amounts of dimeric products (Table I, entry 5).

Due to the relatively high reduction potential of aldehydes, the cyclizations of aldehyde quinone methides **20** and **22** were much more sensitive to reaction conditions than were the corresponding activated alkene cyclizations.[12] The formation of products derived from competitive reduction of the aldehyde could not be eliminated under any of the conditions examined.[13] Although we were able to optimize the reaction conditions to obtain cyclopentanol **21** as the major product, the reaction leading to cyclohexanol **23** was especially capricious. Several runs of the cyclization reaction, under seemingly identical conditions, afforded **23** in yields varying from 30% to 50%.

The mechanism of the cyclization process must involve the initial reduction of the quinone methide to afford a radical anion/dianion that then undergoes cyclization. This conclusion is based on the isolation of dimer byproducts (described above) that retain the intact activated mutiple bond and reduction potentials of the functional groups involved. Utley has shown the first reduction potential of quinone methides that are similar in structure to those used here to be about −1.0 V and the second reduction potential to be approximately 0.5 V more negative.[14a] Reduction potentials for aldehydes normally are in the −1.5 to −2.0 V range.[14b] The precise conditions of the reductive cyclization (solvent, temperature, etc.) and the presence of samarium(II) and -(III) will effect these values.

It is unclear from the available data whether the cyclization occurs at the radical stage or if a second one-electron reduction occurrs followed by cyclization. The oxidation potential of $SmI_2$ (1.55 V) is in the right range to reduce the benzylic radical to the anion before it has a chance to cyclize. In an attempt to resolve this issue, two experiments were conducted. In the first experiment, $SmI_2$ was slowly added to a solution of α,β-unsaturated ester quinone methide **24** at 65 °C, conditions which should favor a radical cyclization, to afford styrene **30** as the major product. Unfortunately, this result does not distinguish between the two pathways since the formation of styrene **30** was presumably the result of competitive $Sm^{3+}$-catalyzed enolization of the quinone methide. In the second experiment, the quinone methide derived from dimethylalkene **32** (synthesized via a Wittig reaction of isopropylidenetriphenylphosphorane and aldehyde **10**) was submitted to the $SmI_2$ cyclization conditions (65 °C) to afford benzylic dimer **33** (eq 2).[15] If cyclized product had

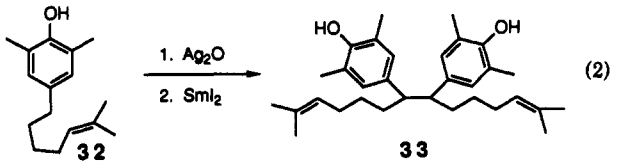
(10) Lipshutz, B. H.; Kozlowski, J.; Wilhelm, R. S. *J. Am. Chem. Soc.* **1982**, *104*, 2305.

(11) The dimers were not fully characterized; however, their $^1H$ NMR spectra showed the expected similarities to dimer **33**. In addition, the dimer in which the alkene had been reduced showed the expected LR-MS spectrum.

(12) Similar problems have been seen with $SmI_2$-induced Barbier coupling reactions of marginally reactive organic halides with aldehydes. For example, see: (a) Souppe, J.; Namy, J. L.; Kagan, H. B. *Tetrahedron Lett.* **1982**, *23*, 3497. (b) Namy, J. L.; Souppe, J.; Collin, J.; Kagan, H. B. *J. Org. Chem.* **1984**, *49*, 2045. (c) Souppe, J.; Danon, L.; Namy, J. L.; Kagan, H. B. *J. Organomet. Chem.* **1983**, *250*, 227.

(13) $SmI_2$ has been commonly used to reduce aldehydes. For the use of ketyl radicals generated from the $SmI_2$ reduction of aldehydes in coupling reactions with alkenes see ref 6 and references cited therein.

(14) (a) Goulart, M. O. F.; Utley, J. H. P. *J. Org. Chem.* **1988**, *53*, 2520. (b) Kyriacou, D. K. *Basics of Electroorganic Synthesis*; John Wiley and Sons: New York, 1981; pp 140–141.




32 33 (2)

been obtained, a radical pathway would be implicated. The failure to see cyclization is consistent with an anionic cyclization; however, the intermediacy of a stable benzylic radical that requires an activated alkene for addition cannot be ruled out.[16,17]

The results of our study are consistent with the intermediacy of benzylic radicals and/or anions in the key carbon–carbon bond-forming reaction. Neither intermediate can be excluded from the available information.

## Conclusion

We have shown that quinone methides can be chemically reduced by $SmI_2$ and that these reduced species react with pendant activated multiple bonds to afford cyclized products in good yield. Formally, the process involves the mild benzylic functionalization of a substituted aromatic compound in the presence of other reactive functional groups. This oxidation–reduction sequence avoids the use of highly labile benzylic halides as precursors to benzylic anions and demonstrates the first use of reduced quinone methides in synthesis. Our work shows that the chemistry of reduced quinone methides can lead to carbon–carbon bond-forming reactions. Since quinone methides are proposed as intermediates in the biosynthesis of lignans and neolignans, our results show it is chemically reasonable to consider biosynthetic pathways that involve reduced quinone methide intermediates. Further studies to determine the nature of the reduced quinone methide intermediate (radical or anion) and to exploit the chemistry of these intermediates in synthesis are in progress.

## Experimental Section[18]

General Information. NMR shifts reported are relative to $CDCl_3$ or $C_6D_6$; coupling constants, $J$, are reported in Hz and refer to apparent peak multiplicities and may not be true coupling constants. HPLC was carried out with an RI detector using a Rainin Dynamax 60-A column 8-μm silica gel column (4.6-mm inside diameter, 25-cm length). Sm(0) was flame dried under Ar prior to use. Solvents for chromatography and recrystallization were distilled prior to use. Commercial compounds were purchased from Ficher Scientific or Aldrich Chemical Co. Concentration refers to removal of solvent under reduced pressure (water aspirator) with a Büchi rotavapor. Unless stated otherwise, all reactions were run under an atmosphere argon in flame-dried glassware.

**1-[4-[(*tert*-Butyldimethylsilyl)oxy]-3,5-dimethylphenyl]-5-hydroxy-1-pentanone (6).** *t*-BuLi (4.2 mL of a 1.93 M solution in pentane, 8.1 mmol) was added dropwise to a stirred solution of aryl bromide **5** (1.28 g, 4.06 mmol) and ether (20 mL) at −78 °C. The resulting white mixture was stirred for 1 h at −78 °C and then transferred dropwise via a cannula cooled in dry ice into a solution of δ valerolactone (0.75 mL, 7.9 mmol) and THF (20 mL) at −78 °C. The resulting solution was allowed to stir for 1 h at −78 °C and was then poured into aqueous saturated $NH_4Cl$ (60 mL). The aqueous layer was extracted with ether (3 × 40 mL). The combined organic extracts were washed with brine (50 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (3:1 hexanes/ethyl acetate followed by 1:1 hexanes/ethyl acetate) afforded 1.08 g (79%) of **6** as a colorless oil: $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.83 (s, 2 H, ArH), 3.86 (t, $J$ = 6.3 Hz, 2 H, $CH_2OH$), 3.16 (t, $J$ = 7.0 Hz, 2 H, $CH_2C(O)Ar$), 2.70 (bs, 1 H, OH), 2.45 (s, 6 H, $ArCH_3$), 2.02 (m, 2 H), 1.85 (m, 2 H), 1.23 (s, 9 H, $SiC(CH_3)_3$), 0.42 (s, 6 H, $Si(CH_3)_2$); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 199.8, 156.7, 130.1, 129.1, 128.6, 62.1, 37.6, 32.2, 25.9, 20.3, 18.7, 17.8, −3.0; IR ($CDCl_3$) 3500, 2957, 1720, 1670, 1597 $cm^{-1}$; MS (EI, 20 eV) $m/z$ 336 ($M^+$, 51), 318 (62), 223 (100); HRMS calcd for $C_{19}H_{32}O_3Si$ 336.2121, found 336.2112.

**1-[4-[(*tert*-Butyldimethylsilyl)oxy]-3,5-dimethylphenyl]-6-hydroxy-1-hexanone (7).** The procedure given previously for the preparation of **6** was carried out with *t*-BuLi (880 μL of a 1.91 M solution in pentane, 1.7 mmol), aryl bromide **5** (265 mg, 0.840 mmol), and ε-caprolactone (70 μL, 0.63 mmol). Flash chromatography (3:1 hexanes/ethyl acetate followed by 1:1 hexanes/ethyl acetate) afforded 216 mg (98%) of aryl ketone **7** as a colorless oil: $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.58 (s, 2 H, ArH), 3.62 (t, $J$ = 6.4 Hz, 2 H, $CH_2OH$), 2.89 (t, $J$ = 7.2 Hz, 2 H, $C(O)CH_2$), 2.39 (bs, 1 H, OH), 2.22 (s, 6 H, $ArCH_3$), 1.74–1.39 (m, 6 H), 1.00 (s, 9 H, $SiC(CH_3)_3$), 0.18 (s, 6 H, $Si(CH_3)_2$); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 199.7, 156.6, 130.2, 129.1, 128.6, 62.4, 38.0, 32.4, 25.9, 25.4, 24.0, 18.7, 17.8, −3.0; IR ($CHCl_3$) 3625, 3486, 2954, 1713, 1671, 1597 $cm^{-1}$; MS (EI, 20 eV) $m/z$ 350 ($M^+$, 26), 278 (79), 223 (100); HRMS calcd for $C_{20}H_{34}O_3Si$ 350.2277, found 350.2268.

**5-[4-[(*tert*-Butyldimethylsilyl)oxy]-3,5-dimethylphenyl]pentanol (8).** Pd/C (5%, 347 mg, 0.163 mmol) was added to a solution of hydroxy ketone **6** (1.04 g, 2.97 mmol) and ethanol (40 mL). The resulting mixture was placed on a hydrogenator at 1 atm of $H_2$ pressure for 12 h, after which the reaction mixture was filtered through silica gel (eluted with ether) and concentrated. Flash chromatography (5:1 hexanes/ethyl acetate followed by 3:1 hexanes/ethyl acetate) afforded 0.844 g (88%) of alcohol **8** as a colorless oil. HPLC (5:1 hexane/ethyl acetate, 1 mL/min, $t_R$ 13.4 min) afforded an analytical sample: $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.77 (s, 2 H, ArH), 3.64 (t, $J$ = 6.6 Hz, 2 H, $CH_2OH$), 2.48 (t, $J$ = 7.6 Hz, 2 H, $CH_2Ar$), 2.18 (s, 6 H, $ArCH_3$), 1.63 (m, 4 H), 1.42 (m, 2 H), 1.03 (s, 9 H, $SiC(CH_3)_3$), 0.179, (s, 6 H, $Si(CH_3)_2$); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 149.9, 135.0, 128.6, 128.1, 63.0, 35.0, 32.7, 31.4, 26.1, 25.4, 18.7, 17.8, −3.0; IR ($CHCl_3$) 3629, 2933, 2859, 1482, 1474, 1255, 1235, 904, 841 $cm^{-1}$; MS (EI, 20 eV) $m/z$ 322 ($M^+$, 62), 247 (13), 210 (23), 209 (100), 191 (16), 75 (16), 73 (15). Anal. Calcd for $C_{19}H_{34}O_2Si$: C, 70.73; H, 10.64. Found: 70.33, 10.29.

**6-[4-[(*tert*-Butyldimethylsilyl)oxy]-3,5-dimethylphenyl]hexanol (9).** The procedure given previously for the preparation of **8** was carried out with ketone **7** (91.7 mg, 0.262 mmol), Pd/C (5%, 28 mg, 0.013 mmol), and ethanol (15 mL). Flash chromatography (5:1 hexanes/ethyl acetate followed by 3:1 hexanes/ethyl acetate) afforded 87 mg (99% yield) of hexanol **9** as a colorless oil. HPLC (5:1 hexane/ethyl acetate, 1 mL/min, $t_R$ 13.4 min) afforded an analytical sample: $^1H$ NMR (300 MHz) δ 6.76 (s, 2 H, ArH), 3.64 (t, $J$ = 6.6 Hz, 2 H, $CH_2OH$), 2.46 (t, $J$ = 7.7 Hz, 2 H, $ArCH_2$), 2.18 (s, 6 H, $ArCH_3$), 1.59–1.53 (m, 4 H), 1.38–1.35 (m, 4 H), 1.03 (s, 9 H, $SiC(CH_3)_3$), 0.18 (s, 6 H, $Si(CH_3)_2$); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 149.9, 135.2, 128.6, 128.1, 63.0, 35.0, 32.7, 31.6, 29.1, 26.1, 25.6, 18.8, 17.8, −3.0; IR ($CHCl_3$) 3625, 2933 $cm^{-1}$; MS (EI, 20 eV) $m/z$ 336 ($M^+$, 33), 209 (100). Anal. Calcd for $C_{20}H_{36}O_2Si$: C, 71.35; H, 10.80. Found: C, 71.74; H, 10.65.

**5-[4-[(*tert*-Butyldimethylsilyl)oxy]-3,5-dimethylphenyl]pentanal (10).** Using the general procedure of Swern and co-workers,[19] a solution of DMSO (87 μL, 1.2 mmol) and $CH_2Cl_2$ (5 mL) was added dropwise to a solution of oxalyl chloride (80 μL, 0.92 mmol) and $CH_2Cl_2$ (5 mL) at −50 °C. The resulting colorless solution was allowed to stir for 10 min, and then a solution of arylpentanol **8** (198 mg, 0.61 mmol) and $CH_2Cl_2$ (10 mL) was

(15) For early examples of using alkenes to probe for radical reactions see: (a) Garst, J. F.; Ayers, P. W.; Lamb, R. C. *J. Am. Chem. Soc.* **1966**, *88*, 4260. (b) Walling, C.; Cooley, J. H.; Ponaras, A. A.; Racah, E. J. *J. Am. Chem. Soc.* **1966**, *88*, 5361.

(16) (a) March, J. *Advanced Organic Chemistry*; John Wiley and Sons: New York, 1985; p 164. (b) The cyclization of benzylic radicals has been shown to be highly dependent upon the reacting partner of the radical; cf. Clerici, A.; Minisci, F.; Porta, O. *Tetrahedron* **1973**, *29*, 2775.

(17) It is possible that a benzylic anion could be formed via addition of iodide to the quinone methide followed by in situ reduction of the resulting benzylic iodide by $SmI_2$. This pathway is precedented in the Barbier reactions of alkyl tosylates with ketones which are thought to involve the formation of an alkyl iodide intermediate in the presence of $SmI_2$: see ref 6, pp 46–47.

(18) General experimental details have been recently reported: see ref 8.

(19) (a) Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480. (b) Luly, J. R.; Dellaria, J. F.; Plattner, J. J.; Soderquist, J. L.; Yi, N. *J. Org. Chem.* **1987**, *52*, 1487.

added dropwise over 10 min. The resulting solution was allowed to stir for 15 min at −50 °C after which a solution of triethylamine (340 μL, 2.5 mmol) and $CH_2Cl_2$ (5 mL) was added. The reaction mixture was warmed to 0 °C in an ice bath. After 1 h the colorless solution was poured into brine (30 mL) and $CH_2Cl_2$ (20 mL). The organic layer was washed sequentially with 1 N HCl (30 mL), brine (30 mL), 30% $Na_2CO_3$ (30 mL), and brine (30 mL). The colorless solution was dried ($Na_2SO_4$) and concentrated to afford 195 mg (99%) of arylpentanal **10** as a pale yellow liquid which was used without purification in subsequent reactions: $^1$H NMR (300 MHz, $CDCl_3$) δ 9.75 (bs, 1 H, C(O)H), 6.78 (s, 2 H, ArH), 2.51 (t, $J$ = 7.0 Hz, 2 H, $ArCH_2$ or $CH_2C(O)$), 2.44 (t, $J$ = 7.0 Hz, 2 H, $CH_2C(O)$ or $ArCH_2$), 2.20 (s, 6 H, $ArCH_3$), 1.64 (m, 4 H), 1.05 (s, 9 H, $SiC(CH_3)_3$), 0.20 (s, 6 H, $Si(CH_3)_2$); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 202.5, 150.0, 134.3, 128.5, 128.1, 43.7, 34.6, 31.0, 26.0, 21.7, 18.6, 17.7, −3.0; IR ($CHCl_3$) 2955, 1722 cm$^{-1}$; MS (EI, 20 eV) $m/z$ 320 ($M^+$, 100), 263 (63), 193 (22); HRMS calcd for $C_{19}H_{32}O_2Si$ 320.2172, found 320.2176.

**6-[4-[(*tert*-Butyldimethylsilyl)oxy]-3,5-dimethylphenyl]hexanal (11).** The procedure given previously for the preparation of **10** was carried out with DMSO (130 μL, 1.8 mmol), $CH_2Cl_2$ (5 mL), oxalyl chloride (120 μL, 1.4 mmol), arylhexanol **9** (302 mg, 0.897 mmol), and triethylamine (500 μL, 3.6 mmol). Concentration afforded 335 mg (112%) of arylhexanal **11** as a pale yellow liquid which was used without purification in subsequent reactions: $^1$H NMR (300 MHz, $CDCl_3$) δ 9.76 (br s, 1 H, C(O)H), 6.77 (s, 2 H, ArH), 2.49 (t, $J$ = 7.3 Hz, 2 H, $ArCH_2$ or $C(O)CH_2$), 2.42 (t, $J$ = 6.9 Hz, 2 H, $C(O)CH_2$ or $ArCH_2$), 2.20 (s, 6 H, $ArCH_3$), 1.69–1.58 (m, 4 H), 1.39–1.36 (m, 2 H), 1.05 (s, 9 H, $SiC(CH_3)_3$), 0.20 (s, 6 H, $Si(CH_3)_2$); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 202.6, 149.9, 134.8, 128.5, 128.0, 43.7, 34.7, 31.2, 28.7, 26.0, 21.9, 18.6, 17.7, −3.0; IR ($CHCl_3$) 2933, 1723 cm$^{-1}$; MS (EI, 20 eV) $m/z$ 334 ($M^+$, 39), 209 (100); HRMS calcd for $C_{20}H_{34}O_2Si$ 334.2328, found 334.2317.

**(*E* and *Z*)-Ethyl 7-[4-[(*tert*-Butyldimethylsilyl)oxy]-3,5-dimethylphenyl]-2-heptenoate (12).** (Carbethoxymethylene)triphenylphosphorane (250 mg, 0.72 mmol) was added to a stirred solution of aldehyde **10** (154 mg, 0.481 mmol) and ether (20 mL) at rt. After 8 h the reaction mixture was poured into brine (50 mL). The aqueous layer was extracted with ether (3 × 30 mL). The organic extracts were combined, washed with brine (50 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (20:1 hexanes/ethyl acetate) afforded 171 mg (91%) of unsaturated ester **12** as a colorless oil (7:1 $E/Z$ mixture, $^1$H NMR): $^{13}$C NMR (75 MHz, $CDCl_3$) δ 166.6, 150.4, 149.9, 149.1, 134.6, 128.5, 128.1, 128.1, 121.3, 119.7, 60.0, 59.7, 34.7, 32.0, 31.2, 31.0, 28.8, 28.6, 27.6, 26.1, 18.7, 17.8, 14.2, −3.0. HPLC (40:1 hexane/ethyl acetate, 1 mL/min, $t_R$ 7.3 min) provided an analytical sample of (*E*)-**12**: $^1$H NMR (300 MHz, $CDCl_3$) δ 6.96 (dt, $J$ = 7.0, 15.6 Hz, 1 H, $CHCHCO_2Et$), 6.75 (s, 2 H, ArH), 5.80 (d, $J$ = 15.6 Hz, 1 H, $CHCO_2Et$), 4.18 (q, $J$ = 7.1 Hz, 2 H, $OCH_2CH_3$), 2.47 (t, $J$ = 7.44 Hz, 2 H, $ArCH_2$), 2.25–2.16 (m, 2 H, $CH_2CHCHCO_2Et$), 2.18 (s, 6 H, $ArCH_3$), 1.63–1.46 (m, 4 H), 1.29 (t, $J$ = 7.1 Hz, 3 H, $OCH_2CH_3$), 1.03 (s, 9 H, $SiC(CH_3)_3$), 0.18 (s, 6 H, $Si(CH_3)_2$); IR ($CHCl_3$) 3006, 1709, 1654 cm$^{-1}$; MS (EI, 20 eV) $m/z$ 390 ($M^+$, 16), 333 (100). Anal. Calcd for $C_{23}H_{38}O_3Si$: C, 70.70; H, 9.82. Found: C, 70.59; H, 9.58.

**(*E* and *Z*)-Ethyl 7-[4-[(*tert*-Butyldimethylsilyl)oxy]-3,5-dimethylphenyl]-2-octenoate (13).** The procedure given previously for the preparation of **12** was carried out with (carbethoxymethylene)triphenylphosphorane (140 mg, 0.40 mmol) and aldehyde **11** (89.7 mg, 0.268 mmol). Flash chromatography (20:1 hexanes/ethyl acetate) afforded 97.6 mg (90.%) of unsaturated ester **13** as a colorless oil (7:1 $E/Z$ mixture, $^1$H NMR). HPLC (40:1, 0.9 mL/min, $t_R$ 6.9 min) provided an analytical sample of (*E*)-**13**: $^1$H NMR (300 MHz, $CDCl_3$) δ 6.98 (dt, $J$ = 7.2, 15.6 Hz, 1 H, (*E*)-$HCCHCO_2Et$), 6.78 (s, 2 H, ArH), 6.21 (dt, $J$ = 7.6, 11.4 Hz, 1 H, (*Z*)-$CHCHCO_2Et$), 5.82 (d, $J$ = 15.6 Hz, 1 H, (*E*)-$CHCO_2Et$), 5.77 (partially obscured d, $J$ = 11.4 Hz, 1 H, (*Z*)-$CHCO_2Et$), 4.20 (q, $J$ = 7.1 Hz, 2 H, $OCH_2$), 2.49 (t, $J$ = 7.4 Hz, 2 H, $ArCH_2$), 2.26–2.14 (m, 2 H), 2.20 (s, 6 H, $ArCH_3$), 1.65–1.34 (m, 6 H), 1.30 (t, $J$ = 7.1 Hz, 3 H, $OCH_2CH_3$), 1.05 (s, 9 H, $SiC(CH_3)_3$), 0.20 (s, 6 H, $Si(CH_3)_2$); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 166.6, 150.4, 149.9, 149.2, 135.0, 128.5, 128.0, 121.2, 119.6, 60.0, 59.6, 34.9, 32.1, 31.3, 29.0, 28.8, 28.6, 27.9, 26.1, 18.7, 17.7, 14.2, −3.0; IR ($CHCl_3$) 2934, 1709, 1474 cm$^{-1}$; MS (EI, 70 eV) $m/z$ 404 ($M^+$, 4), 347 (100), 209 (55). Anal. Calcd for $C_{24}H_{40}O_3Si$: C, 71.22; H, 9.98. Found: C, 71.30; H, 10.10.

**(*E* and *Z*)-6-[4-[(*tert*-Butyldimethylsilyl)oxy]-3,5-dimethylphenyl]-2-heptenenitrile (14).** *n*-BuLi (280 μL of a 2.26 M solution in hexanes, 0.63 mmol) was added to a solution of diethyl cyanomethylphosphonate (110 μL, 0.68 mmol) and ether (18 mL) at −78 °C. The cooling bath was removed, and the reaction mixture was allowed to warm to rt and stirred for 30 min. The resulting white mixture was cooled to −78 °C, and to this was added dropwise a solution of aldehyde **10** (154 mg, 0.481 mmol) and ether (10 mL). Immediately after the addition was completed, the cooling bath was removed and the reaction mixture was allowed to warm to rt and stirred overnight. The reaction mixture was poured into brine (50 mL), and the aqueous layer was extracted with ether (3 × 30 mL). The combined organic extracts were washed with brine (30 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (20:1 hexanes/ethyl acetate followed by 10:1 hexanes/ethyl acetate) afforded 123 mg (74%) of α,β-unsaturated nitrile **14** as a colorless oil (inseparable 2.3:1 $E/Z$ mixture, $^1$H NMR). HPLC (40:1 hexane/ethyl acetate, 1.0 mL/min, $t_R$ 6.7 min) afforded an analytical sample of nitrile **14** as a 2.3:1 $E/Z$ mixture ($^1$H NMR): $^1$H NMR (300 MHz, $CDCl_3$) δ 6.77 (s, 2 H, ArH), 6.76 (s, 2 H, ArH), 6.71 (dt, $J$ = 16.3, 7.0 Hz, 1 H, (*E*)-$HCCHCN$), 6.46 (dt, $J$ = 10.9, 7.7 Hz, 1 H, (*Z*)-$HCCHCN$), 5.31 (apparent d, $J$ = 16.0 Hz, 1 H, (*E*)-$CHCHCN$ and (*Z*)-$CHCHCN$), 2.53–2.41 (m, 3 H), 2.28–2.16 (m, 1 H), 2.20 (s, 6 H, $ArCH_3$), 1.66–1.45 (m, 4 H), 1.04 (s, 9 H, $SiC(CH_3)_3$), 0.19 (s, 6 H, $Si(CH_3)_2$); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 155.9, 155.0, 150.1, 150.0, 134.4, 134.3, 128.8, 128.6, 128.5, 128.2, 128.2, 117.5, 116.0, 99.7, 99.5, 34.8, 34.7, 34.6, 33.2, 31.7, 30.9, 30.8, 27.8, 27.2, 26.3, 26.1, 18.7, 17.8, −2.8, −2.9; IR ($CHCl_3$) 2933, 2225, 1483 cm$^{-1}$; MS (EI, 70 eV) $m/z$ 343 ($M^+$, 1), 286 (100); HRMS calcd for $C_{21}H_{33}NOSi$ 343.2331, found 343.2313.

**(*E* and *Z*)-Ethyl 7-(3,5-Dimethyl-4-hydroxyphenyl)-2-heptenoate (15).** The procedure given previously for the preparation of **12** was carried out with tetra-*n*-butylammonium fluoride (130 μL of a 1.0 M solution in THF, 0.13 mmol) and silyl ether **12** (171 mg, 0.438 mmol). Flash chromatography (10:1 hexanes/ethyl acetate followed by 5:1 hexanes/ethyl acetate) afforded 98 mg of (*E*)-**15** as a colorless oil and 14 mg of (*Z*)-**15** as a colorless oil (92% total yield). HPLC (9:1 hexane/ethyl acetate, 1 mL/min, $t_R$ 11.0 min) provided an analytical sample of (*E*)-**15**: $^1$H NMR (300 MHz, $CDCl_3$) δ 6.96 (dt, $J$ = 15.6, 7.0 Hz, 1 H, $CHCHCO_2Et$), 6.78 (s, 2 H, ArH), 5.81 (d, $J$ = 15.6 Hz, 1 H, $CHCO_2Et$), 4.68 (s, 1 H, ArOH), 4.19 (q, $J$ = 7.1 Hz, 2 H, $OCH_2CH_3$), 2.49 (t, $J$ = 7.4 Hz, 2 H, $ArCH_2$), 2.23 (s, 6 H, $ArCH_3$), 2.25–2.18 (m, 2 H, $CH_2CHCHCO_2Et$), 1.63–1.46 (m, 4 H), 1.29 (t, $J$ = 7.1 Hz, 3 H, $OCH_2CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 166.8, 150.2, 149.2, 133.8, 128.4, 122.8, 121.3, 60.1, 34.8, 32.1, 31.3, 27.6, 15.9, 14.3; IR ($CHCl_3$) 3611, 3007, 1709, 1654 cm$^{-1}$; MS (EI, 20 eV) $m/z$ 276 ($M^+$, 45), 135 (100). Anal. Calcd for $C_{17}H_{24}O_3$: C, 73.90; H, 8.80. Found: C, 73.94; H, 8.74.

**(*E* and *Z*)-Ethyl 8-(3,5-Dimethyl-4-hydroxyphenyl)-2-octenoate (16).** The procedure given previously for the preparation of **15** was carried out with tetra-*n*-butylammonium fluoride (72 μL of a 1.0 M solution in THF, 0.072 mmol) and silyl ether **13** (97.4 mg, 0.241 mmol). Flash chromatography (10:1 hexanes/ethyl acetate followed by 5:1 hexanes/ethyl acetate) afforded 61.2 mg of (*E*)-**16** as a colorless oil and 8.5 mg of (*Z*)-**16** as a colorless oil (99% total yield). HPLC (5:1 hexane/ethyl acetate, 1 mL/min, $t_R$ 6.7 min) provided an analytically pure sample of (*E*)-**16**: $^1$H NMR (300 MHz, $CDCl_3$) δ 6.97 (dt, $J$ = 15.6, 7.0 Hz, 1 H, $HCCHCO_2Et$), 6.78 (s, 2 H, ArH), 5.81 (d, $J$ = 15.6 Hz, 1 H, $CHCO_2Et$), 4.67 (s, 1 H, ArOH), 4.19 (q, $J$ = 7.1 Hz, 2 H, $OCH_2$), 2.47 (t, $J$ = 7.7 Hz, 2 H, $ArCH_2$), 2.23 (s, 6 H, $ArCH_3$), 2.21–2.16 (m, 2 H, $CH_2CHCHCO_2Et$), 1.76–1.26 (m, 6 H), 1.30 (t, $J$ = 7.1 Hz, 3 H, $OCH_2CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 166.8, 150.1, 149.4, 134.1, 128.4, 122.8, 121.2, 60.1, 34.9, 32.1, 31.6, 28.8, 27.9, 15.9, 14.2; IR ($CHCl_3$) 3609, 2934, 1709, 1654 cm$^{-1}$; MS (EI, 70 eV) $m/z$ 290 ($M^+$, 20), 135 (100). Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.43; H, 9.04. Found: C, 74.31; H, 8.88.

**(*E* and *Z*)-6-(3,5-Dimethyl-4-hydroxyphenyl)-2-heptenenitrile (17).** The procedure given previously for the preparation of **12** was carried out with tetra-*n*-butylammonium fluoride (110 μL of a 1.0 M solution in THF, 0.11 mmol) and silyl ether **14** (123 mg, 0.358 mmol). Flash chromatography (10:1 hexane/ethyl acetate followed by 5:1 hexane/ethyl acetate) afforded 68.4 mg

of phenol 17 as a colorless oil (83%, 2.3:1 mixture of *E*/*Z* isomers). HPLC (9:1 hexane/ethyl acetate, 1 mL/min, $t_R$ 9.0 min) provided an analytically pure sample of $\alpha,\beta$ unsaturated nitrile as a 2.3:1 *E*/*Z* mixture ($^1$H NMR): $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.78 (s, 2 H, ArH), 6.77 (s, 2 H, ArH), 6.71 (dt, $J$ = 16.3, 7.0 Hz, 1 H, (*E*)-C*H*CHCN), 6.47 (dt, $J$ = 10.9, 7.7 Hz, 1 H, (*Z*)-C*H*CHCN), 5.31 (dm, $J$ = 16.3 Hz, 2 H, (*E*)-CHCN and (*Z*)-CHCN), 2.53–2.41 (m, 3 H), 2.28–2.20 (m, 1 H), 2.23 (s, 6 H, $ArCH_3$), 1.67–1.40 (m, 4 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 155.9, 155.0, 150.2, 133.5, 133.4, 128.4, 128.4, 122.9, 122.8, 117.5, 99.7, 99.5, 34.6, 34.6, 33.2, 31.7, 31.0, 27.7, 27.1, 15.9; IR ($CHCl_3$) 3610, 2936, 2226, 1633 cm$^{-1}$; MS (EI, 20 eV) $m/z$ 229 ($M^+$, 41), 135 (100); HRMS calcd for $C_{15}H_{19}NO$ 229.1467, found 229.1468.

**5-(3,5-Dimethyl-4-hydroxyphenyl)pentanal (18).** The procedure given previously for the preparation of **12** was carried out with tetra-*n*-butylammonium fluoride (89 $\mu$L of a 1 M solution in THF, 0.089 mmol) and silyl ether **10** (95.4 mg, 0.298 mmol). Concentration afforded 77.4 g (126%) of aldehyde **18** as a pale yellow oil which was used without purification in the subsequent cyclization reaction due to instability: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.75 (t, $J$ = 1.7 Hz, 1 H, C(O)H), 6.78 (s, 2 H, ArH), 4.60 (bs, 1 H, ArOH), 2.53–2.42 (m, 4 H), 2.22 (s, 6 H, $ArCH_3$), 1.68–1.60 (m, 4 H); IR ($CDCl_3$) 3617, 2975, 1722, 1489 cm$^{-1}$.

**6-(3,5-Dimethyl-4-hydroxyphenyl)hexanol (19).** The procedure given previously for the preparation of **12** was carried out with tetra-*n*-butylammonium fluoride (250 $\mu$L of a 1 M solution in THF, 0.25 mmol) and silyl ether **11** (275 mg, 0.823 mmol). Concentration afforded 219 mg of aldehyde **19** (121%) as a pale yellow oil which was used without purification in the subsequent cyclization reaction due to instability: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.76 (t, $J$ = 1.6 Hz, 1 H, C(O)H), 6.77 (s, 2 H, ArH), 4.65 (bs, 1 H, ArOH), 2.45 (m, 4 H), 2.22 (s, 6 H, $ArCH_3$), 1.70–1.24 (m, 6 H); IR ($CDCl_3$) 3611, 2933, 2859, 1722, 1489, 1462, 1319, 1198, 1150, 1021 cm$^{-1}$.

**(1*S**,2*S**)-2-(3,5-Dimethyl-4-hydroxyphenyl)cyclopentanol (21). From Phenol 18.** $Ag_2O$ (160 mg, 0.69 mmol) was added to a solution of phenol **18** (13.8 mg, 0.0669 mmol) and benzene-$d_6$ (1 mL) at 65 °C. After 2 h the pale green reaction mixture was filtered through a plug of $Na_2CO_3$ (THF) and dried over $Na_2CO_3$. This solution was filtered through glass wool and was generally used immediately but could be stored overnight. Concentration of a similar solution afforded quinone methide **20** as a yellow oil: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.80 (s, 1 H, C(O)H), 7.26 (s, 1 H, ArH), 6.88 (s, 1 H, ArH), 6.24 (t, $J$ = 8.2 Hz, 1 H, ArCH), 2.58–1.20 (m, 6 H), 2.04 (s, 3 H, $ArCH_3$), 1.99 (s, 3 H, $ArCH_3$).

$CH_2I_2$ (54 $\mu$L, 0.67 mmol) was added to a suspension of Sm(0) (110 mg, 0.73 mmol) and THF (13 mL) at 0 °C. The resulting mixture was allowed to stir at 0 °C for 1 h followed by 1 h at rt. To the resulting violet-blue solution of $SmI_2$ at 35 °C was added quinone methide **20** (13.4 mL of a 5 mM solution in THF, 0.0669 mmol) via syringe pump over 1.8 h. Upon completion of addition the blue reaction mixture was cooled and then poured into aqueous saturated $NaHCO_3$ (30 mL) and ether (20 mL). The aqueous layer was extracted with ether (3 × 20 mL). The combined organic extracts were washed with brine (30 mL), dried ($MgSO_4$) and concentrated. Flash chromatography (5:1 hexanes/ethyl acetate followed by 3:1 hexanes/ethyl acetate) afforded 7.1 mg (67% from alcohol **8**) of *trans*-cyclopentanol **21** as a white solid. The minor isomer was not isolated, but $^1$H NMR of the crude reaction mixture indicated that the diastereoselectivity of the reaction was >5:1. Preparative TLC (3:1 hexane/ethyl acetate) provided an analytically pure sample of *trans*-cyclopentanol **21**: mp 110–112 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.87 (s, 2 H, ArH), 4.09 (apparent q, $J$ = 7.4 Hz, 1 H, C*H*OH), 2.73 (apparent q, $J$ = 7.4 Hz, 1 H, ArCH), 2.23 (s, 6 H, $ArCH_3$), 2.20–2.04 (m, 2 H), 1.86–1.62 (m, 4 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 150.8, 134.6, 127.4, 123.1, 80.4, 53.7, 33.7, 31.9, 21.5, 16.0; IR ($CHCl_3$) 3609, 2960 cm$^{-1}$; MS (EI, 20 eV) $m/z$ 206 ($M^+$, 56), 135 (100); HRMS calcd for $C_{13}H_{18}O_2$ 206.1307, found 206.1297.

**From Cuprate 31.** CuCN (47 mg, 0.53 mmol) was azeotropically dried with toluene (2 × 2 mL) with successive purging with argon. Ether (1.0 mL) was added, and the slurry was cooled to −78 °C. In a separate flask, *t*-BuLi (1.0 mL of a 1.91 M solution in pentane, 1.91 mmol) was added dropwise to a solution of 4-bromo-2,6-dimethyl-1-(*tert*-butyldimethylsilyl)phenol (**5**) (301 mg, 0.955 mmol) and ether (15 mL) at −78 °C. The resulting mixture was allowed to stir for 1 h at −78 °C and was then transferred dropwise via a dry ice cooled cannula into the CuCN/ether slurry at −78 °C. The mixture was warmed to −20 °C and stirred for 30 min. Cyclopentene oxide (41.7 $\mu$L, 0.478 mmol) was then added dropwise to the cuprate **31** at −20 °C. The cooling bath was removed, and the reaction mixture was allowed to warm to rt. After 12 h the reaction mixture was poured into aqueous saturated $NH_4Cl$ (30 mL). The aqueous layer was extracted with ethyl acetate (3 × 30 mL). The combined organic extracts were washed with brine (75 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (10:1 hexanes/ethyl acetate followed by 5:1 hexanes/ethyl acetate) afforded 42.5 mg (28%) of the silyl ether corresponding to **21**. The procedure given previously for the preparation of **12** was carried out with tetra-*n*-butylammonium fluoride (40 $\mu$L of a 1.0 M solution in THF, 0.040 mmol) and the above silyl ether (42.5 mg, 0.132 mmol) to afford 22.9 mg (84%) of **21**. The $^1$H NMR spectra, $^{13}$C NMR spectra, melting point, and TLC mobility were identical to **21** prepared via reductive cyclization.

**(1*S**,2*S**)- and (1*R**,2*S**)-2-(3,5-Dimethyl-4-hydroxyphenyl)cyclohexanol (23).** The procedure given previously for the preparation of **21** was carried out with $Ag_2O$ (82 mg, 0.35 mmol), phenol **19** (13.0 mg, 0.0590 mmol) and benzene-$d_6$ for 2 h to afford quinone methide **22**: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.25 (s, 1 H, C(O)H), 6.95 (s, 1 H, ArH), 6.46 (s, 1 H, ArH), 5.61 (t, $J$ = 8.1 Hz, ArCH), 2.10 (s, 3 H, $ArCH_3$), 2.07 (s, 3 H, $ArCH_3$), 1.86 (apparent q, $J$ = 7.6 Hz, 2 H, $CHCH_2$), 1.72–1.67 (m, 2 H), 1.41–1.12 (m, 2 H), 1.02–0.84 (m, 2 H).

To a solution of $SmI_2$ from $CH_2I_2$ (48 $\mu$L, 0.59 mmol), Sm(0) (98 mg, 0.65 mmol), and THF at 35 °C was added quinone methide **22** (1 mM solution in THF (59 mL), 0.059 mmol) over 8 h. After workup, flash chromatography (5:1 hexanes/ethyl acetate followed by 3:1 hexanes/ethyl acetate) afforded 6.5 mg (50% from alcohol **9**) of cyclohexanol **23** as a 1:1 mixture of diastereomers (colorless oil). Preparative TLC (3:1 hexanes/ethyl acetate) afforded an analytically pure sample of *cis*- and *trans*-cyclohexanols **23** as white solids. Hi-$R_f$ diastereomer: mp 128–130 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.87 (s, 1 H, ArH), 4.52 (bs, 1 H, ArOH), 3.96 (bs, 1 H, CHO*H*), 2.63 (dt, $J$ = 12.6, 2.8 Hz, 1 H, C*H*OH), 2.24 (s, 6 H, $ArCH_3$), 2.22–1.25 (m, 9 H); $^{13}$C NMR $\delta$ (125 MHz, $CDCl_3$) 150.8, 135.4, 127.8, 123.0, 70.7, 47.0, 32.7, 26.3, 24.6, 19.6, 16.0. IR ($CDCl_3$) 3607, 2934, 1725, 1712 cm$^{-1}$; MS (EI, 20 eV) $m/z$ 220 ($M^+$, 71), 161 (41), 135 (100); HRMS calcd for $C_{14}H_{20}O_2$ 220.1463, found 220.1452. Low-$R_f$ diastereomer: mp 155–157 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.86 (s, 2 H, ArH), 4.55 (bs, 1 H, ArOH), 3.62–3.54 (m, 1 H, C*H*OH), 2.32–1.24 (m, 9 H), 2.23 (s, 6 H, $ArCH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 151.0, 134.6, 127.9, 123.2, 74.6, 52.4, 34.3, 33.5, 26.2, 25.1, 16.0. IR ($CDCl_3$) 3700, 3610, 2934, 1733, 1716 cm$^{-1}$; MS (EI, 70 eV) $m/z$ 220 ($M^+$, 35), 161 (33), 135 (100); HRMS calcd for $C_{14}H_{20}O_2$ 220.1463, found 220.1468.

**(1*S**,2*S**)- and (1*R**,2*S**)-2-(3,5-Dimethyl-4-hydroxyphenyl)-1-[(ethoxycarbonyl)methyl]cyclopentane (25).** The procedure given previously for the preparation of **21** was carried out with $Ag_2O$ (180 mg, 0.78 mmol), phenol **15** (14.1 mg, 0.0510 mmol), and benzene-$d_6$ (1.5 mL) for 1 h to afford quinone methide **24**: $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 6.94 (dt, $J$ = 15.6, 7.0 Hz, 1 H, C*H*CHCO$_2$Et), 6.91 (s, 1 H, ArH), 6.46 (s, 1 H, ArH), 5.82 (dt, $J$ = 15.6, 1.5 Hz, 1 H, CHCO$_2$Et), 5.54 (t, $J$ = 8.1 Hz, 1 H, ArCH), 4.06 (q, $J$ = 7.1 Hz, 2 H, $OCH_2$), 2.09 (s, 3 H, $ArCH_3$), 2.06 (s, 3 H, $ArCH_3$), 1.84 (apparent q, $J$ = 7.6 Hz, 2 H, $ArCHCH_2$), 1.76–1.66 (m, 2 H, $CH_2$), 1.72–1.65 (m, 2 H, $CH_2CHCHCO_2Et$), 1.00 (t, 3 H, $J$ = 7.1 Hz, $OCH_2CH_3$).

To a solution of $SmI_2$ from $CH_2I_2$ (48 $\mu$L, 0.60 mmol), Sm(0) (99 mg, 0.66 mmol), and THF (12 mL) at 65 °C was added quinone methide **24** (10.2 mL of a 5.0 mM solution in THF, 0.0510 mmol) over 1.6 h. After workup, flash chromatography (10:1 hexanes/ethyl acetate followed by 5:1 hexanes/ethyl acetate) afforded 12.3 mg (87%) of arylcyclopentane ester **25** as a colorless oil (inseparable 1:1 mixture of diastereomers). HPLC (9:1 hexane/ethyl acetate, 1 mL/min, $t_R$ 9.0) provided an analytically pure sample of ester **25** (1:1 mixture of diastereomers, $^1$H NMR): $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.81 (s, 2 H, ArH), 6.74 (s, 2 H, ArH), 4.47 (bs, 2 H, ArOH), 4.03 (q, $J$ = 7.1 Hz, 2 H, $OCH_2$), 4.01 (q, $J$ = 7.1 Hz, 2 H, $OCH_2$), 3.15 (apparent q, $J$ = 7.6 Hz, 1 H, ArCH, 2.61–2.53 (m, 1 H, ArCH), 2.51–2.35 (m, 2 H, $CH_2CO_2Et$), 2.50–1.24 (m, 18 H), 2.22 (s, 12 H, $ArCH_3$), 1.19 (t, 6 H, $J$ = 7.1 Hz,

$OCH_2CH_3$); $^{13}C$ NMR (125 MHz, $CDCl_3$) δ 173.8, 173.1, 150.5, 135.5, 134.2, 128.5, 127.8, 122.8, 122.4, 60.0, 60.0, 51.8, 47.3, 44.5, 40.4, 38.8, 36.2, 35.2, 32.0, 31.0, 30.2, 23.6, 23.5, 16.0, 16.0, 15.9, 14.2; IR ($CHCl_3$) 3610, 3006, 1724 $cm^{-1}$; MS (EI, 70 eV) $m/z$ 276 ($M^+$, 23), 188 (100); HRMS calcd for $C_{17}H_{24}O_3$ 276.1725, found 276.1718.

**(1*S**,2*S**)- and (1*R**,2*S**)-2-(3,5-Dimethyl-4-hydroxyphenyl)-1-[(ethoxycarbonyl)methyl]cyclohexane (27).** The procedure given previously for the preparation of **21** was carried out with $Ag_2O$ (160 mg, 0.70 mmol), phenol **16** (13.2 mg, 0.0454 mmol), and benzene-$d_6$ (1.5 mL) for 1 h to afford quinone methide **26**: $^1H$ NMR (300 MHz, $C_6D_6$) δ 7.00 (dt, $J$ = 15.8, 7.0 Hz, 1 H, C*H*CHCO$_2$Et), 6.96 (s, 1 H, ArH), 6.48 (s, 1 H, ArH), 5.87 (dt, $J$ = 15.6, 1.25 Hz, 1 H, CHCO$_2$Et), 5.62 (t, $J$ = 8.1 Hz, 1 H, ArCH), 4.06 (q, $J$ = 7.1 Hz, 2 H, $OCH_2$), 2.10 (s, 3 H, $ArCH_3$), 2.07 (s, 3 H, $ArCH_3$), 1.91–1.84 (m, 2 H), 1.77–1.71 (m, 2 H), 1.00 (t, $J$ = 7.1 Hz, 3 H, $OCH_2CH_3$), 1.04–0.93 (m, 4 H).

To a solution of $SmI_2$ from $CH_2I_2$ (37 μL, 0.46 mmol), Sm(0) (77 mg, 0.51 mmol), and THF (9 mL) at 65 °C was added quinone methide **26** (40 mL of a 1.15 mM solution in THF, 0.0454 mmol) over 5.3 h. After workup, flash chromatography (5:1 hexanes/ethyl acetate) afforded 9.2 mg (70%) of arylcyclohexane **27** as a colorless oil (inseparable 1:1 mixture of diastereomers). HPLC (9:1 hexane/ethyl acetate, 1 mL/min, $t_R$ 8.6 min) provided an analytically pure sample of ester **27** (1:1 mixture of diastereomers, $^1H$ NMR): $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.77 (s, 4 H, ArH), 4.49 (s, 2 H, ArOH), 4.01 (q, $J$ = 7.1 Hz, 2 H, $OCH_2$), 3.99 (q, $J$ = 7.1 Hz, 2 H, $OCH_2$), 2.78 (m, 1 H, ArCH), 2.44 (m, 1 H, ArCH), 2.34–0.85 (m, 22 H), 2.22 (s, 6 H, $ArCH_3$), 2.21 (s, 6 H, $ArCH_3$), 1.18 (t, $J$ = 7.1 Hz, 3 H, $OCH_2CH_3$), 1.17 (t, $J$ = 7.1 Hz, 3 H, $OCH_2CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 173.8, 173.5, 150.4, 150.3, 137.2, 136.5, 127.7, 122.8, 122.5, 60.0, 60.0, 49.6, 44.9, 39.9, 39.9, 37.0, 35.9, 32.8, 31.8, 30.1, 26.8, 26.5, 26.2, 25.6, 20.4, 16.0, 16.0, 14.2; IR ($CHCl_3$) 3608, 2985, 1730 $cm^{-1}$; MS (EI, 20 eV) $m/z$ 290 ($M^+$, 50), 202 (100), 161 (31); HRMS calcd for $C_{18}H_{26}O_3$ 290.1882, found 290.1888.

**(1*S**,2*S**)- and (1*R**,2*S**)-2-(3,5-Dimethyl-4-hydroxyphenyl)-1-(cyanomethyl)cyclopentane (29).** The same procedure given previously for the preparation of **21** was carried out with $Ag_2O$ (330 mg, 1.4 mmol), phenol **17** (21.9 mg, 0.0956 mmol), and benzene-$d_6$ (2 mL) at 65 °C for 12 h to afford quinone methide **28** (2.3:1 mixture of $E/Z$ isomers) as a pale red solution: $^1H$ NMR (300 MHz, $C_6D_6$) δ 6.88 (s, 1 H, ArH), 6.86 (d, $J$ = 1 Hz, 1 H), 6.46 (s, 2 H, ArH), 5.84 (dt, $J$ = 16.3, 6.9 Hz, 1 H, C*H*CHCN), 5.56–5.41 (m, 3 H, ArCH, C*H*CHCN), 4.54–4.45 (m, 2 H, CHC*H*CN), 2.10 (s, 3 H, $ArCH_3$), 2.10 (s, 3 H, $ArCH_3$), 2.08 (s, 3 H, $ArCH_3$), 2.06 (s, 3 H, $ArCH_3$), 1.94–0.77 (m, 12 H).

To a solution of $SmI_2$ from $CH_2I_2$ (77 μL, 0.96 mmol), Sm(0) (160 mg, 1.1 mmol), and THF (35 mL) at 65 °C was added quinone methide **28** (19 mL of a 5 mM solution in THF, 0.0956 mmol) over 2.5 h. After workup, flash chromatography (10:1 hexanes/ethyl acetate followed by 5:1 hexanes/ethyl acetate) afforded 17 mg (78% yield) of arylcyclopentane **29** as a colorless oil (1:1 mixture of diastereomers, $^1H$ NMR). HPLC (10:1 hexane/ethyl acetate, 0.8 mL/min, trans: $t_R$ 18.2 min, cis: $t_R$ 19.2 min) provided analytical samples of the *cis*- and *trans*-nitriles. Low-$R_f$ diastereomer ($t_R$ 19.2 min): $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.81 (s, 2 H, ArH), 4.55 (s, 1 H, ArOH), 2.53 (dt, $J$ = 16.5 Hz, 3.3 Hz, 1 H, ArCH), 2.23 (s, 6 H, $ArCH_3$), 2.41 (dd, $J$ = 16.5 Hz, 3.3 Hz, $CH_2CN$), 2.20 (1 H), 1.55 (m, 8 H); $^{13}C$ NMR (125 MHz, $CDCl_3$) δ 150.9, 134.1, 127.4, 123.2, 119.0, 51.0, 44.2, 34.9, 31.2, 23.3, 20.6, 16.0; IR ($CHCl_3$) 3610, 2959, 2254 $cm^{-1}$; MS (EI, 20 eV) $m/z$ 229 ($M^+$, 100), 161 (44); HRMS calcd for $C_{15}H_{19}NO$ 229.1467, found 229.1474. High-$R_f$ diastereomer ($t_R$ 18.2 min): $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.76 (s, 2 H, ArH), 4.54 (bs, 1 H, ArOH), 3.19 (apparent q, $J$ = 7.7 Hz, 1 H, ArCH), 2.50–2.43 (m, 1 H, C*H*CH$_2$CN), 2.23 (s, 6 H, $ArCH_3$), 2.09–1.57 (m, 8 H); $^{13}C$ NMR (125 MHz, $CDCl_3$) δ 150.8, 132.5, 128.3, 122.9, 120.1, 47.2, 41.0, 30.7, 29.5, 23.2, 19.3, 16.0; IR ($CHCl_3$) 3609, 2959, 2261 $cm^{-1}$; MS (EI, 20 eV) $m/z$ 229 ($M^+$, 100), 161 (88); HRMS calcd for $C_{15}H_{19}NO$ 229.1467, found 229.1453.

**Ethyl 7-(3,5-Dimethyl-4-hydroxyphenyl)-2,6-heptadienoate (30).** $SmI_2$ (0.055 M) was added via syringe pump to a solution of quinone methide **24** (0.171 mmol) and THF (34 mL) at 65 °C until the blue color of $SmI_2$ persisted (ca. 2 mL). The resulting pale blue reaction mixture was cooled to rt and poured into aqueous saturated $NaHCO_3$ (50 mL) and ether (30 mL). The aqueous layer was extracted with ether (3 × 50 mL). The combined organic extracts were washed with brine (100 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (5:1 hexanes/ethyl acetate) afforded 30.0 mg (64%) of styrene **30** as a colorless oil: $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.02 (partially obscured dt, $J$ = 15.7, 6.5 Hz, 1 H, C*H*CHCO$_2$Et), 6.97 (s, 2 H, ArH), 6.28 (d, $J$ = 15.7 Hz, 1 H, ArCH or CHCO$_2$Et), 6.01 (partially obscured dt, $J$ = 15.8, 6.4 Hz, 1 H, ArCHC*H*), 5.86 (d, $J$ = 15.6 Hz, 1 H, ArCH or CHCO$_2$Et), 4.77 (bs, 1 H, ArOH), 4.19 (q, $J$ = 7.1 Hz, 2 H, $OCH_2CH_3$), 2.40–2.31 (m, 4 H), 2.23 (s, 6 H, $ArCH_3$), 1.29 (t, 3 H, $OCH_2CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 166.7, 151.6, 148.4, 130.4, 129.6, 126.3, 126.2, 123.0, 121.7, 60.2, 32.2, 31.4, 15.9, 14.2; IR ($CDCl_3$) 3609, 2982, 1709, 1603 $cm^{-1}$; MS (EI, 20 eV) 274 ($M^+$, 12), 161 (100); HRMS calcd for $C_{17}H_{22}O_3$ 274.1569, found 274.1564.

**7-(3,5-Dimethyl-4-hydroxyphenyl)-2-methyl-2-heptene (32).** *n*-BuLi (630 μL of a 2.3 M solution in hexanes, 1.4 mmol) was added to a suspension of freshly dried (160 °C, 0.05 mmHg) isopropropyltriphenylphosphonium bromide (590 mg, 1.5 mmol) and THF (15 mL) at −78 °C. The cooling bath was removed, and the orange mixture was allowed to warm to rt and was then stirred for 30 min. The resulting red solution was cooled to −78 °C, and to this was added dropwise a solution of aldehyde **10** (197 mg, 0.615 mmol) and THF (10 mL). Immediately after the addition was completed, the cooling bath was removed and the red reaction mixture was allowed to warm to rt. After 4 h the reaction mixture was poured into brine (25 mL). The aqueous layer was extracted with ether (3 × 20 mL). The combined organic extracts were washed with brine (50 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (20:1 hexanes/ethyl acetate) afforded 195 mg (91%) of 7-[3,5-dimethyl-4-[(*tert*-butyldimethylsilyl)oxy]-phenyl]-2-methyl-2-heptene as a colorless oil: $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.84 (s, 2 H, ArH), 5.20 (t, $J$ = 7.0 Hz, 1 H, *H*CC(CH$_3$)$_2$), 2.54 (t, $J$ = 7.7 Hz, 2 H, $ArCH_2$), 2.26 (s, 6 H, $ArCH_3$), 2.07 (m, 2 H), 1.76 (s, 3 H, (*Z*)-CHCC*H*$_3$), 1.70–1.60 (m, 2 H), 1.68 (s, 3 H, (*E*)-CHCC*H*$_3$), 1.48–1.38 (m, 2 H), 1.11 (s, 9 H, SiC(CH$_3$)$_3$, 0.26 (s, 6 H, Si(CH$_3$)$_2$); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 149.8, 135.3, 131.1, 128.6, 128.0, 124.8, 35.0, 31.3, 29.6, 27.9, 26.1, 25.7, 18.7, 17.8, 17.7, −3.0; IR ($CHCl_3$) 3611, 2966 $cm^{-1}$. The procedure given previously for the preparation of **12** was carried out with tetrabutylammonium fluoride (170 μL of a 1.0 M solution in THF, 0.17 mmol) and the above silyl ether (195 mg, 0.562 mmol). Flash chromatography (20:1 hexanes/ethyl acetate followed by 10:1 hexanes/ethyl acetate) afforded 122 mg (93%) of phenol **32** as a colorless oil. HPLC (9:1 hexane/ethyl acetate, 1 mL/min, $t_R$ 9.0 min) provided an analytically pure sample of dimethylalkene **32**: $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.79 (s, 2 H, ArH), 5.12 (m, 1 H, *H*C(CH$_3$)$_2$), 4.45 (s, 1 H, ArOH), 2.48 (t, $J$ = 7.7 Hz, 2 H, $ArCH_2$), 2.23 (s, 6 H, $ArCH_3$), 2.04–1.96 (m, 2 H, CHC*H*$_2$), 1.69 (s, 3 H, (*Z*)-CHC*H*$_3$), 1.61 (s, 3 H, (*E*)-CHC*H*$_3$), 1.58–1.52 (m, 2 H), 1.41–1.34 (m, 2 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 150.0, 134.5, 131.2, 128.5, 124.7, 122.7, 35.0, 31.5, 29.6, 27.9, 25.7, 17.7, 15.9; IR ($CHCl_3$) 3612, 2969 $cm^{-1}$; MS (EI, 20 eV) $m/z$ 232 ($M^+$, 82), 161 (98), 135 (100). Anal. Calcd for $C_{16}H_{24}O$: C, 82.68; H, 10.43. Found: C, 82.49; H, 10.38.

**7,8-Bis(3,5-dimethyl-4-hydroxyphenyl)-2,13-dimethyl-2,12-tetradecadiene (33).** The procedure given previously for the preparation of **21** was carried out with $Ag_2O$ (490 mg, 2.1 mmol), phenol **32** (32.9 mg, 0.142 mmol), and benzene-$d_6$ (1.5 mL) for 1 h to afford the corresponding quinone methide: $^1H$ NMR (300 MHz, $C_6D_6$) δ 7.02 (s, 1 H, ArH), 6.48 (s, 1 H, ArH), 5.75 (t, $J$ = 8.1 Hz, 1 H, ArCH), 5.11–5.06 (m, 1 H, C*H*C(CH$_3$)$_2$), 2.19–2.03 (m, 2 H, CHC*H*$_2$), 2.07 (s, 3 H, $ArCH_3$), 2.05 (s, 3 H, $ArCH_3$), 1.90 (apparent q, $J$ = 7.1 Hz, 2 H, CHC*H*$_2$), 1.65 (s, 3 H, $ArCH_3$), 1.48 (s, 3 H, $ArCH_3$), 1.35–1.28 (m, 2 H).

To a solution of $SmI_2$ from $CH_2I_2$ (110 μL, 1.4 mmol), Sm(0) (240 mg, 1.56 mmol), and THF (28 mL) at 65 °C was added the above quinone methide (28 mL of a 5 mM solution in THF, 0.142 mmol) dropwise over 3.7 h. After workup, flash chromatography (10:1 hexanes/ethyl acetate followed by 5:1 hexanes/ethyl acetate) afforded 13.6 mg of the high $R_f$ diastereomer (colorless oil) and 13.3 mg of the low $R_f$ diastereomer (white solid) of dimer **33** (82% total yield). High $R_f$ diastereomer (oil): $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.43 (s, 4 H, ArH), 5.03 (m, 2 H, C*H*CCH$_3$), 4.43 (s, 2 H, ArOH), 2.62 (m, 2 H, ArCH), 2.79–0.86 (m, 12 H), 2.15 (s, 12 H, $ArCH_3$), 1.64 (s, 3 H, (*Z*)-CHCC*H*$_3$), 1.55 (s, 3 H, (*E*)-CHCC*H*$_3$);

$^{13}$C NMR (75 MHz, $CDCl_3$) δ 150.0, 134.2, 131.1, 129.6, 124.8, 121.4, 50.1, 32.5, 28.1, 25.7, 17.6, 15.9; IR ($CHCl_3$) 3608, 3002, 1489 cm$^{-1}$; MS (FAB, positive ion, nitrobenzyl alcohol matrix) *m/z* 461 ($MH^+$, 1), 135 (100); FAB-HRMS calcd for $C_{32}H_{45}O_2$ 461.3420, found 461.3423. Low $R_f$ diastereomer (white solid): mp 110–112 °C; $^1$H NMR (300 MHz, $CDCl_3$) δ 6.72 (s, 4 H, ArH), 4.88 (t, *J* = 6.8 Hz, 2 H, $CHCCH_3$), 4.47 (s, 2 H, ArOH), 2.42 (m, 2 H, ArCH), 2.24 (s, 12 H, $ArCH_3$), 1.79–0.86 (m, 12 H), 1.58 (s, 6 H, (*Z*)-$CHCCH_3$), 1.46 (s, 6 H, (*E*)-$CHCCH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 150.0, 136.4, 130.8, 128.4, 124.9, 122.3, 51.4, 34.1, 27.8, 27.7, 25.6, 17.6, 16.1; IR ($CHCl_3$) 3609, 2930, 1489 cm$^{-1}$; MS (FAB, positive ion, nitrobenzyl alcohol matrix) *m/z* 461 ($MH^+$, 1), 161 (25), 135 (100); MS (FAB, negative ion, 1-thioglycerol matrix) *m/z* 461 ($MH^-$, 52), 147 (100); HRMS (FAB, positive ion, nitrobenzyl alcohol matrix) calcd for $C_{32}H_{45}O_2$ ($MH^+$) 461.3420 found 461.3397.

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**Supplementary Material Available:** $^1$H NMR and $^{13}$C NMR spectra for compounds **6**, **7**, **10**, **11**, **14**, **17**, **21**, **23**, **25**, **27**, **29**, **30**, **32**, and **33** and $^1$H NMR spectra for compounds **18**, **19**, **20**, **22**, **24**, **26**, **28** (41 pages). This material is contained in many 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.

# Preparation and Reactivity of the Adducts of Ketene Alkylsilyl Acetals with Ethyl Propiolate in the Presence of Titanium Tetrachloride

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The reaction of ketene alkylsilyl acetals with ethyl propiolate in the presence of $TiCl_4$ led to intermediates whose reactivity was studied with electrophiles such as $H_2O$, $D_2O$, NBS, NCS, and PhSeCl to form glutaconate derivatives. Except in the case of the dimethylketene trimethylsilyl acetal, for which the reaction was stereospecific, with other ketene acetals the selectivity was lower. Similar results were observed in the reaction of these titanium intermediates with aldehydes and ketones. The results were interpretated as the formation of vinylic titanium intermediates (more stabilized in the case of the dimethylketene acetal) in equilibrium with the titanium allenolates.

## Introduction

Numerous methods have been developed for preparing α-functionalized α,β-ethylenic esters. Among the straightforward procedures to access to such intermediates, the most promising for their simplicity employ the DABCO-catalyzed coupling of aldehydes with acrylates[1] or [α-(alkoxycarbonyl)vinyl]metal derivatives. Various metals have been used for the preparation of these vinylmetal compounds, such as Li,[2] Al,[3] Cu,[4] Sn,[5] Ge,[6] Pb,[7] Zn,[8] Pt,[9] Co,[10] Hg,[2b] Ru,[11] and Pd.[12,13] The most common way to prepare these metallic intermediates is the 1,4-addition of organometallic compounds to 2-alkynoates. Wide synthetic applications of this reaction were made in the case

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