Formation of Carbon–Carbon Bonds via Quinone Methide-Initiated Cyclization Reactions

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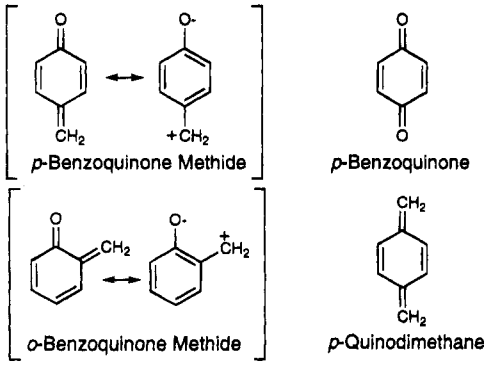
p-Quinone methides were found to be excellent electrophilic cyclization initiators for the formation of six-membered rings. Cyclizations to form five- and seven-membered rings were also studied. Oxidation of 2,6-disubstituted phenols with Ag_2O afforded the corresponding quinone methides. A wide range of cyclization terminators/nucleophiles were found to be effective in the cyclizations, including: allylsilane, β-keto esters, furan, pyrrole, indole, and a number of alkenes. The yields of the cyclizations were generally high.

Introduction

Quinone methides are interesting compounds that have been proposed as intermediates in a large number of chemical and biological processes.[1] They are structurally similar to benzoquinones and quinodimethanes; however, their chemistry is quite different. The asymmetry introduced by the presence of two electronically different substituents, carbonyl and methylidene, on the cyclohexadiene imparts a strong dipolar character to quinone methides not found in benzoquinones and quinodimethanes.[2] The exocyclic alkylidene is electrophilic and the carbonyl oxygen is basic. In spite of their simplicity, the dipolar valence-bond resonance structures that can be written for these compounds are descriptive of their chemistry. HMO calculations on *p*-benzoquinone methide corroborate this view of the quinone methide, where a substantial negative charge resides on the oxygen and a significant positive charge on the exocyclic alkylidene.[2b,d]



The parent quinone methides, *o*- and *p*-benzoquinone methide, are quite unstable and matrix isolation techniques were required to observe them spectroscopically.[3,4] Substitution on the quinone methide nucleus provides stability to the system. Indeed, many highly substituted quinone methides are stable, naturally occurring compounds.[5] The application of quinone methides to synthesis has been largely limited to the use of *in situ*-generated *o*-quinone methides as heterodienes in Diels–Alder type reactions.[6] In contrast, there has been little application of *p*-quinone methides as synthesis intermediates.[7]

p-Quinone methides have been proposed as intermediates in biosynthesis,[8] enzyme inhibition,[8c,d] insect cuticle chemistry,[9] wood lignin chemistry,[10] and release mechanisms in photographic processes.[11] In addition, *o*-quinone methides have been proposed to play an important role in the chemistry and mode of action of several classes of antitumor compounds.[12] The importance of these compounds in so many different processes led us to initiate a program aimed at studying the chemistry of quinone methides in detail.

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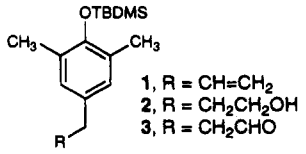
One possible arena in which to examine the synthesis, stability, and reactivity of quinone methides is cyclization reactions that form carbon–carbon bonds. Such a study should allow the electrophilicity of the quinone methide to be probed using cyclization terminators/nucleophiles of varying reactivity. Until the initiation of this work, the application of quinone methide-initiated cyclizations had been limited to reactions in which the terminator was an electron-rich benzene ring.[7,13] The goal of the research presented here is to determine what types of cyclization terminators/nucleophiles are compatible with quinone methide-initiated cyclizations.[14,15] It seemed likely that quinone methides could be activated to afford reactive benzylic cation intermediates under extremely mild conditions.

All of the substrates in this study incorporated 2,6-dialkyl or 2,6-dialkoxy substitution that allowed the quinone methides to be isolated and characterized. The origin of the stabilization afforded by the 2,6-disubstitution has been proposed to be due to steric hindrance to polymerization.[1] In addition, Soucek and co-workers have studied substituted 2,6-di-*tert*-butyl *p*-benzoquinone methides.[2a–c] These workers proposed that the steric interaction between the carbonyl oxygen of the quinone methide and the 2,6-*tert*-butyl groups induced a distortion of the quinonoid ring to a boat-like conformation to relieve the steric interaction. Substituents smaller than *tert*-butyl might also produce a steric interaction that brings the carbonyl carbon out of the plane of the diene, resulting in decreased overlap between the carbonyl and the diene. In effect, this decreases the contribution of the dipolar resonance structure shown above and thus, the electrophilicity of the exocyclic alkylidene. The observed stability of the 2,6-disubstituted quinone methides is likely due to a combination of the two effects: steric hindrance to intermolecular reactions and nonplanarity of the carbonyl and the diene.

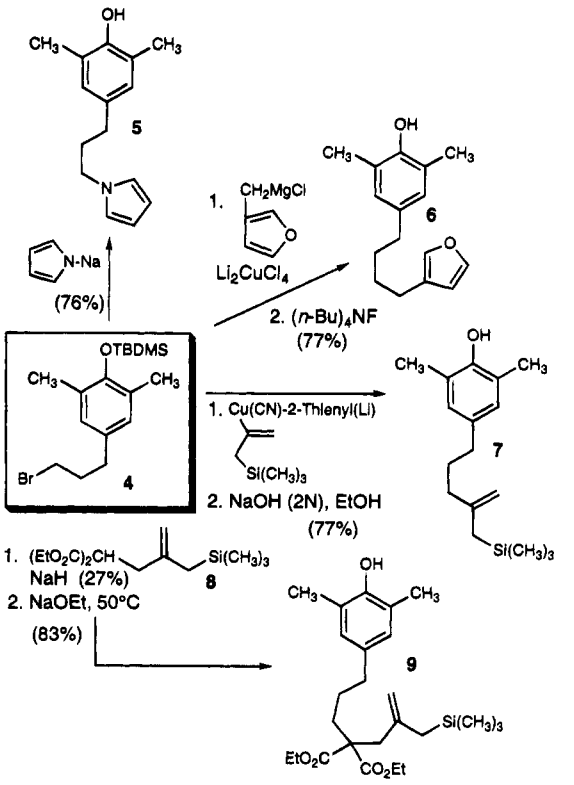
Results and Discussion

Synthesis of the Cyclization Substrates. Several versatile intermediates containing 2,6-disubstituted phenols were used to prepare a number of different cyclization substrates. Hydroboration/oxidation of readily available alkene[16] **1** afforded alcohol **2** in 76% yield. Oxidation of **2** with pyridinium dichromate[17] provided **3** in 58% yield. Compounds **2** and **3** were used as precursors to several different cyclization substrates.

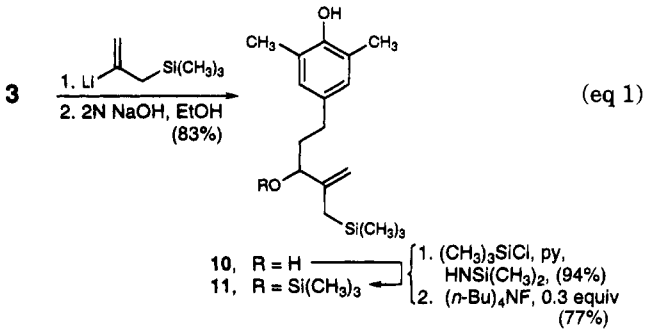


Treatment of alcohol **2** with carbon tetrabromide and triphenylphosphine afforded bromide **4** in 65% yield (see Scheme 1 for structure).[18] Displacement of the bromide with the appropriate nucleophile, followed by desilylation, afforded pyrrole **5**, furan **6**, and allylsilanes **7** and **9** (Scheme 1). In the case of **5**, a separate deprotection step was unnecessary; alkylation of the sodium salt of pyrrole followed by workup afforded the deprotected phenol directly.

Scheme 1



Condensation of aldehyde **3** with 2-lithio-3-(trimethylsilyl)-1-propene[19] followed by selective deprotection of the silyl ether in the presence of the allylsilane afforded phenol **10** (eq 1). Attempts to carry out this desilylation with catalytic fluoride resulted in competing cleavage of the trimethylsilyl group on the allylsilane. Selective



(eq 1)

protection of the secondary alcohol as the trimethylsilyl ether was achieved by silylation of the phenol and the alcohol, followed by selective removal of the phenolic silyl group with catalytic fluoride ion to afford **11** in 72% yield from **10**.

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(13) There are examples of intermolecular reactions in which quinone methides react with other carbon based nucleophiles, see ref 1.

(14) For preliminary work on the intramolecular reaction of quinone methides with carbon nucleophiles see: (a) Angle, S. R.; Turnbull, K. D. *J. Am. Chem. Soc.* **1989**, *111*, 1136. (b) Angle, S. R.; Louie, M. S.; Mattson, H. L.; Yang, W. *Tetrahedron Lett.* **1989**, *30*, 1193. (c) Angle, S. R.; Frutos, R. P. *J. Chem. Soc., Chem. Commun.* **1993**, 171. (d) Angle, S. R.; Louie, M. S. *Tetrahedron Lett.* **1993**, *34*, 4751.

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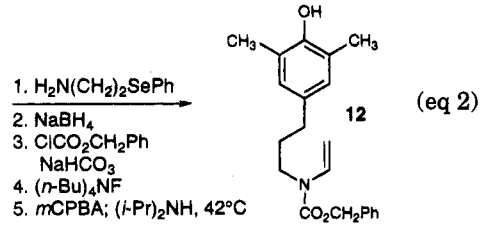
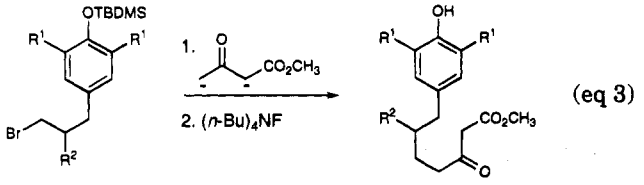
Aldehyde **3** was converted to enecarbamate **12** via the five-step sequence shown in eq 2. Reductive amination of **3** with 2-(phenylseleno)ethylamine[20] afforded the secondary amine that was protected as the carbobenzyloxy (CBZ) carbamate. Removal of the silyl protecting group on the phenol, followed by oxidation to the selenoxide and elimination, afforded **12**.[20]



(eq 2)

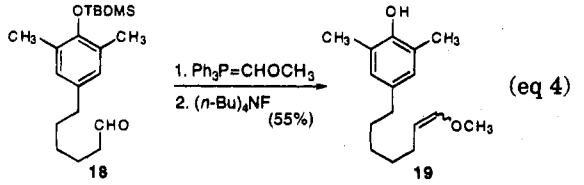
Substrates containing a β-keto ester terminator (**15**–**17**) were prepared by alkylation of the Weiler dianion[21] with bromides **4**, **13**, and **14** (see Experimental Section for preparation) followed by desilylation of the phenols (eq 3). Wittig olefination of aldehyde **18**[22] followed by treatment with fluoride ion gave alkene **19** as a 1:1 *E*/*Z* mixture in 55% yield (eq 4).



(eq 3)

4, $R^1 = CH_3$, $R^2 = H$
13, $R^1 = OCH_3$, $R^2 = H$
14, $R^1 = CH_3$, $R^2 = CH_3$

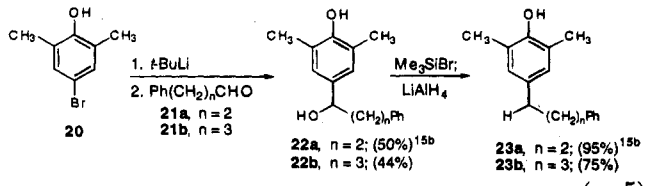
15, $R^1 = CH_3$, $R^2 = H$; (71%)
16, $R^1 = OCH_3$, $R^2 = H$; (63%)
17, $R^1 = CH_3$, $R^2 = CH_3$; (59%)



(eq 4)

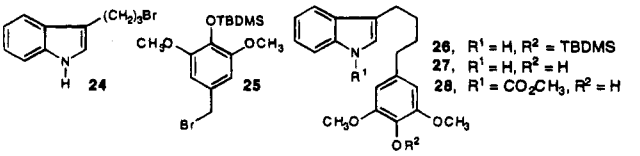
18 **19**

Treatment of phenol **20** with excess *tert*-butyllithium resulted in formation of the corresponding phenoxide aryllithium. This dianion was then condensed with aldehydes **21** to afford benzylic alcohols **22** (eq 5). Removal of the benzylic alcohol was accomplished by treatment of **22** with bromotrimethylsilane to provide the benzylic bromide,[23] which was reduced with lithium aluminum hydride to give **23a**[15b] in 95% yield and **23b** in 75% yield.



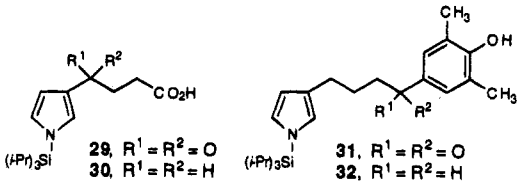
(eq 5)

Indole-containing substrates **27** and **28** were prepared from bromide **24**. Conversion of **24** to the dianion upon treatment with 3 equiv of *tert*-butyllithium, followed by condensation with benzylic bromide **25** in the presence of copper(I) cyanide, provided **26** in 37–45% yield. In the absence of copper(I) cyanide the yield of **26** was considerably lower, 7–18%. Removal of the silyl ether gave phenol **27** in 94% yield. *N*-Acylation of indole **26** with methyl chloroformate, followed by removal of the silyl protecting group on the phenol afforded **28** in 50% yield.



26, $R^1 = H$, $R^2 = TBDMS$
27, $R^1 = H$, $R^2 = H$
28, $R^1 = CO_2CH_3$, $R^2 = H$

Readily available keto acid **29** was used to prepare pyrrole-containing substrate **32**.[24] Direct reduction of the ketone functionality in **29** to a methylene group proved troublesome; however, a two-step procedure provided the desired product **30** in 82% overall yield. Treatment of **29** with sodium borohydride afforded the alcohol, which spontaneously lactonized to the γ-lactone. Hydrogenolysis (H_2, Pd/C) of the lactone then afforded **30**. Conversion of acid **30** to the Weinreb amide,[25] followed by condensation with the dianion derived from bromophenol **20** (see eq 5 for structure) provided **31** in 66% yield. Treatment of benzylic ketone **31** with H_2 (53 psi) in the presence of Pd/C gave **32** in 51% yield.



Synthesis of the Quinone Methides. Oxidation of the phenols with Ag_2O (1.2–20 equiv)[26] afforded the corresponding quinone methides within 15–60 min. In general, a larger excess of Ag_2O resulted in shorter reaction times. An exception to this generalization was the oxidation of pyrrole **5** with 10.1 equiv of Ag_2O; this phenol required 13 h for complete oxidation. In this case, it may be that the pyrrole, or a minor impurity, poisoned the surface of the Ag_2O thereby slowing the oxidation. The quinone methides proved to be quite stable and could be stored neat or in solution for several days with little or no decomposition. In most cases, the oxidation was carried out in CH_2Cl_2, C_6D_6, or $CDCl_3$. The progress of the reaction was monitored by ^1H NMR or TLC, and on consumption of starting material, the reaction mixture was filtered through Celite or glass wool, and if necessary, dried over Na_2SO_4 or K_2CO_3 to provide a solution of quinone methide (>95% pure by ^1H NMR analysis). In several cases, the quinone methides were extensively characterized, and in others the formation of the quinone methide was verified by ^1H NMR analysis and it was then used immediately in the cyclization reaction.

Prior to synthesis of the cyclization substrates, the stability of the terminators to the oxidation conditions was determined. For example, a $CDCl_3$ suspension of allyltrimethylsilane and Ag_2O (10 equiv) was monitored

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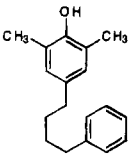
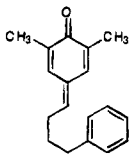
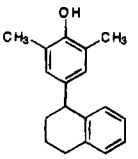
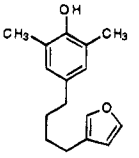
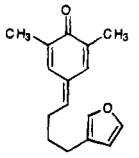
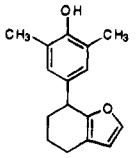
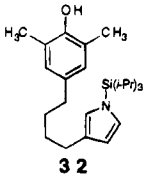
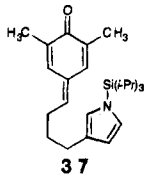
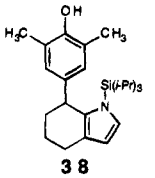
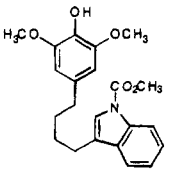
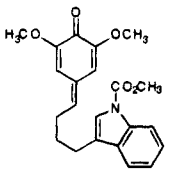
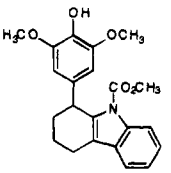
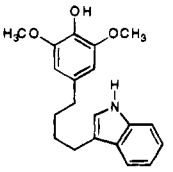
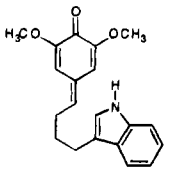
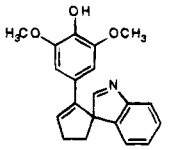
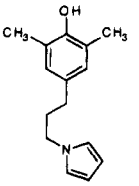
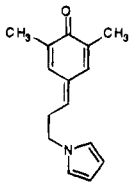
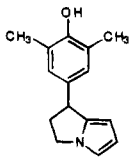
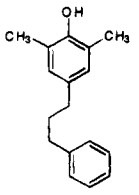
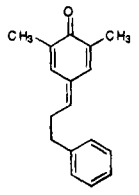
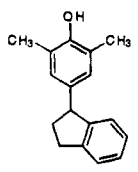
Table 1. Quinone Methide-Initiated Cyclization Reactions

Entry	Phenol	Quinone Methide	Lewis Acid	Product(s)	Yield (%)
1	 **23b**	 **33**	$ZnCl_2$	 **34**	93
2	 **6**	 **35**	$ZnCl_2$	 **36**	83
3	 **32**	 **37**	$ZnCl_2$	 **38**	98
4	 **28**	 **39**	$ZnCl_2$	 **40**	81
5	 **27**	 **41**	none	 **42**	90
6	 **5**	 **43**	$ZnCl_2$	 **44**	62
	 **23a**	 **45**	$ZnCl_2$	 **46**	—

by ^1H NMR spectroscopy for several hours. No reaction or decomposition of the allylsilane was observed.

Cyclization Studies: Electrophilic Substitution with Aromatic Terminators. Table 1 shows several quinone methide-initiated cyclizations that form six-membered rings upon electrophilic substitution. In all but one case, (entry 5) zinc chloride was added to initiate the cyclization. Since the solubility of zinc chloride in CH_2Cl_2, C_6D_6, and $CDCl_3$ is sparing at best, the reactions can be viewed as catalytic in Lewis acid. The relative reactivity of the terminators varied considerably. The phenyl-terminated cyclization, entry 1, possessed the least reactive terminator.[27] Examination of rate data for electrophilic bromination and acylation of monosubstituted pyrroles showed them to be $>10^9$ times more reactive than simple monosubstituted benzenes.[28] Furans were $>10^3$ times more reactive than monosubstituted

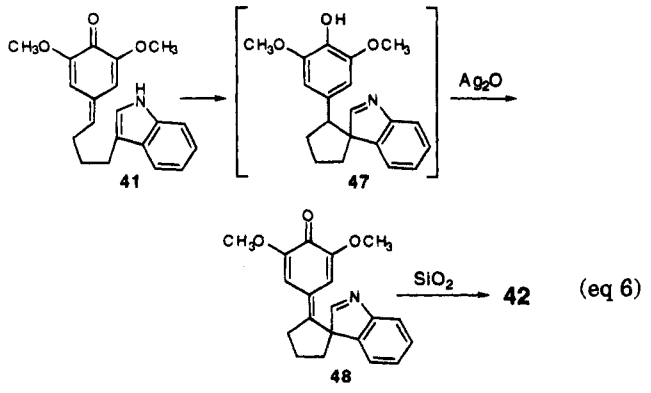
(27) Mayr, H.; Bartl, J.; Hagen, G. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1613.

(28) Marino, G. Electrophilic Substitutions of Five-Membered Rings. *Advances in Heterocyclic Chemistry;* Katritzky, A. R., Boulton, A. J., Eds.; Academic Press: New York, 1971; pp 235–315.

benzenes.[28] Thus, the range of reactivities of the terminators in Table 1 covered many orders of magnitude. These examples showed that quinone methide-initiated cyclizations are compatible with virtually all aromatic cyclization terminators/nucleophiles that underwent electrophilic substitution.

An examination of Table 1 showed the cyclizations affording six-membered rings to be high-yielding, efficient processes. The least reactive terminator, phenyl (entry 1), affords a virtually identical yield of cyclization product as the most reactive terminator, pyrrole (entry 3). In a communication of this work,[14b] the yield for the **33** to **34** transformation was reported as 67%. Since this time, we have found that simply drying the quinone methide by chasing with CH_2Cl_2 to remove traces of water, followed by treatment with zinc chloride, resulted in a 93% yield for the cyclization reaction.

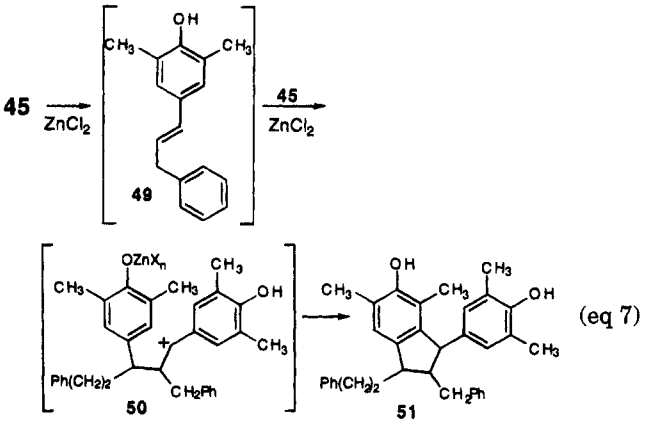
N-Acylindole **28** (entry 4) afforded cyclized product **40** in 81% yield. In the case of unprotected indole **27** (entry 5), the quinone methide (**41**) could not be observed by ^{1}H NMR and the expected product analogous to **40** was not formed. No Lewis acid was required; cyclization occurred spontaneously. Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed quinone methide **48** to be the product of the reaction (eq 6). Stirring **48** in a suspension of silica gel and chloroform followed by flash chromatography afforded styrene **42** in 90% overall yield from **27**. The formation of **48** must have occurred by oxidation of **27** to quinone methide **41** which was then attacked by the indole at C(3) to afford **47** (eq 6). Oxidation of **47** by excess Ag_2O then provided quinone methide **48**. While **48** could not be purified, the crude material was >90% pure by ^{1}H NMR analysis. The structure assignment of **48** was based on its spectral data and chemical behavior. The ^{1}H NMR spectrum showed two sets of resonances for the hydrogens of the methoxy groups (δ 3.78 and δ 3.09), and the imine methine hydrogen appeared as a singlet at δ 8.21. The presence of the quinone methide carbonyl was indicated by a resonance at δ 175.5 in the ^{13}C NMR spectrum.



(eq 6)

Entries 6 and 7 in Table 1 showed that the formation of five-membered rings must be examined on an individual basis. Pyrrole **43** afforded a modest 62% yield of cyclization product **44**. The low yield was due to the instability of product **44**, which rapidly decomposed upon standing. At low concentrations (0.001−0.006 M), the 62% yield was reproducible. At higher concentrations (ca. 0.1 M), **44** was obtained in lower yield and intractable products were obtained in 20−80% yield. The concentration dependent yield may be due to intermolecular reactions competing with, or subsequent to, the intramolecular cyclization. The cyclization of **43** occurred in a five-membered transition state with only two sp^3 centers in the ring that is being formed. This must have resulted in poor overlap of the cyclization terminator/nucleophile with the benzylic cation generated upon activation of the quinone methide.

The attempted cyclization of **45**, with a less reactive phenyl terminator, afforded dihydro(1*H*)indene **51** in 73% yield (eq 7); none of the desired cyclization product **46** was observed. The formation of dimer **51** is believed to have occurred via zinc chloride-mediated enolization of the quinone methide to styrene **49** which then acted as a nucleophile toward a second quinone methide to afford benzylic cation **50**. This then underwent intramolecular electrophilic aromatic substitution to afford **51** (eq 7). This mechanism is well precedented in the acid-mediated dimerization of styrenes[29] and in other work from our laboratory.[15]

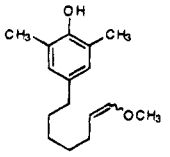
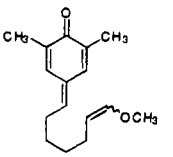
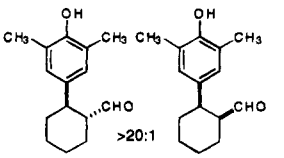
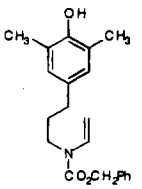
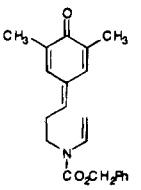
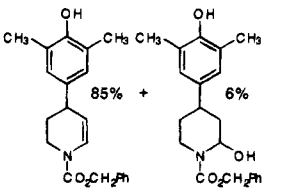
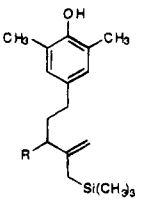
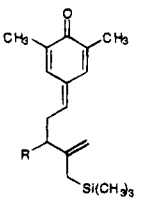
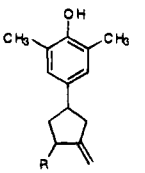
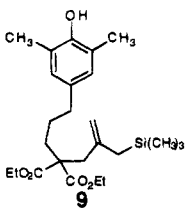
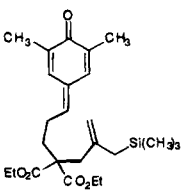
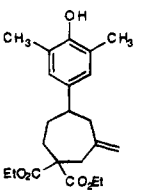
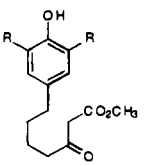
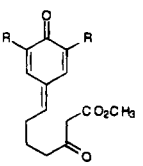
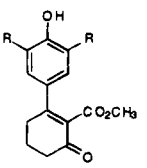
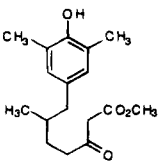
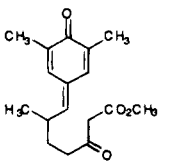
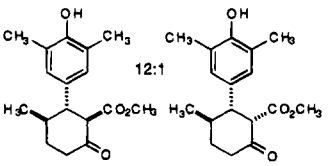


(eq 7)

Cyclization Studies: Alkene and β-Keto Ester Terminators. In an effort to expand the utility of the quinone methide-initiated cyclization reactions, a series of alkene terminators was examined. Again, the substitution on the quinone methide was kept constant, the goal of the study being the examination of the range of terminators that can be employed in the cyclization. Entry 1 in Table 2 shows that an exocyclic enol ether is an acceptable terminator. The Lewis acid of choice was Ti(O*i*-Pr)$_3$Cl (−40 °C to room temperature, 1 h) which allowed the *trans*-product **53** to be isolated in 58% yield as a >20:1 mixture of **53**:**54**. The use of $TiCl_4$ afforded products in similar yields; however, the isomer ratio was 2.4:1 (^{1}H NMR) after 5 min reaction time at −40 °C, and 8.2:1 (^{1}H NMR) after 1 h reaction time at −40 °C. The stereoselectivity resulted from epimerization after the cyclization and not from a stereoselective cyclization. Entry 2 showed that the electron rich alkene, in this case an enecarbamate, can be endocyclic to the six-membered ring that is formed in the cyclization. Product enecarbamate **56** was obtained in excellent yield. Allylsilane **58** underwent smooth cyclization to afford methylene cyclopentane **61** in 83% yield after treatment with tetrabutylammonium fluoride (Table 2, entry 3). The crude cyclization product was a mixture of phenol and the corresponding trimethylsilyl ether, thus necessitating the treatment with fluoride ion. In contrast to the formation of the five-membered ring with a pyrrole terminator (Table 1, entry 6), the yields of this allylsilane-terminated cyclization were not concentration dependent.

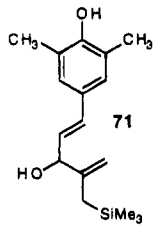
(29) Cf. MacMillan, J.; Martin, I. L.; Morris, D. J. *Tetrahedron* **1969**, *25*, 905.

Table 2. Quinone Methide-Initiated Cyclization Reactions

Entry	Phenol	Quinone Methide	Lewis Acid	Product(s)	Yield (%)
1	 **19**	 **52**	$Ti(OiPr)_3Cl$	 >20:1 **53** **54**	58
2	 **12**	 **55**	$ZnCl_2$	 85% + 6% **56** **57**	90
3	 **7**, R = H	 **58**, R = H	$ZnCl_2$	 **61**, R = H	83
4	**10**, R = OH	**59**, R = OH	$ZnCl_2$	—	—
5	**11**, R = $OSiMe_3$	**60**, R = $OSiMe_3$	$ZnCl_2$	**62**, R = $OSiMe_3$	82
6	 **9**	 **63**	$ZnCl_2$	 **64**	98
7	 **15**, R = CH_3	 **65**, R = CH_3	none	 **67**, R = CH_3	76
8	**16**, R = OCH_3	**66**, R = OCH_3	none	**68**, R = OCH_3	78
9	 **17**	 **69**	$ZnCl_2$	 12:1 **70a** **70b**	73

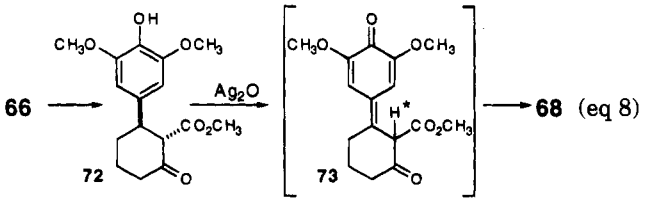
In an effort to examine the preparation of functionalized carbocycles via this methodology, the effect of an oxygen substituent two carbons removed from the quinone methide alkylidene carbon was studied with allylsilanes **59** and **60** (Table 2, entries 4 and 5). Phenol **10** underwent smooth oxidation to quinone methide **59**, which was observed by ^1H NMR spectroscopy. Treatment of **59** with $ZnCl_2$ did not afford any of the desired cyclization product; only intractable product mixtures were observed. In an attempt to increase the nucleophilicity of the allyl silane, **59** was treated with tetrabutylammonium fluoride. The product of the reaction was unstable styrene **71**, not the desired cyclization adduct. Analysis of the ^1H NMR spectrum of the crude reaction mixture showed the transformation to be virtually quantitative. Flash chromatography on deactivated (Et_3N) silica gel gave **71** in 64% isolated yield. Oxidation of silyl ether **11** to quinone methide **60**, followed by

treatment with $ZnCl_2$ afforded cyclization product **62** in 82% yield as a 5:1 mixture of diastereomers. The cyclization is thus compatible with an adjacent silyl ether, but not an adjacent alcohol. This is presumably due to $ZnCl_2$-mediated decomposition of the quinone methide facilitated by complexation with the free alcohol, and not the silyl ether.



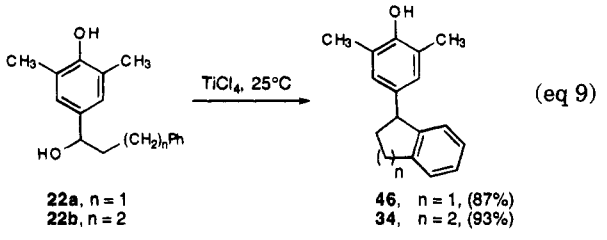
The formation of a seven-membered ring was studied with the cyclization of quinone methide **63** (entry 6, Table 2). Methylenecycloheptane **64** was obtained in 98% yield after treatment with tetrabutylammonium fluoride.

Several substrates incorporating a β-keto ester cyclization terminator were also examined (Table 2, entries 7–9). Oxidation of phenol **15** with Ag_2O (4.2 equiv) afforded cyclohexenone **67** in 76% yield. In this case, $ZnCl_2$ was not required to initiate the cyclization. A ^1H NMR spectrum of quinone methide **65** was obtained by careful monitoring of the oxidation. Oxidation of phenol **16** with Ag_2O (20 equiv) afforded a solution of **66** which was treated directly with $ZnCl_2$ (excess Ag_2O was not removed) to afford **68** and **72** in 78 and 20% yields, respectively (eq 8). The formation of cyclohexenones **68** (and **67**) must result from cyclization of the initially formed quinone methide to give the expected cyclohexanone **72** (eq 8). This was then oxidized by excess Ag_2O to quinone methide **73**, which in turn suffered loss of the acidic hydrogen doubly activated by the ketone and ester functionalities (H*, eq 8). In support of this notion, cyclohexanone **72** was resubmitted to the oxidation conditions to afford **68**.



The introduction of a methyl substituent adjacent to the quinone methide alkylidene (Table 2, entry 9) slowed the second oxidation, and cyclohexanone products were isolated in good yield. This example showed that the addition of a β-keto ester to a quinone methide can be reversible. The initial cyclization of quinone methide **69** gave **70** as a 1:1:1 mixture (^1H NMR analysis) of three diastereomers. Treatment of this mixture with $ZnCl_2$ afforded **70** as a 1.8:1 mixture of two diastereomers (**70a/70b**) after workup. Preparative TLC of this mixture afforded a 73% yield of **70a** as a 12:1 mixture of **70a/70b**, indicative of equilibration upon chromatography. This 12:1 mixture could be converted to a 1:1 mixture of diastereomers (**70a/70b**) by treatment with $NaOCH_3$ in CH_3OH or stirring with a suspension of silica gel in ethyl acetate. These results support the assignment of the mixture of epimers at the stereogenic center bearing the methyl ester. Due to the rapid epimerization of **70b** (the minor diastereomer) to a mixture **70a/70b** favoring **70a**, this diastereomer (**70b**) could not be characterized. The ^1H NMR spectrum of the major diastereomer showed a signal for the benzylic hydrogen as a triplet (J = 11.7 Hz) at δ 2.81 indicative of an axial hydrogen coupled to two adjacent axial hydrogens. This net epimerization of the three diastereomers initially formed in the cyclization to two diastereomers must occur via complexation of the Lewis acid with the β-keto ester to reversibly open the cyclohexanone ring to afford quinone methide **69**. Reclosure of the ring by addition to the quinone methide could then ultimately afford the thermodynamically favored products **70a** and **70b** with the aryl and methyl groups in an equatorial orientation.

Comparison of the Efficiency of Cyclizations with Preformed Quinone Methides vs in Situ-Generated Benzylic Cations. The difficulty seen in the cyclization of quinone methide **45** to form a five-membered ring (Table 1, entry 7) appeared to be in contrast to a similar cyclization of a benzylic alcohol upon treatment with a Lewis acid.[30] In an effort to probe the possible difference in cationic intermediates, benzylic alcohols **22a** and **22b** were treated with $TiCl_4$ (4 equiv). The six-membered cyclization substrate **22b** afforded tetralin **34** in 93% yield after 10 min at 25 °C (eq 9). Benzylic alcohol **22b** afforded tetralin **34** in the same yield as quinone methide **33** (entry 1, Table 1). Treatment of the five-membered cyclization substrate **22a** with $TiCl_4$ afforded the desired cyclization product **46** in 87% yield (eq 9). In contrast, quinone methide **45** failed to afford any cyclization product **46** under the same conditions (Table 1, entry 7). If a benzylic cation is involved in the reaction, one would expect the quinone methide and benzylic alcohol to provide the same cation and afford the same products. This is clearly not the case and implies that the quinone methide cyclizations are going through a cationic intermediate that has a sp^2 hybridized center adjacent to the aromatic ring. The benzylic alcohol on the other hand must experience significant assistance from the incoming cyclization terminator/nucleophile in the ionization step, and a benzylic cation is not formed.[31] The quinone methide presumably experiences unfavorable overlap in the transition state for cyclization due to



22a, n = 1
22b, n = 2

46, n = 1, (87%)
34, n = 2, (93%)

the two sp^3 centers in the transition state and the attempted cyclization failed. The alcohol, which presumably does not proceed via a free benzylic cation, does not encounter these problems with poor orbital overlap and the cyclization succeeds.

Conclusion

Quinone methides are versatile cyclization initiators that provide easy access to benzylic cation intermediates.

(30) Angle, S. R.; Louie, M. S. *J. Org. Chem.* **1991**, *56*, 2853.

(31) For reactions proposed to involve nucleophile assistance in displacement of a leaving group in the benzylic position see: (a) Bonnet-Delpon, D.; Cambillau, C.; Charpentier-Morize, M.; Jacquot, R.; Mesureur, D.; Ourevitch, M. *J. Org. Chem.* **1988**, *53*, 754. (b) Heck, R.; Winstein, S. *J. Am. Chem. Soc.* **1957**, *79*, 3105. (c) Mason, T. J. *J. Chem. Soc. Perkin Trans. 2* **1975**, 1664. (d) Ando, T.; Yamawaki, J.; Saito, Y. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 219.

Their formation and activation are compatible with highly reactive cyclization terminators such as pyrroles, as well as relatively unreactive cyclization terminators such as enecarbamates. The application of quinone methide-initiated cyclization reactions to the synthesis of natural products is currently under investigation.

Experimental Section[32]

General Information. NMR spectra were recorded on a JEOL FX200, General Electric QE-300, or GN-500 NMR; coupling constants (J) are reported in hertz and refer to apparent peak multiplicities and may not necessarily be true coupling constants; abbreviations used are as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentuplet, br = broad. UV spectra were recorded on a diode array spectrophotometer. HPLC was carried out with an refractive index detector using a 25 cm column (4.6 mm i.d.) packed with 8 μm of silica gel. Capillary GC was carried out using an FID detector on a 25 m HP-101 (methyl silicone) column. The following standard GC parameters were used unless indicated otherwise: flow rate = 60 mL/min; injector temp = 200 °C; detector temperature = 280 °C; temperature program = 40–280 °C at 18 °C/min, initial time = 1 min. The abbreviation rt is used for room temperature. The molarities indicated for alkyllithiums were established by titration with 2,5-dimethoxybenzyl alcohol.[33] In cases where synthetic intermediates or products were isolated by "aqueous workup" (aqueous solution, organic solvent, drying agent), the procedure was to quench the reaction mixture with the indicated aqueous solution, dilute with the indicated organic solvent, separate the organic layer, extract the aqueous layer several times with the organic solvent, dry the combined organic extracts over the indicated drying agent, and remove the solvent under reduced pressure (water aspirator) with a rotary evaporator. The pH 6 buffer was prepared by dissolving 23.2 g of KH_2PO_4 and 4.3 g of Na_2HPO_4 (anhydrous) in water and diluting to a volume of 1 L. Unless stated otherwise, all reactions were run under an atmosphere of nitrogen or argon in flame- or oven-dried glassware.

1-[(*tert*-Butyldimethylsilyl)oxy]-2,6-dimethyl-4-(2-propenyl)benzene (1). TBDMS-Cl (2.15 g, 14.3 mmol) and imidazole (1.76 g, 26.0 mmol) were added to a stirred solution of 2,6-dimethyl-4-(2-propenyl)phenol[34] (2.10 g, 13.0 mmol) in DMF (26 mL) at rt. After 4 h, aqueous workup (H_2O, ether, $MgSO_4$) afforded a yellow oil. Flash chromatography (20:1 hexanes/ethyl acetate) gave silyl ether **1** (3.07 g, 86%) as a clear oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.78 (s, 2 H, ArH), 6.03–5.88 (m, 1 H), 5.07 (br d, J = 12.5 Hz, 1 H), 5.02 (dd, J = 3.9, 1.7 Hz, 1 H), 3.26 (d, J = 6.7 Hz, 2 H), 2.18 (s, 6 H), 1.03 (s, 9 H), 0.17 (s, 6 H); IR ($CDCl_3$) 1638, 1483, 1473, 1465 cm^{-1}.

3-[4-[(*tert*-Butyldimethylsilyl)oxy]-3,5-dimethylphenyl]-1-propanol (2). BH_3·THF (30 mL of a 1.0 M solution in THF, 30 mmol) was added dropwise to a stirred solution of alkene **1** (7.67 g, 27.7 mmol) in THF (100 mL) at 0 °C over 10 min. The resulting mixture was stirred for 10 min and then the ice bath was removed and stirring was continued an additional 2 h. The reaction mixture was cooled to 0 °C and then NaOH (10.2 mL of a 3 N solution) and H_2O_2 (10.2 mL of a 30% solution) were slowly added. After stirring for 15 min, the cooling bath was removed and stirring was continued for 1 h. Aqueous workup (H_2O, ether, $MgSO_4$) afforded a clear oil. Flash chromatography (5:1 hexanes/ethyl acetate) afforded alcohol **2** (6.19 g, 76%) as a clear oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.81 (s, 2 H), 3.66 (t, J = 6.4 Hz, 2 H), 2.58 (t, J = 7.5 Hz, 2 H), 2.20 (s, 6 H), 1.86 (m, 2 H), 1.05 (s, 9 H), 0.20 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.9, 135.0, 129.4, 129.1, 63.2, 35.1, 32.0, 26.9, 19.5, 18.6, −2.2; IR (neat) 3650–3050, 1480, 1390, 1360 cm^{-1}; MS (EI, 20 eV) m/z 294 (M$^+$, 100), 219 (76), 179 (12); HRMS calcd for $C_{17}H_{30}O_2Si$ 294.2016, found 294.2015.

3-[4-[(*tert*-Butyldimethylsilyl)oxy]-3,5-dimethylphenyl]-propanal (3). PDC[17] (1.15 g, 3.05 mmol) was added to a stirred solution of alcohol **2** (500 mg, 1.70 mmol) in CH_2Cl_2 (8.5 mL) at rt. The resulting solution was stirred for 20 h. Ether (10 mL) was added, and after 5 min, the reaction mixture was filtered through silica gel (ether). Concentration afforded a yellow oil which was purified by flash chromatography (20:1 hexanes/ethyl acetate) to afford aldehyde **3** (288 mg, 58%) as a clear oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.82 (s, 1 H), 6.79 (s, 2 H), 2.83 (m, 2 H), 2.73 (m, 2 H), 2.19 (s, 6 H), 1.03 (s, 9 H), 0.18 (s, 6 H); ^{13}C (75 MHz, $CDCl_3$) δ 202.5, 150.8, 132.7, 128.5, 45.4, 30.0, 27.3, 26.1, 18.7, 17.7, −2.9; IR (CH_2Cl_2) 1724, 1484, 1474 cm^{-1}; MS (CI, CH_4) m/z 293 (MH$^+$, 9), 292 (M$^+$, 35), 235 (100); HRMS calcd for $C_{17}H_{28}O_2Si$ 292.1859, found 292.1886.

4-(3-Bromopropyl)-1-[(*tert*-butyldimethylsilyl)oxy]-2,6-dimethylbenzene (4). According to the general procedure of Hooz and Gilani,[18] $(Ph)_3P$ (1.68 g, 6.40 mmol) was added to a stirred solution of CBr_4 (2.10 g, 6.32 mmol) and alcohol **2** (931 mg, 3.17 mmol) in ether (10.3 mL) at rt. The resulting viscous yellow solution was stirred for 4 h, ether (20 mL) was added, and stirring was continued for an additional 20 min. Aqueous workup (H_2O, ether, $MgSO_4$) afforded a clear oil containing a white solid ($(Ph)_3PO$). Flash chromatography (hexanes) afforded bromide **4** (737 mg, 65%) as a clear oil that solidified upon standing in the freezer: mp < 25 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.79 (s, 2 H), 3.40 (t, J = 6.8 Hz, 2 H), 2.64 (t, J = 6.8 Hz, 2 H), 2.16 (s, 6 H), 2.12 (t, J = 6.8 Hz, 2 H), 1.05 (s, 9 H), 0.20 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.1, 133.8, 129.6, 129.2, 35.2, 34.1, 33.9, 29.9, 19.5, 18.6, −2.1; IR (CCl_4) 1475, 1438, 1228 cm^{-1}; MS (EI, 20 eV) m/z 358 (M$^+$, 100), 356 (M$^+$, 96), 301 (86), 299 (88); HRMS calcd for $C_{17}H_{29}OSiBr$ 356.1172, found 356.1171.

2,6-Dimethyl-4-[3-(pyrrol-1-yl)propyl]phenol (5). Pyrrole (0.28 mL, 4.0 mmol) was slowly added to a stirred suspension of NaH (97%, 99.2 mg, 4.01 mmol) in DMF (5.0 mL) at rt. After gas evolution ceased, the suspension was cooled to 0 °C and bromide **4** (270 mg, 0.800 mmol) dissolved in DMF (1.1 mL) was slowly added. The resulting solution was stirred for 20 min at 0 °C. Aqueous workup (H_2O, pH adjusted to 4.5 with H_3PO_4, ethyl acetate, Na_2SO_4) afforded 219 mg of crude product. Flash chromatography (7:1 hexanes/ethyl acetate) afforded **5** as a green viscous liquid (139 mg, 76%; purity by GC = 95.9%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.77 (s, 2 H), 6.66 (t, J = 2.1 Hz, 2 H), 6.15 (t, J = 2.1 Hz, 2 H), 4.49 (s, 1 H), 3.87 (t, J = 7.1 Hz, 2 H), 2.48 (t, J = 7.6 Hz, 2 H), 2.22 (s, 6 H), 2.10–2.00 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.2, 132.4, 128.3, 123.0, 120.3, 108.0, 48.6, 33.0, 31.7, 15.7; IR (neat) 3528, 2925, 1499 cm^{-1}; UV (EtOH) λ_{max} 362, 278, 204 nm; MS (EI, 20 eV) m/z 229 (M$^+$, 39), 81(100); HRMS calcd for $C_{15}H_{19}NO$ 229.1467, found 229.1463.

2,6-Dimethyl-4-[3-(furan-3-yl)butyl]phenol (6). A solution of 3-(chloromethyl)furan[35] (138 mg, 1.23 mmol) and THF (1 mL) was added dropwise to Mg (29.7 mg, 1.24 mmol) and THF (1 mL). The resulting solution was refluxed until no Mg was visible, then cooled to 0 °C and a solution of bromide **4** (201 mg, 0.562 mmol) in THF (1 mL) was added, followed immediately by the addition of a solution of Li_2CuCl_4 (0.1 mL of a 0.1 M solution in THF, 0.01 mmol).[36] The resulting suspension was stirred for 1 h at 0 °C. Aqueous workup (H_2O, ether, Na_2SO_4) afforded crude product (248 mg). Flash chromatography (20:1 hexanes/ethyl acetate) afforded 1-[(*tert*-butyldimethylsilyl)oxy]-2,6-dimethyl-4-[4-(3-furanyl)butyl]benzene (198 mg, 94%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 (t, J = 1.5 Hz, 1 H), 7.20 (br s, 1 H), 6.76 (s, 2 H), 6.75 (br s, 1 H), 2.54–2.36 (m, 4 H), 2.18 (s, 6 H), 1.65–1.55 (m, 4 H), 1.03 (s, 9 H), 0.18 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.9, 142.6, 138.8, 135.0, 128.7, 128.6, 125.1, 111.0,

(32) Some general experimental details have recently been reported: Angle, S. R.; Mattson-Arnaiz, H. L. *J. Am. Chem. Soc.* **1992**, *114*, 9782, and ref 30.

(33) Winkle, M. R.; Lansinger, J. M.; Ronald, R. C. *J. Chem. Soc., Chem. Commun.* **1980**, 87.

(34) The 4-propenylphenols were prepared via Claisen rearrangement of the corresponding *O*-allylphenols according to the general procedure of Tarbell and Kincaid described in ref 16.

(35) Tanis, S. P. *Tetrahedron Lett.* **1982**, *23*, 3115.

(36) Tamura, M.; Kochi, J. *Synthesis* **1971**, 303.

34.8, 31.2, 29.7, 26.1, 24.6, 18.7, 17.8, −2.9; IR (CCl_4) 2931, 2859 cm^{-1}; UV (EtOH) λ_{max} 276, 206 nm; MS (EI, 20 eV) m/z 358 (M^+, 81), 301 (76), 61 (100); HRMS calcd for $C_{22}H_{34}O_2Si$ 358.2328, found 358.2317. (n-Bu)$_4$NF (0.24 mL of a 1 M solution in THF, 0.24 mmol) was added to a stirred solution of the above silyl phenol (56.1 mg, 0.154 mmol) in THF (1 mL). The resulting solution was stirred at rt for 15 min. Concentration and flash chromatography (4:1 hexanes/ethyl acetate) afforded **6** (29.7 mg, 82%) as colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.34 (s, 1 H), 7.19 (s, 1 H), 6.78 (s, 2 H), 6.25 (s, 1 H), 4.46 (s, 1 H), 2.47 (t, J = 6 Hz, 2 H), 2.43 (t, J = 6 Hz, 2 H), 2.22 (s, 6 H), 1.59 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.1, 142.6, 138.7, 134.2, 128.4, 125.1, 122.7, 111.0, 34.8, 31.4, 29.6, 24.6, 15.9; IR (CCl_4) 3638, 2938, 1610, 1525, 1480 cm^{-1}; UV (EtOH) λ_{max} 280, 206 nm; MS (EI, 20 eV) 244 (M^+, 92), 135 (100); HRMS calcd for $C_{16}H_{20}O_2$ 244.1463, found 244.1470.

2,6-Dimethyl-4-[4-[(trimethylsilyl)methyl]-4-pentenyl]-phenol (7). t-BuLi (2.9 mL of a 1.7 M solution in pentane, 4.9 mmol) was added dropwise over 5 min to a stirred solution of 2-bromo-3-(trimethylsilyl)-1-propene[19] (477 mg, 2.47 mmol) in THF (2.5 mL) at −78 °C. The resulting yellow solution was stirred at −78 °C for 45 min and then added via a dry ice-jacketed cannula to a solution of lithium 2-thienylcyanocuprate[37] (10.3 mL of a 0.25 M solution in THF (Aldrich), 2.57 mmol). The resulting brown solution was stirred at −78 °C for 15 min, and then a solution of bromide **4** (417 mg, 1.17 mmol) in THF (0.5 mL) was added. The resulting brown solution was allowed to warm to rt, heated to 35 °C, and stirred for 65 h.[37] The reaction mixture was then poured into a stirred solution of 9:1 saturated aqueous NH_4Cl/concentrated NH_4OH (100 mL). After 30 min, aqueous workup (H_2O, ether, $MgSO_4$) afforded 463 mg (100%) of the crude allylsilane as a brown oil. Due to difficulty in purification, the crude product was used directly in the desilylation reaction. An analytical sample was prepared by flash chromatography (40:1:0.1 hexane/ethyl acetate/Et_3N) of a portion (45 mg) of this material to afford 1-[(*tert*-butyldimethylsilyl)oxy]-2,6-dimethyl-4-[4-[(trimethylsilyl)methyl]-4-pentenyl]benzene as a light yellow oil: ^1H NMR (300 MHz, $CDCl_3$) δ 6.78 (s, 2 H), 4.61(s, 1 H), 4.53 (s, 1 H), 2.48 (t, J = 7.7 Hz, 2 H), 2.19 (s, 6 H), 1.98 (t, J = 7.6 Hz, 2 H), 1.65−1.79 (m, 2 H), 1.25 (m, 2H), 1.04 (s, 9 H), 0.18 (s, 6 H), 0.01 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.4, 147.6, 135.0, 129.3, 128.1, 106.9, 37.2, 34.7, 29.7, 26.5, 18.7, 18.1, 17.5, −1.3, −3.0; IR (CCl_4) 1633, 1484, 1300 cm^{-1}; MS (EI, 20 eV) m/z 390 (M^+, 7), 262 (100), 205 (46); HRMS calcd for $C_{23}H_{42}Si_2O$ 390.2774, found 390.2791. Aqueous NaOH (10.7 mL of a 2 N solution, 21.4 mmol) was added to a solution of the above crude silyl ether (418 mg, 1.07 mmol) in THF/ethanol (1:1, 6 mL). The resulting solution was stirred at rt for 72 h. Aqueous workup (saturated aqueous NH_4Cl/concentrated NH_4OH solution (9:1 v/v, 25 mL), ether, $MgSO_4$) afforded 341 mg of a yellow oil. Flash chromatography (20:1:0.1 hexanes/ethyl acetate/Et_3N) afforded phenol **7** (229 mg, 77%) as a clear oil: ^1H NMR (300 MHz, $CDCl_3$) δ 6.80 (s, 2 H), 4.61 (s, 1 H), 4.53 (s, 1 H), 4.47 (s, 1 H), 2.48 (t, J = 7.7 Hz, 2 H), 2.23 (s, 6 H), 1.99 (t, J = 7.5 Hz, 2 H), 1.76−1.66 (m, 2 H), 1.54 (s, 2 H), 0.01 (s, 9 H); ^{13}C (75 MHz, $CDCl_3$) δ 152.3, 147.7, 134.4, 128.7, 122.9, 107.1, 38.0, 34.9, 30.1, 27.0, 16.1, −1.1; IR (CCl_4) 3630, 1632, 1488 cm^{-1}; MS (EI, 20 eV) m/z 276 (M^+, 2), 220 (68), 148 (100); HRMS calcd for $C_{17}H_{28}SiO$ 276.1910, found 276.1914.

2,6-Dimethyl-4-{4,4-bis(ethoxycarbonyl)-6-[(trimethylsilyl)methyl]-6-heptenyl}phenol (9). A solution of diester **8**[38] (221 mg, 0.770 mmol) in THF was added to a stirred suspension of NaH (18.5 mg, 0.770 mmol) in THF (2.5 mL) at 0 °C. The resulting solution was stirred for 10 min and allowed to warm to rt, and then a solution of bromide **4** (197.5 mg, 0.616 mmol) in THF (0.3 mL) was added. The resulting solution was stirred for 10 min and then heated to 55 °C for 12 h. After cooling, the reaction mixture was poured into a solution of 9:1 saturated aqueous NH_4Cl/concentrated NH_4OH. Aqueous workup (H_2O, ether, Na_2SO_4) followed by flash chromatography (20:1 hexanes/ethyl acetate) afforded the silyl ether of **9** (93.6 mg, 27%) as a clear oil. A portion of this material (67.0 mg, 0.119 mmol) was added to a solution of NaOEt (from Na 82 mg, 3.6 mmol) in ethanol (2 mL) and heated to 55 °C for 9 h. Aqueous workup (saturated aqueous NH_4Cl/concentrated NH_4OH, ether, Na_2SO_4) followed by flash chromatography (6:1 hexanes/ethyl acetate) afforded **9** (44.2 mg, 83%) as a clear oil: ^1H NMR (300 MHz, $CDCl_3$) δ 6.75 (s, 2 H, ArH), 4.63 (s, 1 H), 4.58 (s, 1 H), 4.53 (s, 1 H), 4.15 (m, 4 H), 2.62 (s, 2 H), 2.47 (t, J = 7.6 Hz, 2 H), 2.21 (s, 6 H), 1.96 (m, 2 H), 1.45 (m, 2 H), 1.40 (s, 2 H), 1.23 (t, J = 7.1 Hz, 6 H), 0.01 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.7, 150.2, 142.2, 133.5, 128.4, 122.7, 111.7, 61.0, 57.3, 39.6, 35.1, 31.6, 27.4, 26.3, 15.9, 14.0, −1.5; IR (CCl_4) 3621, 3529, 2957, 1731, 1630, cm^{-1}; MS (EI, 20 eV) m/z 448 (M^+, 100), 433 (22), 375 (24); HRMS calcd for $C_{25}H_{40}O_5Si$ 448.2646, found 448.2645. Anal. Calcd for $C_{25}H_{40}O_5Si$: C, 66.92; H, 8.99. Found: C, 66.80; H, 8.80.

(±)-2,6-Dimethyl-4-[3-hydroxy-4-[(trimethylsilyl)-methyl]-4-pentenyl]phenol (10). t-BuLi (0.48 mL of a 1.7 M solution in pentane, 0.82 mmol) was added dropwise to a stirred solution of 2-bromo-3-(trimethylsilyl)-1-propene[19] (79.3 mg, 0.410 mmol) in THF (1 mL) at −78 °C. The resulting yellow solution was stirred at −78 °C for 1 h and then added via a dry ice jacketed cannula to a solution of aldehyde **3** (100 mg, 0.342 mmol) in THF (1 mL) at −78 °C. The resulting yellow solution was stirred at −78 °C for 30 min and then the cooling bath was removed. After warming to rt, the reaction mixture was stirred an additional 30 min and then poured into a H_2O/ether mixture (1:1, 10 mL). Aqueous workup (H_2O, ether, $MgSO_4$) afforded a yellow oil. Flash chromatography (10:1:0.025 hexane/ethyl acetate/Et_3N) afforded 1-[(*tert*-butyldimethylsilyl)oxy]-2,6-dimethyl-4-[3-hydroxy-4-[(trimethylsilyl)methyl]-4-pentenyl]benzene (116 mg, 83%) as a viscous white oil: ^1H NMR (300 MHz, $CDCl_3$) δ 6.83 (s, 2 H), 4.96 (d, J = 1.1 Hz, 1 H), 4.70 (s, 1 H), 3.97 (dd, J = 7.7, 3.9 Hz, 1 H), 2.74−2.51 (m, 2 H), 2.31 (s, 6 H), 2.00−1.71 (m, 2 H), 1.54 (ABq, J = 13.8 Hz, $\Delta\nu$ = 66.5 Hz, 2 H), 1.06 (s, 9 H), 0.20 (s, 6 H), 0.04 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.0, 149.9, 134.5, 128.7, 128.2, 107.0, 74.8, 37.4, 31.1, 26.1, 22.6, 18.7, 17.8, −1.2, −3.0; IR (CCl_4) 3635, 1640, 1491, 1480 cm^{-1}; MS (EI, 20 eV) m/z 406 (M^+, 8), 262 (100); HRMS calcd for $C_{23}H_{42}O_2Si_2$ 406.2723, found 406.2720. NaOH (4.5 mL of a 2 N solution, 9.0 mmol) was added to a THF/ethanol solution (1:1 v/v, 2 mL) of a sample of the above silylated phenol (178 mg, 0.437 mmol). After stirring for 48 h at rt, aqueous workup (saturated aqueous NH_4Cl/concentrated NH_4OH solution (9:1 v/v, 10 mL), ether, $MgSO_4$) afforded a clear oil. Flash chromatography (20:1:0.1 hexanes/ethyl acetate/Et_3N) afforded phenol **10** (128 mg, 99%) as a clear oil: ^1H NMR (300 MHz, $CDCl_3$) δ 6.83 (s, 2 H), 4.96 (s, 1 H), 4.71 (s, 1 H), 4.67 (s, 1 H), 3.98 (dt, J = 4.0, 5.9 Hz, 1 H), 2.72−2.49 (m, 2 H), 2.24 (s, 6 H), 1.59 (d, J = 4.1 Hz, 1 H), 1.54 (ABq, J = 14.0 Hz, $\Delta\nu$ = 64.5 Hz, 2 H), 0.04 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.2, 149.9, 133.5, 128.5, 122.9, 107.1, 75.0, 37.8, 31.1, 22.5, 15.9, −1.2; IR (CCl_4) 3628, 1632, 1587, 1488 cm^{-1}; MS (EI, 20 eV) m/z 292 (M^+, 6), 144 (26), 135 (100); HRMS calcd for $C_{17}H_{28}O_2Si$ 292.1859, found 292.1869.

(±)-2,6-Dimethyl-4-[4-[(trimethylsilyl)methyl]-3-[(trimethylsilyl)oxy)]-4-pentenyl]phenol (11). Me_3SiCl (0.275 mL, 1.97 mmol) was added to a solution of **10** (229 mg, 0.783 mmol) and hexamethyldisilazane (415 μL, 1.97 mmol) in pyridine (7.8 mL). After stirring at rt for 3 h, aqueous workup (H_2O, ether, combined organic layers washed with saturated aqueous $CuSO_4$, $MgSO_4$) afforded 2,6-dimethyl-4-[4-[(trimethylsilyl)methyl]-3-[(trimethylsilyl)oxy]-4-pentenyl]-1-[(trimethylsilyl)oxy]benzene (322 mg, 94%) as a clear oil: ^1H NMR (300 MHz, $CDCl_3$) δ 6.80 (s, 2 H), 4.94 (d, J = 1.3 Hz, 1 H), 4.67 (d, J = 0.7 Hz, 1 H), 3.96 (dd, J = 7.3, 4.6 Hz, 1 H), 2.63−2.53 (m, 1 H), 2.48−2.37 (m, 1 H), 2.18 (s, 6 H), 1.92−1.80 (m, 1 H), 1.77−1.65 (m, 1 H), 1.50 (ABq, J = 14.1 Hz, $\Delta\nu$ = 54.0 Hz, 2 H), 0.25 (s, 9 H), 0.12 (s, 9 H), 0.05 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.0, 149.7, 134.5, 128.9, 128.3, 106.8, 78.0, 38.3, 31.3, 22.1, 16.2, 0.7, −1.0, −2.8; IR (CCl_4) 1639, 1485 cm^{-1}; MS (EI, 20 eV) m/z 436 (M^+, 3), 216 (100), 207 (36);

(37) Lipshutz, B. H.; Koerner, M.; Parker, D. A. *Tetrahedron Lett.* **1987**, *28*, 945. This cuprate reaction was much slower than expected, perhaps due to the effect of the trimethylsilyl group.

(38) Diester **8** was prepared by alkylation of the sodium salt of diethyl malonate with 1-bromo-2-[(trimethylsilyl)methyl]-2-propene (Molander, G. A.; Shubert, D. C. *Tetrahedron Lett.* **1986**, *27*, 787).

HRMS calcd for $C_{23}H_{44}O_2Si_3$ 436.2649, found 436.2652. (n-Bu)$_4$NF (50 μL of a 1 M solution in THF, 0.050 mmol) was added to a stirred solution of the above bis-silyl ether (73.3 mg, 0.168 mmol) in $CDCl_3$ (2 mL). After 5 min, aqueous workup (H_2O, ether, Na_2SO_4) afforded crude product. Flash chromatography (10:1:0.25 hexanes/ethyl acetate/Et_3N) afforded impure **11** (51.1 mg) which was subjected to a second flash chromatography (20:1:0.1 hexanes/ethyl acetate/triethylamine) to afford **11** (47.2 mg, 77%) as a clear oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.81 (s, 2 H), 4.94 (s, 1 H), 4.67 (d, J = 0.7 Hz, 1 H), 4.49 (s, 1 H), 3.98 (dd, J = 7.1, 4.7 Hz, 1 H), 2.63–2.52 (m, 1 H), 2.47–2.36 (m, 1 H), 2.23 (s, 6 H), 1.89–1.62 (m, 2 H), 1.49 (ABq, J = 14.4 Hz, $\Delta\nu$ = 53.2 Hz, 2 H), 0.13 (s, 9 H), 0.03 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.5, 149.2, 134.5, 129.0, 123.2, 108.6, 77.9, 38.7, 31.6, 21.9, 16.3, 0.8, -0.4; IR (CCl_4) 3640, 1640, 1492 cm^{-1}; MS (EI, 20 eV) m/z 364 (M$^+$, 1), 216 (100), 135 (27); HRMS calcd for $C_{20}H_{36}O_2Si_2$ 364.2255, found 364.2254.

2,6-Dimethyl-4-[3-[(*N*-benzyloxycarbonyl)-*N*-ethenylamino]propyl]phenol (12). A solution of 2-(phenylseleno)-ethylamine (364 mg, 1.82 mmol)[20] in CH_2Cl_2 (1.6 mL) was added dropwise to a stirred suspension of aldehyde **3** (487 mg, 1.67 mmol) and $MgSO_4$ (199 mg, 1.65 mmol) in CH_2Cl_2 (2.8 mL) at 0 °C. The resulting suspension was stirred for 2 h at 0 °C and then CH_3OH (2.4 mL) and $NaBH_4$ (74.5 mg, 1.97 mmol) were added sequentially. After stirring at 0 °C for 30 min, H_2O (2.0 mL) was added and the resulting suspension was stirred for 15 min. Aqueous workup (H_2O, CH_2Cl_2, K_2CO_3) afforded 1-[(*tert*-butyldimethylsilyl)oxy]-2,6-dimethyl-4-[3-[*N*-[2-(phenylseleno)ethyl]amino]propyl]benzene (859 mg) as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53–7.49 (m, 2 H), 7.26–7.24 (m, 3 H), 6.76 (s, 2 H), 3.05 (t, J = 6.6 Hz, 2 H), 2.87 (t, J = 6.6 Hz, 2 H), 2.61 (t, J = 7.2 Hz, 2 H), 2.50 (t, J = 7.7 Hz, 2 H), 2.17 (s, 6 H), 1.75 (m, 3 H), 1.03 (s, 9 H), 0.18 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.0, 134.4, 132.8, 129.7, 129.1, 128.6, 128.2, 127.0, 48.9, 48.8, 32.6, 31.7, 28.4, 26.1, 18.7, 17.8, −3.0; IR ($CDCl_3$) 3695, 3691, 2932, 2859, 1479 cm^{-1}. Benzyl chloroformate (400 μL, 1.80 mmol) was added to a two-phase mixture of the above crude amine (859 mg), saturated aqueous $NaHCO_3$ (3 mL), and CH_2Cl_2 (3 mL). The resulting two-phase solution was stirred at rt for 8 h. Aqueous workup (H_2O, CH_2Cl_2, K_2CO_3) afforded 863 mg of a yellow oil. Flash chromatography (9:1 hexane/ethyl acetate) afforded 826 mg (85%) of 1-[(*tert*-butyldimethylsilyl)oxy]-2,6-dimethyl-4-[3-[*N*-(benzyloxycarbonyl)-*N*-[2-phenylseleno)ethyl]amino]propyl]-benzene as a clear oil: ^{1}H NMR (300 MHz, $CDCl_3$, 45 °C) δ 7.59–7.10 (m, 10 H), 6.75 (s, 2 H), 5.15 (s, 2 H), 3.52 (m, 2H), 3.31 (t, J = 6.9 Hz, 2 H), 3.05 (br m, 2 H), 2.46 (t, J = 6.9 Hz, 2 H), 2.21 (s, 6 H), 1.81 (m, 2 H). 1.07 (s, 9 H), 0.22 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$, 45 °C) δ 155.9, 150.2, 136.8, 133.9, 132.3, 129.0, 128.5, 128.2, 127.9, 126.9, 67.0, 47.7 (br), 32.2, 30.3, 26.1, 25.0, 18.7, 17.8, −3.0; IR (CCl_4) 2931, 1703, 1473, 1254 cm^{-1}; MS (EI, 50 eV) m/z 611 (M$^+$, 28), 306 (41), 91 (100); HRMS calcd for $C_{33}H_{45}NO_3SeSi$ 611.2334, found 611.2339. (n-Bu)$_4$NF (1.2 mL of a 1 M solution in THF, 1.2 mmol) was added dropwise to a stirred solution of the above silyl phenol in THF (4.2 mL) at 0 °C. The resulting mixture was allowed to warm to rt and stirred for 20 min. Aqueous workup (H_2O, ethyl acetate, Na_2SO_4) afforded 580 mg of an amber oil. Flash chromatography (5:1 hexanes/ethyl acetate) afforded 2,6-dimethyl-4-[3-[*N*-(benzyloxycarbonyl)-*N*-[2-(phenylseleno)-ethyl]amino]propyl]phenol (474 mg, 77%) as a clear oil: ^{1}H NMR (300 MHz, $CDCl_3$, 50 °C) δ 7.53–7.11 (m, 10 H), 6.73 (s, 2 H), 5.12 (s, 2 H), 4.45 (s, 1 H), 3.50 (t, J = 7.5 Hz, 2 H), 3.29 (t, J = 7.5 Hz, 2 H), 3.02 (br m, 2 H), 2.43 (t, J = 7.5 Hz, 2H), 2.20 (s, 6 H), 1.78 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.8, 150.4, 136.5, 132.5, 132.2, 128.2, 128.0 (br), 127.9, 127.2, 66.9, 47.6, 32.2, 30.2 (br), 24.8, 15.8; IR (CCl_4) 3621, 2934, 1704, 1489, 1478 cm^{-1}; MS (EI, 50 eV) m/z 497 (M$^+$, 7), 340 (26), 161 (22), 91 (100); HRMS calcd for $C_{27}H_{31}NO_3Se$ 497.1469, found 497.1480. A solution of m-CPBA (143.2 mg, 0.829 mmol) in CH_2Cl_2 (1.25 mL) was added dropwise to a stirred solution of the above phenol (187 mg, 0.378 mmol) and CH_2Cl_2 (2.5 mL) at 0 °C. The resulting solution was stirred for 90 min and then diisopropylamine (1.55 mL, 11.1 mmol) was added. The resulting solution was refluxed for 20 h and then allowed to cool to rt. Aqueous workup ($NaHCO_3$, CH_2Cl_2, Na_2SO_4) afforded 402 mg of a brown oil. Medium pressure liquid chromatography (9:1 hexanes/ethyl acetate) afforded **12** (66.0 mg, 54%) as an amber oil: ^{1}H NMR (300 MHz, $CDCl_3$, 45 °C) δ 7.45–7.29 (m, 5 H), 7.11 (m, 1 H), 6.79 (s, 2 H), 5.23 (s, 2 H), 4.70 (br m, 1 H), 4.27–4.23 (m, 2 H), 3.59 (t, J = 7.5 Hz, 2 H), 2.53 (t, J = 7.8 Hz, 2 H), 2.23 (s, 6 H), 1.89 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$, 45 °C, C=O not observed) δ 150.4, 136.2, 132.9, 132.5 (br), 128.5, 128.3, 128.1, 127.9, 123.0, 91.8, 67.8, 43.1, 32.2, 28.6, 15.8; IR (CCl_4) 3621, 2924, 1716, 1630, 1197, 1176 cm^{-1}.

4-(3-Bromopropyl)-1-[(*tert*-butyldimethylsilyl)oxy]-2,6-dimethoxybenzene (13) The same procedure used for the preparation of **2** from **1** was carried out with 2,6-dimethoxy-4-(3-propenyl)phenol[34] (5.97 g, 30.8 mmol). Flash chromatography (20:1 hexanes/ethyl acetate) afforded 5.46 g of 3-[4-[(*tert*-butyldimethylsilyl)oxy]-3,5-dimethoxyphenyl]-1-propanol (57%) as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.38 (s, 2 H), 3.78 (s, 6 H), 3.65 (t, J = 6.5 Hz, 2 H), 2.63 (apparent t, J = 7.5 Hz, 2 H), 1.87 (m, 2 H), 1.01 (s, 9 H), 0.12 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.3, 134.3, 132.2, 105.3, 62.0, 55.6, 34.2, 32.2, 25.7, 18.6, −4.8; IR ($CDCl_3$) 1588, 1511, 1465, 1423 cm^{-1}; MS (EI, 20eV) m/z 326 (M$^+$, 5), 269 (100), 254 (24); HRMS calcd for $C_{17}H_{30}O_4Si$ 326.1913, found 326.1899. The same procedure used for the preparation of **4** from **2** was carried out with the above alcohol (3.58 g, 10.9 mmol). Flash chromatography (20:1 hexanes/ethyl acetate) afforded **13** (2.64 g, 62%) as a clear oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.37 (s, 2 H), 3.78 (s, 6 H), 3.38 (t, J = 6.5 Hz, 2 H), 2.69 (apparent t, J = 7.3 Hz, 2 H), 2.18–2.10 (m, 2 H), 1.01 (s, 9 H), 0.12 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.5, 132.9, 132.6, 105.5, 55.7, 34.2, 34.1, 33.2, 25.8, 18.7, −4.7; IR ($CDCl_3$) 1589, 1512, 1464, 1423 cm^{-1}; MS (EI, 20eV) m/z 390 (M$^+$, 3), 388 (M$^+$, 3), 333 (100), 331 (93); HRMS calcd for $C_{17}H_{29}BrO_3Si$ 388.1069, found 388.1076.

(±)-4-(3-Bromo-2-methylpropyl)-1-[(*tert*-butyldimethylsilyl)oxy]-2,6-dimethylbenzene (14). The same procedure used for the preparation of **2** from **1** was carried out with 2,6-dimethyl-4-(2-methylpropenyl)phenol[34] (9.00 g, 30.6 mmol). Flash chromatography (6:1 hexanes/ethyl acetate) afforded (±)-3-[4-[(*tert*-butyldimethylsilyl)oxy]-3,5-dimethylphenyl]-2-methyl-1-propanol (6.04 g, 64%) as a clear oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.81 (s, 2 H), 3.54 (dd, J = 10.5, 6.2 Hz, 1 H), 3.46 (dd, J = 10.5, 5.9 Hz, 1 H), 2.64 (dd, J = 13.5, 6.3 Hz, 1 H), 2.31 (dd, J = 13.4, 8.0 Hz, 1 H), 2.23 (s, 6 H), 1.97–1.87 (m, 1 H), 1.08 (s, 9 H), 0.94 (d, J = 6.7 Hz, 3 H), 0.23 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.0, 133.1, 129.3, 128.0, 65.5, 38.8, 37.7, 26.0, 18.6, 17.7, 16.5, −1.2; IR (neat) 3350, 1742, 1480, 1473, 1464, 1438, 1388 cm^{-1}; MS (CI, CH_4) m/z 309 (MH$^+$, 26), 308 (M$^+$, 100), 233 (38), 209 (71); HRMS calcd for $C_{18}H_{32}O_2Si$ 308.2178, found 308.2172. The same procedure used for the preparation of **4** from **2** was carried out with the above alcohol (3.73 g, 12.1 mmol). Flash chromatography (hexane) afforded bromide **14** (2.47 g, 55%) as a clear oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.77 (s, 2 H), 3.39 (dd, J = 9.8, 4.9 Hz, 1 H), 3.30 (dd, J = 9.8, 5.8 Hz, 1 H), 2.60 (dd, J = 13.6, 7.2 Hz, 1 H), 2.41 (dd, J = 13.7, 6.9 Hz, 1 H), 2.19 (s, 6 H), 2.09–1.99 (m, 1 H), 1.03 (s, 9 H), 1.03 (obscured m, 3 H), 0.19 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.4, 132.2, 129.4, 128.2, 40.8, 40.2, 37.2, 26.2, 18.9, 17.8, −2.9; IR (neat) 1478, 1472, 1461, 1432, 1387, 1375, 1359 cm^{-1}; MS (EI, 20eV) m/z 372 (M$^+$, 100), 370 (M$^+$, 91), 273 (92), 271 (76); HRMS calcd for $C_{18}H_{31}BrOSi$ 370.1328, found 370.1315.

Methyl 7-(3,5-Dimethyl-4-hydroxyphenyl)-3-oxoheptanoate (15). According to the general procedure of Weiler,[21] ethyl acetoacetate (0.80 mL, 7.14 mmol) was added dropwise to a stirred suspension of NaH (202 mg, 8.15 mmol) in THF (24 mL) at 0 °C. The resulting solution was stirred for 10 min, and then n-BuLi (3.2 mL of a 2.4 M solution in hexanes, 7.8 mmol) was added dropwise. After stirring an additional 10 min at 0 °C, a solution of bromide **4** (265 mg, 0.741 mmol) in THF (0.5 mL) was added and the resulting solution was stirred at rt for 30 min. Aqueous workup (1 N HCl, ether, $MgSO_4$) afforded a yellow oil. Flash chromatography (10:1 hexanes/ethyl acetate) afforded 228 mg (78%) of product. (n-Bu)$_4$NF (0.41 mL of a 1 M solution in THF, 0.41 mmol) was added to

a solution of a similar sample of the above silyl ether (114 mg, 0.289 mmol) in THF (1.8 mL) at rt. After stirring for 90 min, aqueous workup (H_2O, ether, $MgSO_4$) afforded crude product as a yellow oil. Flash chromatography (3:1 hexanes/ethyl acetate) afforded **15** (69.1 mg, 91%) as a clear oil: ^1H NMR (300 MHz, $CDCl_3$) δ 6.77 (s, 2 H), 4.85 (br s, 1 H), 3.74 (s, 3 H), 3.44 (s, 2 H), 2.51 (m, 4 H), 2.22 (s, 6 H), 1.60 (br s, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.6, 168.5, 151.1, 134.3, 129.2, 123.8, 53.1, 49.8, 43.7, 35.5, 31.9, 23.9, 16.7; IR (CCl_4) 3620, 3005, 2922, 2855, 1755, 1722, 1658, 1628 cm^{-1}; MS (EI, 20 eV) m/z 278 (M^+, 40), 260 (18), 135 (100); HRMS calcd for $C_{16}H_{22}O_4$ 278.15186, found 278.15181. Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 69.34; H, 8.12.

Methyl 7-(3,5-dimethoxy-4-hydroxyphenyl)-3-oxoheptanoate (16). The procedure described above for the preparation of **15** was carried out with bromide **13** (202 mg, 0.519 mmol) to afford crude product as a yellow oil. Three successive flash chromatographies (5:1 hexanes/ethyl acetate; 10:1 hexanes/ethyl acetate; 15:1 hexanes/ethyl acetate) afforded the silyl ether (142 mg, 64%) as a clear oil. Desilylation of a portion of this material (48.7 mg, 0.115 mmol) according to the procedure described for **15** above, afforded crude **16** as a yellow oil. Flash chromatography (3:1 hexanes/ethyl acetate) afforded **16** (34.8 mg, 98%) as a clear oil: ^1H NMR (300 MHz, $CDCl_3$) δ 6.40 (s, 2 H), 5.37 (s, 1 H), 3.89 (s, 6 H), 3.74 (s, 3 H), 3.45 (s, 2 H), 2.57 (apparent q, J = 6.4 Hz, 4 H), 1.63 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.6, 167.6, 146.8, 133.1, 132.7, 104.8, 56.2, 52.3, 49.0, 42.8, 35.9, 30.9, 23.0; IR (CCl_4) 3572, 1754, 1732, 1664, 1623, 1519, 1470 cm^{-1}; MS (EI, 20 eV) m/z 310 (M^+, 100), 278 (41), 167 (61); HRMS calcd for $C_{16}H_{22}O_6$ 310.1417, found 310.1416.

(±)-Methyl 7-(3,5-dimethyl-4-hydroxyphenyl)-6-methyl-3-oxoheptanoate (17). The procedure described above for the preparation of **15** was carried out with bromide **14** (300 mg, 0.809 mmol) to afford crude product as a yellow oil. Flash chromatography (gradient: 15:1, 10:1, 5:1 hexanes/ethyl acetate) afforded recovered bromide **14** (61.5 mg, 20%) and product silyl ether (174 mg, 53%; 66% based on recovered **14**) as a clear oil. Desilylation of a portion of this material (70.2 mg, 0.173 mmol) according to the procedure described for **15** above, afforded crude **17** as a yellow oil. Flash chromatography (10:1 hexanes/ethyl acetate) afforded **17** (45.7 mg, 90%) as a clear oil: ^1H NMR (300 MHz, $CDCl_3$) δ 6.74 (s, 2 H), 4.48 (br s, 1 H), 3.73 (s, 3 H), 3.43 (s, 2 H), 2.61–2.45 (m, 3 H), 2.32–2.25 (m, 1 H), 2.22 (s, 6 H), 1.75–1.60 (m, 2 H), 1.50–1.37 (m, 1 H), 0.85 (d, J = 6.4 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.9, 167.7, 150.3, 132.4, 129.2, 122.7, 52.3, 48.9, 42.6, 40.9, 34.5, 30.0, 19.2, 15.9; IR (CCl_4) 3638, 3541, 1759, 1734, 1666, 1637, 1500, 1461 cm^{-1}; MS (EI, 20 eV) m/z 292 (M^+, 21), 135 (100); HRMS calcd for $C_{17}H_{24}O_4$ 292.1675, found 292.1675.

(*E* and *Z*)-7-(3,5-Dimethyl-4-hydroxyphenyl)-1-methoxy-1-heptene (19). *n*-BuLi (0.33 mL of a 2.26 M solution in hexanes, 0.75 mmol) was added to a stirred solution of (methoxymethyl)triphenylphosphonium chloride[39] (296 mg, 0.86 mmol) and ether (30 mL) at −78 °C. The cooling bath was removed, and the reaction mixture was allowed to warm to rt and stirred for 1 h. The resulting orange mixture was cooled to −78 °C, and a solution of aldehyde **18**[22] (193 mg, 0.576 mmol) in ether (15 mL) was added dropwise. Immediately after the addition was completed, the cooling bath was removed and the reaction mixture was allowed to warm to rt and stirred overnight. Aqueous workup (brine, ether, K_2CO_3) followed by filtration through silica gel (deactivated with 5% NEt_3 in hexanes, hexanes) afforded (*E* and *Z*)-7-[4-[(*tert*-butyldimethylsilyl)oxy]-3,5-dimethylphenyl]-1-methoxy-1-heptene (176 mg, 84%) as a colorless oil (1:1 *E*/*Z* mixture, ^1H NMR) which was used in the subsequent desilylation reaction: ^1H NMR (300 MHz, $CDCl_3$) δ 6.80 (s, 2 H), 6.31 (d, J = 12.6 Hz, 1 H), 5.89 (d, J = 6.2 Hz, 1 H), 4.75 (dt, J = 12.6, 7.2 Hz, 1 H), 4.37 (apparent q, J = 7.0 Hz, 1 H), 3.60 (s, 3 H), 3.50 (s, 3 H), 2.49 (t, J = 7.7 Hz, 2 H), 2.22 (s, 6 H), 2.07–1.94 (m, 2 H), 1.63–1.37 (m, 6 H), 1.07 (s, 9 H), 0.21 (s, 6 H); IR ($CDCl_3$) 2920, 1470 cm^{-1}. Treatment of the above silyl ether (176 mg, 0.485 mmol) with $(n\text{-Bu})_4NF$ (0.15 mL of a 1.0 M solution in THF, 0.15 mmol) followed by aqueous workup (H_2O, ether) and flash chromatography (column packed with 5% NEt_3 in hexanes; gradient 20:1 followed by 10:1 hexanes/ethyl acetate) afforded **19** (78 mg, 65%) as a colorless oil (1:1 *E*/*Z* mixture, ^1H NMR): ^1H NMR (300 MHz, $CDCl_3$) δ 6.78 (s, 2 H), 6.27 (d, J = 12.6 Hz, 1 H), 5.86 (d, J = 6.2 Hz, 1 H), 4.72 (dt, J = 12.6, 7.2 Hz, 1 H), 4.50 (s, 1 H), 4.33 (apparent q, J = 6.9 Hz, 1 H), 3.56 (s, 3 H), 3.49 (s, 3 H), 2.46 (t, J = 7.7 Hz, 2 H), 2.22 (s, 6 H), 2.18–1.90 (m, 2 H), 1.58–1.21 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.1, 146.8, 145.9, 134.5, 134.4, 128.4, 128.3, 122.8, 122.7, 107.0, 103.0, 59.4, 55.8, 35.0, 31.7, 30.6, 29.6, 29.0, 28.7, 27.5, 23.7, 15.9; IR ($CDCl_3$) 3450, 2900, 1480 cm^{-1}; MS (EI, 50 eV) m/z 248 (M^+, 9), 161 (17), 135 (100).

1-(3,5-Dimethyl-4-hydroxyphenyl)-4-phenyl-1-butanol (22b). *t*-BuLi (30.0 mL of a 1.0 M pentane solution, 30.0 mmol) was added dropwise to a stirred solution of phenol **20** (3.00 g, 14.9 mmol) and THF (149 mL) at −78 °C. The solution was stirred for 2 h and then aldehyde **21b**[40] (2.50 g, 16.9 mmol) was added dropwise. The resulting solution was allowed to warm to 0 °C. After 30 min, aqueous workup (pH 6 buffer, ether, $MgSO_4$) and recrystallization (ether/hexanes) of the crude product afforded **22b** (1.77 g, 44%) as white needles: mp 111–112 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.28–7.14 (m, 5 H), 6.93 (s, 2 H), 4.59 (s, 1 H), 4.55 (t, J = 6.0 Hz, 1 H), 2.63 (t, J = 7.3 Hz, 2 H), 2.24 (s, 6 H), 1.86–1.60 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.5, 142.2, 136.0, 128.3, 128.2, 126.2, 125.6, 123.2, 74.3, 38.2, 35.6, 27.6, 16.0; IR (CCl_4) 3619, 3029, 2944, 1489 cm^{-1}; MS (EI, 70 eV) m/z 270 (M^+, 2), 161(100), 91(13). Anal Calcd for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 80.02; H, 8.26.

2,6-Dimethyl-4-(4-phenylbutyl)phenol (23b). Following the general procedure of Jung and Hatfield,[23] bromotrimethylsilane (70 μL, 0.52 mmol) was added to a stirred solution of alcohol **22b** (108 mg, 0.400 mmol) and ether (10 mL). After 10 min, the yellow solution was cooled to 0 °C and $LiAlH_4$ (160 mg, 4.3 mmol) was added. After 30 min, wet ether was carefully added and the resulting mixture was filtered through silica gel, dried ($MgSO_4$), and concentrated to afford crude **23b** (99.8 mg). Flash chromatography (7:1 hexanes/ethyl acetate) afforded **23b** (76.1 mg, 75%) as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.30–7.16 (m, 5 H), 6.78 (s, 2 H), 4.45 (s, 1 H), 2.63 (t, J = 7.1 Hz, 2 H), 2.51 (t, J = 7.1 Hz, 2 H), 2.22 (s, 6 H), 1.64 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.1, 142.6, 134.2, 128.4, 128.4, 128.2, 125.6, 122.7, 35.8, 34.9, 31.4, 31.1, 15.8; IR (neat) 3574, 2930, 2655, 1603, 1488 cm^{-1}; UV (CH_3CN) λ_{max}, nm (log ϵ) 278 (3.43), 230 (3.43), 218 (3.42), 214 (3.45), 210 (3.22); MS (EI, 70 eV) m/z 254 (M^+, 29), 135 (100), 91(15); HRMS calcd for $C_{18}H_{22}O$ 254.1671, found 254.1661. Anal. Calcd for $C_{18}H_{22}O$: C, 84.99; H, 8.72. Found: C, 84.91; H, 8.75.

1-[(*tert*-Butyldimethylsilyl)oxy]-2,6-dimethoxy-4-[4-(indol-3-yl)butyl]benzene (26). *t*-BuLi (4.0 mL of a solution 1.33 M in pentane, 5.3 mmol) was added to a solution of **24**[41] (421 mg, 1.78 mmol) and THF (10 mL) at −78 °C under nitrogen. After stirring for 5 min, a solution of CuCN (334 mg, 3.53 mmol) in THF (2 mL) was added. The reaction mixture was allowed to warm to 0 °C, stirred for 5 min, and then cooled back to −78 °C. A solution of **25**[42] (639 mg, 1.78 mmol) and THF (25 mL) was added. After 50 min, the reaction was quenched by the addition of CH_3OH (0.5 mL) and H_2O (25 mL). Aqueous workup (H_2O, ethyl acetate, Na_2SO_4), concentration, and flash chromatography (4:1 hexanes/ethyl acetate) afforded **26** (286 mg, 37%) as colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.91 (br s, 1 H), 7.61 (d, J = 7.8 Hz, 1 H), 7.35 (d, J = 8.0 Hz, 1 H), 7.19 (dt, J = 0.6, 7.3 Hz, 1 H), 7.11

(39) Levine, S. G. *J. Am. Chem. Soc.* **1958**, *80*, 6150.

(40) Aldehyde **21b** was prepared from the commercially available acid via reduction ($LiAlH_4$) and oxidation under Swern conditions.

(41) (a) Bromide **24** was prepared from the commercially available alcohol in 90% yield by treatment with CBr_4 and $P(Ph)_3$.[18] (b) For a detailed experimental see: Yang, W. Ph.D. Dissertation, University of California, Riverside, 1991.

(42) Benzylic bromide **25** was prepared from commercially available 3,5-dimethoxy-4-hydroxybenzaldehyde in three steps: [TBDMSCl, imidazole, CH_2Cl_2, 3h, rt (84%); $NaBH_4$, CH_3OH (99%); TMSBr, THF (92%)].[41b]

(dt, J = 0.6, 7.0 Hz, 1 H), 6.94 (s, 1 H), 6.36 (s, 2 H), 3.78 (s, 6 H), 2.80 (t, J = 6.9 Hz, 2 H), 2.59 (t, J = 7.1 Hz, 2 H), 1.73 (m, 4 H), 1.03 (s, 9 H), 0.14 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.3, 136.3, 135.2, 132.2, 127.6, 121.8, 121.0, 119.0, 118.9, 116.8, 111.0, 105.4, 55.7, 36.0, 31.4, 29.7, 25.8, 25.0, 18.7, −4.5; IR (CCl_4) 3491, 2934, 2858, 1588, 1514 cm^{-1}; MS (EI, 20 eV) m/z 439 (M^+, 10), 382 (100); HRMS calcd for $C_{26}H_{37}NO_3Si$ 439.2543, found 439.2552.

2,6-Dimethoxy-4-[4-(indol-3-yl)butyl]phenol (27). (n-Bu)$_4$NF (0.2 mL, of a 1 M solution in THF, 0.2 mmol) was added to a stirred solution of **26** (63.2 mg, 0.15 mmol) and THF (2 mL) at 0 °C. After 15 min, concentration and flash chromatography (1:1 hexanes/ethyl acetate) afforded **27** (44.5 mg, 94%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (br s, 1 H), 7.63 (d, J = 7.7 Hz, 1 H), 7.35 (d, J = 8.0 Hz, 1 H), 7.20 (t, J = 7.2 Hz, 1 H), 7.12 (t, J = 7.3 Hz, 1 H), 6.95 (s, 1 H), 6.42 (s, 2 H), 5.40 (s, 1 H), 3.87 (s, 6 h), 2.81 (t, J = 6.9 Hz, 2 H), 2.61 (t, J = 7.2 Hz, 2 H), 1.77 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.8, 136.3, 133.9, 132.6, 127.5, 121.7, 121.1, 119.0, 118.9, 116.6, 111.0, 104.9, 56.2, 36.0, 31.6, 29.7, 25.0; IR (CCl_4) 3558, 3491, 2936, 2857, 1617, 1519 cm^{-1}; MS (EI, 20 eV) m/z 325 (M^+, 75), 167 (14), 130 (100); HRMS calcd for $C_{20}H_{23}NO_3$ 325.1678, found 325.1681.

2,6-Dimethoxy-4-{4-[*N*-(methoxycarbonyl)indol-3-yl]-butyl}phenol (28). t-BuLi (0.33 mL of a 1.33 M solution in pentane, 0.45 mmol) was added to a stirred solution of **26** (189 mg, 0.430 mmol) and THF (5 mL) at −78 °C. After 5 min, methyl chloroformate (37 μL, 0.47 mmol) was added and the resulting solution was stirred for 10 min. After quenching with CH_3OH (0.5 mL), aqueous workup (H_2O, ethyl acetate, Na_2SO_4) followed by flash chromatography (20:1 hexanes/ethyl acetate) afforded 1-[(*tert*-butyldimethylsilyl)oxy]-2,6-dimethoxy-4-{4-[*N*-(methoxycarbonyl)indol-3-yl]butyl}benzene (120.9 mg, 57%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (d, J = 7.3 Hz, 1 H), 7.52 (d, J =7.5 Hz, 1 H), 7.35 (s, 1 H), 7.34 (t, J = 6.9 Hz, 1 H), 7.25 (t, J = 7.5 Hz, 1 H), 6.36 (s, 2 H), 4.03 (s, 3 H), 3.77 (s, 6 H), 2.72 (t, J = 6.6 Hz, 2 H), 2.59 (t, J = 6.9 Hz, 2 H), 1.75 (m, 4 H), 1.02 (s, 9 H), 0.13 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.5, 151.4, 135.6, 134.9, 132.3, 130.8, 124.5, 122.6, 122.03, 122.8, 119.1, 115.2, 105.4, 55.7, 53.6, 35.9, 31.2, 28.6, 25.8, 24.7, 18.7, −4.6; IR (CCl_4) 2955, 2935, 1740, 1588, 1514, 1445, 1382 cm^{-1}; MS (EI, 20 eV) m/z 497 (M^+, 6), 440 (100), 251 (18), 209 (36); HRMS calcd for $C_{28}H_{39}NO_5Si$ 497.2598, found 497.2580. (n-Bu)$_4$NF (0.21 mL, 1 M in THF solution, 0.21 mmol) was added to a solution of the above silylated phenol (52.3 mg, 0.105 mmol) and THF (2 mL) at rt. After 5 min, concentration and flash chromatography (4:1 hexanes/ethyl acetate) afforded **28** (33.2 mg, 87%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (d, J = 7.1 Hz, 1 H), 7.52 (d, J = 7.6 Hz, 1 H), 7.35 (s, 1 H), 7.34 (t, J = 8.7 Hz, 1 H), 7.25 (t, J = 7.34 Hz, 1 H), 6.40 (s, 2 H), 5.38 (br s, 1 H), 4.03 (s, 3 H), 3.87 (s, 6 H), 2.73 (t, J = 6.7 Hz, 2 H), 2.60 (t, J = 6.9 Hz, 2 H), 1.75 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.5, 146.8, 135.6, 133.5, 132.7, 130.7, 124.5, 122.6, 121.9, 121.8, 119.0, 115.2, 104.9, 56.2, 53.6, 35.9, 31.4, 28.6, 24.7; IR (CCl_4) 3556, 2937, 1740, 1615, 1518, 1457 cm^{-1}; MS (EI, 20 eV) m/z 383 (M^+, 100), 188 (21); HRMS calcd for $C_{22}H_{25}NO_5$ 383.1733, found 383.1719.

4-Oxo-4-[1-(triisopropylsilyl)pyrrol-3-yl]butyric Acid (29). According to the general procedure of Muchowski et al.,[24] succinic anhydride (538 mg, 5.38 mmol) was added to a stirred suspension of anhydrous $AlCl_3$ (1.32 g, 9.90 mmol) in 1,2-dichloroethane (20 mL) at rt. The resulting solution was stirred for 20 min and then cooled to 0 °C. A solution of *N*-(triisopropylsilyl)pyrrole[24] (1.00 g, 4.48 mmol) in 1,2-dichloroethane (6.0 mL) was added over 5 min and the resulting solution was stirred for 15 min then slowly brought to reflux. After 12 h, the reaction mixture was cooled to rt, poured into ice−water (100 mL), and acidified to pH 4 with aqueous 10% HCl. Aqueous workup (H_2O, CH_2Cl_2, Na_2SO_4) afforded a brown oil (2.96 g). Filtration through silica gel (ethyl acetate) and concentration afforded **29** as a colorless oil (1.39 g, 96%) which rapidly turned brown upon standing: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (s, 1 H), 6.73 (s, 2 H), 3.16 (t, J = 6.9 Hz, 2 H), 2.77 (t, J = 6.6 Hz, 2 H), 1.47 (septet, J = 7.5 Hz, 3 H), 1.12 (d, J = 7.5 Hz, 18 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.1, 176.5, 130.4, 127.6, 126.3, 111.3, 34.6, 29.0, 18.1, 12.1; IR (CCl_4) 3600−2500, 2946, 1713, 1672, 1528 cm^{-1}; MS (CI, NH_3) m/z 324 (MH^+, 100), 280 (25); HRMS calcd for $C_{17}H_{30}NO_3Si$ (MH^+) 324.1995, found 324.1984.

4-[1-(Triisopropylsilyl)pyrrol-3-yl]butyric Acid (30). $NaBH_4$ (4.68 g, 124 mmol) was slowly added to a stirred solution of **29** (2.00 g, 6.18 mmol) in absolute ethanol (75 mL), at 0 °C. After 90 min, aqueous workup (pH 5 buffer, CH_2Cl_2, $MgSO_4$) afforded crude lactone as a colorless oil (1.57 g, 83%). Material of this purity was suitable for use in the next step. Flash chromatography (CH_2Cl_2) afforded an analytical sample of lactone as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.78 (s, 1 H), 6.76 (d, J = 2.7 Hz, 1 H), 6.29 (br s, 1 H), 5.54 (dd, J = 7.5, 6.6 Hz, 1 H), 2.62 (m, 2 H), 2.51 (m, 1 H), 2.32 (m, 1 H), 1.43 (septet, J = 7.5 Hz, 3 H), 1.10 (d, J = 7.5 Hz, 18 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.4, 125.2, 123.9, 122.4, 108.6, 77.7, 29.8, 29.5, 17.8, 11.6; IR (CCl_4) 2895, 1781 cm^{-1}. A suspension of the above lactone (1.50 g, 4.88 mmol) and 5% Pd/C (104 mg; 1 mol % Pd) in ether (150 mL) was shaken under a hydrogen atmosphere (53 psi, rt) for 16 h then filtered through Celite and concentrated to afford **30** as a colorless oil (1.49 g, 99%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.70 (d, J = 2.1 Hz, 1 H), 6.53 (s, 1 H), 6.14 (br s, 1 H), 2.58 (t, J = 7.5 Hz, 2 H), 2.37 (t, J = 7.5 Hz, 2 H), 1.91 (m, 2 H), 1.42 (septet, J = 7.5 Hz, 3 H), 1.09 (d, J = 7.5 Hz, 18 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.8, 125.2, 124.8, 122.0, 111.1, 33.9, 26.8, 26.5, 18.4, 12.2; IR (CCl_4) 3300−2900, 2859, 1709 cm^{-1}; MS (CI, CH_4) m/z 310 (MH^+, 100), 309 (M^+, 60), 185 (40); HRMS calcd for $C_{17}H_{32}NO_2Si$ (MH^+) 310.2202, found 310.2188.

1-(3,5-Dimethyl-4-hydroxyphenyl)-4-[1-(triisopropylsilyl)pyrrol-3-yl]-1-butanone (31). 1,1′-Carbonyldiimidazole (893 mg, 5.51 mmol) was added to a stirred solution of **30** (1.42 g, 4.59 mmol) in CH_2Cl_2 (25 mL) at rt. After stirring for 30 min, CO_2 evolution had ceased and *N*,*O*-dimethylhydroxylamine hydrochloride[25] (626 mg, 6.42 mmol) was added. The resulting solution was stirred at rt for 2 h and concentrated, and the crude product was taken up in hexane (50 mL). Aqueous workup (saturated aqueous NH_4Cl, hexane, Na_2SO_4) and concentration afforded *N*-methoxy-*N*-methyl-4-[1-(triisopropylsilyl)-3-pyrrolyl]butanamide as a brown oil (1.54 g, 95%). Material of this purity was suitable for use in the next step. An analytical sample was prepared by flash chromatography (gradient 4:1 to 0:1 hexanes/ethyl acetate) to provide the amide as a colorless oil which turned brown after several hours: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.68 (d, J = 1.8 Hz, 1 H), 6.54 (s, 1 H), 6.15 (br s, 1 H), 3.61 (s, 3 H), 3.16 (s, 3 H), 2.55 (t, J = 7.5 Hz, 2 H), 2.43 (t, J = 7.8 Hz, 2 H), 1.92 (m, 2 H), 1.41 (septet, J = 7.5 Hz, 3 H), 1.06 (d, J = 7.5 Hz, 18 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.9, 125.2, 124.0, 121.3, 110.6, 61.1, 32.1, 31.4, 26.6, 25.8, 17.8, 11.6; IR (CCl_4) 2906, 2894, 1674, 1464 cm^{-1}. n-BuLi (1.0 mL of a 2.3 M solution in hexanes, 2.3 mmol) was added to a stirred solution of 4-bromo-2,6-dimethylphenol (456 mg, 2.27 mmol) in THF (40.0 mL) at −78 °C. After 15 min, t-BuLi (2.8 mL of a 1.6 M solution in pentane, 4.5 mmol) was added and the resulting bright yellow solution was stirred for 45 min. A portion of this dianion solution (11.2 mL of the 0.057 M (theor) solution, 0.64 mmol) was added via cannula to a cold (−78 °C) solution of the above amide (150 mg, 0.425 mmol) in THF (6.0 mL). After stirring for 4 h at −78 °C, the solution was slowly poured into a stirred 0 °C solution of saturated aqueous NH_4Cl (200 mL). Aqueous workup (H_2O, ether, $MgSO_4$) afforded crude product (256 mg) as a yellow oil. Flash chromatography (5:1 hexanes/ethyl acetate) afforded **31** (123 mg, 70%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (s, 2 H), 6.71 (d, J = 2.1 Hz, 1 H), 6.55 (s, 1 H), 6.17 (br s, 1 H), 5.08 (s, 1 H), 2.92 (t, J = 7.5 Hz, 2 H), 2.59 (t, J = 7.2 Hz, 2 H), 2.27 (s, 6 H), 1.99 (m, 2 H),1.42 (septet, J = 7.5 Hz, 3 H), 1.08 (d, J = 7.5 Hz, 18 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.9, 156.4, 129.7, 129.3, 125.2, 124.2, 122.8, 121.5, 110.6, 37.7, 26.5, 25.9, 17.9, 15.8, 11.7; IR (CCl_4) 3612, 2947, 2870, 1684 cm^{-1}; MS (CI, NH_3) m/z 414 (MH^+, 100); HRMS calcd for $C_{25}H_{40}NO_2Si$ (MH^+) 414.2828, found 414.2806.

1-(3,5-Dimethyl-4-hydroxyphenyl)-4-[1-(triisopropylsilyl)pyrrol-3-yl]butane (32). A suspension of **31** (17.0 mg, 0.0411 mmol) and 5% Pd/C (5.0 mg, 5.7 mol% Pd) in diethyl

ether (2.0 mL) was shaken under an atmosphere of hydrogen (53 psi, rt) for 16 h. Filtration through Celite and concentration followed by HPLC (20:1 hexane/ethyl acetate, 1.0 mL/min, t_R = 7.9 min) afforded **32** (8.4 mg, 51%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.78 (s, 2 H), 6.69 (t, J = 2.4 Hz, 1 H), 6.51 (s, 1 H), 6.14 (br s, 1 H), 4.44 (s, 1 H), 2.50 (m, 4 H), 2.21 (s, 3 H), 1.62 (m, 4 H), 1.42 (septet, J = 7.2 Hz, 3 H), 1.09 (d, J = 7.2 Hz, 18 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.0, 134.7, 128.4, 126.2, 123.9, 122.6, 121.1, 110.6, 34.9, 31.6, 30.7, 26.8, 17.9, 15.9, 11.7; IR (CCl_4) 3019, 2954, 2865, 1464 cm^{-1}.

General Procedure for Oxidation of a Phenol to a Quinone Methide. Neat Ag_2O (1.2–20 equiv) was added to a solution of phenol in the indicated solvent and the suspension was stirred or shaken for the time noted at the temperature indicated. The progress of the oxidation was monitored by ^{1}H NMR and/or TLC. When the oxidation was complete, the suspension was filtered through a plug of glass wool to afford a solution of quinone methide. In cases where the quinone methide was dried, the above solution was dried over K_2CO_3 or Na_2SO_4, and chased with toluene or CH_2Cl_2.

General Procedure for Cyclization Reactions. The Lewis acid was added to a stirred solution of cyclization substrate at the temperature noted. After the indicated time, normal "aqueous workup" afforded crude product.

2,6-Dimethyl-4-(4-phenylbutylidene)-2,5-cyclohexadien-1-one (33). According to the general quinone methide preparation, phenol **23b** (44.4 mg, 0.175 mmol) and Ag_2O [131 mg, 0.565 mmol; $CDCl_3$ (0.8 mL), 15 min, rt] afforded a solution of **33**. Concentration afforded a sample for analysis (yellow oil): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32–7.17 (m, 6 H), 6.88 (s, 1 H), 6.30 (t, J = 8.1 Hz, 1 H), 2.69 (t, J = 7.6 Hz, 2 H), 2.51 (q, J = 7.5 Hz, 2 H), 2.04 (s, 3 H), 2.01 (s, 3 H), 1.87 (p, J = 7.5 Hz, 2 H); ^{13}C NMR 126.0, 35.2, 30.7, 28.3, 16.7, 16.0; IR (CCl_4) 2978, 2898, 1628 cm^{-1}; UV (CH_3CN) λ_{max} 326, 322, 318, 310, 288, 284, 210 nm; MS (EI, 70 eV) 252 (M^+, 19), 161 (65), 91 (100); HRMS calcd for $C_{18}H_{20}O$ 252.1514, found 252.1508.

(±)-2,6-Dimethyl-4-(1,2,3,4-tetrahydronaphthalen-1-yl)phenol (34). From 22b. $TiCl_4$ (0.33 mL, 3.11 mmol) was added to a solution of alcohol **22b** (210 mg, 0.778 mmol) and CH_2Cl_2 at rt. After 5 min aqueous workup ($NaHCO_3$, CH_2Cl_2, $MgSO_4$) afforded crude product (200 mg) as a yellow semisolid. Recrystallization (ether/hexanes) afforded **46** (186 mg, 95%) as a white solid: mp 80–81 °C.

From 33. According to the general cyclization procedure, quinone methide **33** (43 mg, 0.17 mmol; dried by chasing with CH_2Cl_2) [$CDCl_3$ (17 mL), $ZnCl_2$ (0.34 mL of a 1.0 M ether solution, 0.34 mmol), rt, 15 min; aqueous workup (pH 6 buffer, CH_2Cl_2, $MgSO_4$)] afforded 48.1 mg of crude **34** as an oil. Flash chromatography (7:1 hexanes/ethyl acetate) gave 39.6 mg (93%) of **34** as a pale yellow oil which crystallized upon standing to give a white solid: mp 80–81 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.12–7.01 (m, 4 H), 6.82 (s, 2 H), 4.47 (s, 1 H), 3.97 (t, J = 6.6 Hz, 1 H), 2.97–2.77 (m, 2 H), 2.20 (s, 6 H), 2.11 (m, 1 H), 1.96–1.71 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.3, 140.0, 139.1, 137.4, 130.1, 128.9, 128.8, 125.7, 125.5, 122.7, 44.9, 33.5, 29.8, 21.3, 16.0; IR (CCl_4) 3621, 2933, 1488, 1449 cm^{-1}; UV (CH_3CN) λ_{max} 276, 216 nm; MS (EI, 70 eV) m/z 252 (M^+, 34), 130 (100); HRMS calcd for $C_{18}H_{20}O$ 252.1514, found 252.1504.

2,6-Dimethyl-4-[4-(furan-3-yl)butylidene]-2,5-cyclohexadien-1-one (35). According to the general quinone methide preparation, phenol **6** (16.8 mg, 0.069 mmol) and Ag_2O [20.3 mg, 0.086 mmol; $CDCl_3$ (0.6 mL), 100 min, rt] afforded a solution of **35**. Concentration of this solution afforded a sample of **35** for analysis: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (s, 1 H), 7.25 (s, 1 H), 7.22 (s, 1 H), 6.89 (s, 1 H), 6.30 (t, J = 6 Hz, 1 H), 6.27 (s, 1 H), 2.56–2.47 (m, 4 H), 2.04 (s, 3 H), 2.00 (s, 3 H), 1.80 (tt, J = 7, 7 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.7, 147.4, 142.9, 139.0, 138.5, 136.4, 134.7, 132.2, 129.8, 124.0, 110.7, 29.4, 28.3, 24.3, 16.7, 16.0; IR (CCl_4) 2978, 2827, 1646, 1627, 1579, 1445 cm^{-1}; UV ($CDCl_3$) λ_{max} 282, 242 nm; MS (EI, 70 eV) m/z 242 (M^+, 100), 161 (74), 91 (39); HRMS calcd for $C_{16}H_{18}O_2$ 242.1307, found 242.1316

(±)-2,6-Dimethyl-4-(4,5,6,7-tetrahydrobenzofuran-7-yl)phenol (36). According to the general cyclization procedure, quinone methide **35** (from 16.8 mg of **6**, 0.069 mmol) [$CDCl_3$ (0.6 mL), $ZnCl_2$ (10.2 mg, 0.075 mmol), rt, 15 min; aqueous workup (H_2O, $CHCl_3$, Na_2SO_4)] afforded crude product. Flash chromatography (4:1 hexanes/ethyl acetate) afforded **36** (13.9 mg, 83%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (s, 1 H), 6.71 (s, 2 H), 6.25 (s, 1 H), 4.50 (s, 1 H), 3.89 (t, J = 6 Hz, 1 H), 2.52 (m, 2 H), 2.20 (s, 6 H), 1.86–1.66 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.8, 150.8, 140.9, 135.3, 127.9, 122.9, 118.4, 110.1, 40.1, 34.1, 22.4, 21.5, 16.0; IR (CCl_4) 3620, 2934, 1503, 1488 cm^{-1}; UV (EtOH) λ_{max} 280, 206 nm; MS (EI, 20 eV) m/z 242 (M^+, 100), 227 (43), 199 (37); HRMS calcd for $C_{16}H_{18}O_2$ 242.1307, found 242.1304.

2,6-Dimethyl-4-[4-[1-(triisopropylsilyl)pyrrol-3-yl]-butylidene]-2,5-cyclohexadien-1-one (37). According to the general quinone methide preparation, phenol **32** (7.5 mg, 0.019 mmol) and Ag_2O [62.0 mg, 0.268 mmol; $CDCl_3$ (1.0 mL), 20 min, rt] afforded a solution of **37**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (s, 1 H), 6.88 (s, 1 H), 6.71 (t, J = 2.1 Hz, 1H) 6.53 (s, 1 H), 6.35 (t, J = 8.1 Hz, 1 H), 6.14 (s, 1 H), 2.54 (apparent dt, J = 21.4, 7.2 Hz, 4 H), 2.02 (s, 3 H), 1.99 (s, 3 H), 1.82 (m, 2 H), 1.42 (septet, J = 7.5 Hz, 3 H), 1.09 (d, J = 7.5 Hz, 18 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.8, 149.0, 138.7, 136.2, 134.5, 131.8, 130.0, 124.9, 124.3, 121.3, 110.5, 30.5, 28.6, 26.6, 17.8, 16.8, 16.1, 11.6; IR (CCl_4) 3620, 2946, 2870, 1618, 1575 cm^{-1}.

(±)-7-(3,5-Dimethyl-4-hydroxyphenyl)-1-(triisopropylsilyl)-4,5,6,7-tetrahydroindole (38). According to the general cyclization procedure, quinone methide **37** (from 7.5 mg of **32**, 0.019 mmol) [$CDCl_3$ (1.0 mL), $ZnCl_2$ (25.6 mg, 0.194 mmol), rt, 5 min; concentration] afforded crude product as a brown oil (8.0 mg) which was purified by HPLC (15:1 hexane/ethyl acetate, 1.0 mL/min, t_R = 6.1 min) to afford **38** (7.3 mg, 98%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.73 (d, J = 2.7 Hz, 1 H), 6.53 (s, 2 H), 6.10 (d, J = 2.7 Hz, 1 H), 4.42 (s, 1 H), 4.15 (br s, 1 H), 2.62 (m, 2 H), 2.17 (s, 6 H), 2.10–1.97 (m, 2 H), 1.80–1.50 (m, 2 H), 1.21 (septet, J = 7.2 Hz, 3 H), 1.02 (d J = 7.2 Hz, 9 H), 0.82 (d, J = 7.2 Hz, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.0, 137.9, 133.0, 128.6, 124.9, 122.1, 121.8, 108.7, 39.8, 33.8, 23.3, 18.4, 18.1, 17.2, 15.9, 13.0; IR (CCl_4) 2932, 2869, 1559 cm^{-1}; MS (CI, NH_3) m/z 398 (MH^+, 100), 397 (M^+, 45); HRMS calcd for $C_{25}H_{40}NOSi$ (MH^+) 398.2879, found 398.2873.

2,6-Dimethoxy-4-[4-[*N*-(methoxycarbonyl)indol-3-yl]-butylidene]-2,5-cyclohexadien-1-one (39). According to the general quinone methide preparation, phenol **28** (32.8 mg, 0.0856 mmol) and Ag_2O [40.1 mg, 0.173 mmol; $CDCl_3$ (0.6 mL), 5 min, rt] afforded a solution of **39**. Concentration of a portion of this solution afforded a sample of **39** for analysis: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (br d, J = 7.0 Hz, 1 H) 7.51 (d, J = 7.6 Hz, 1 H), 7.36 (s, 1 H), 7.36–7.22 (m, 2 H), 6.42 (s, 1 H), 6.23 (t, J = 8.3 Hz, 1 H), 6.21 (s, 1 H), 4.01 (s, 3 H), 3.77 (s, 3 H), 3.67 (s, 3 H), 2.78 (t, J = 7.1 Hz, 2 H), 2.56 (dt, J = 7.5, 7.5 Hz, 2 H), 2.01 (tt, J = 7.2, 7.1 Hz, 2 H); IR (CCl_4), 2956, 2935, 1739, 1659, 1590 cm^{-1}; MS (EI, 50 eV) 381 (M^+, 40), 193 (77), 188 (100), 161 (69); HRMS calcd for $C_{22}H_{23}O_5N$ 381.1576, found 381.1593.

(±)-1-(3,5-Dimethoxy-4-hydroxyphenyl)-9-(methoxycarbonyl)-1,2,3,4-tetrahydrocarbazole (40). According to the general cyclization procedure, quinone methide **39** (from 32.8 mg of **28**, 0.0856 mmol) [$CDCl_3$ (1.0 mL), $ZnCl_2$ (15.2 mg, 0.112 mmol), rt, 2 min; aqueous workup (H_2O, $CHCl_3$, Na_2SO_4)] afforded crude product. Concentration and chromatography (4:1 hexanes/ethyl acetate) afforded **40** (26.4 mg, 81%) as a white solid: mp 150–152 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 (d, J = 7.5 Hz, 1 H), 7.50 (d, J = 7.3 Hz, 1 H), 7.29 (p, J = 6.1 Hz, 2 H), 6.24 (s, 2 H), 5.36 (s, 1 H), 4.65 (br s, 1 H), 2.85 (dt, J = 16.4, 3.9 Hz, 1 H), 2.67 (dt, J = 16.3, 7.8 Hz, 1 H), 2.17 (m, 1 H), 1.95 (m, 1 H), 1.77 (br t, J = 4.0 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.8, 146.8, 137.0, 136.2, 135.4, 132.9, 129.5, 124.2, 122.7, 119.5, 118.0, 115.6, 104.4, 56.4, 53.0, 40.9, 33.6, 21.2, 17.8; IR (CCl_4) 3555, 2939, 1742, 1613 cm^{-1}; MS (EI, 20 eV) 381 (M^+, 84), 322 (100), 227 (61); HRMS calcd for $C_{22}H_{23}NO_5$ 381.1576, found 381.1576.

(±)-2,3-Didehydro-2-(3,5-dimethoxy-4-hydroxyphenyl)-spiro[cyclopentane-1,3′-[3*H*]indole] (42) and (±)-2-(3,5-Dimethoxy-4-oxo)-2,5-cyclohexadienylidene]spiro[cyclopentane-1,3′-[3*H*]indole] (48). According to the general quinone methide preparation, phenol **27** (17.6 mg, 0.054 mmol)

and Ag_2O [125 mg, 0.54 mmol; $CDCl_3$ (0.6 mL), 30 min, rt] afforded a solution of **48**. Concentration of a portion of this solution afforded a sample of **48** for analysis: ^1H NMR (300 MHz, $CDCl_3$) δ 8.21 (s, 1 H), 7.71 (d, J = 7.6 Hz, 1 H), 7.42 (m, 1 H), 7.30 (d, J = 8.4 Hz, 2 H), 6.42 (s, 1 H), 5.11 (s, 1 H), 3.78 (s, 3 h), 3.21 (t, J = 6.1 Hz, 2 H), 3.09 (s, 3 H), 2.27 (m, 2 H), 2.14 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.5, 175.2, 154.2, 153.1, 151.9, 151.3, 146.2, 128.4, 127.5, 125.6, 122.2, 121.6, 107.0, 105.2, 68.9, 55.5, 54.9, 37.2, 34.9, 25.2; MS (EI, 20 eV) m/z 321 (M^+, 100), 290 (6); HRMS calcd for $C_{20}H_{19}NO_3$ 321.1365, found 321.1365. Silica gel (10.1 mg) was added to a solution of quinone methide **48** (from 17.6 mg of phenol **27**, 0.054 mmol) and $CHCl_3$ (1 mL) at rt. After 1 min, concentration and flash chromatography (4:1 hexanes/ethyl acetate) afforded **42** (15.6 mg, 90% from **27**) as an orange oil: ^1H NMR (300 MHz, $CDCl_3$) δ 8.20 (s, 1 H), 7.69 (d, J = 7.6 Hz, 1 H), 7.36 (dt, J = 1.2, 7.5 Hz, 1 H), 7.31 (d, J = 6.5 Hz, 1 H), 7.24 (t, J = 7.2 Hz, 1 H), 6.49 (t, J = 2.5 Hz, 1 H), 5.98 (s, 2 H), 5.50 (s, 1 H) 3.57 (s, 3 H), 2.82 (m, 2 H), 2.54 (ddd, J = 13.2, 5.9, 8.1 Hz, 1 H), 2.16 (ddd, J = 13.1, 5.3, 8.0 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.1, 154.8, 146.5, 143.3, 141.8, 134.2, 131.0, 128.1, 126.8, 126.1, 122.2, 121.2, 102.0, 70.9, 55.8, 33.7, 31.7; IR (CCl_4) 3552, 2959, 2937, 1608 cm^{-1}; MS (EI, 20 eV) m/z 321 (M^+, 100), 306 (4); HRMS calcd for $C_{20}H_{19}NO_3$ 321.1365, found 321.1368.

2,6-Dimethyl-4-[3-(pyrrol-1-yl)propylidene]-2,5-cyclohexadien-1-one (43). According to the general quinone methide preparation, phenol **5** (125 mg, 0.539 mmol) and Ag_2O [1.26 g, 5.44 mmol; CH_2Cl_2 (7.0 mL), 13h, rt] afforded a solution of quinone methide. Concentration of a similar reaction mixture afforded a sample for analysis (orange oil): ^1H NMR (300 MHz, $CDCl_3$) δ 7.11 (t, J = 1.1 Hz, 1 H), 6.85 (s, 1 H), 6.65 (t, J = 2.0 Hz, 2 H), 6.19–6.13 (m, 3 H), 4.07 (t, J = 6.8 Hz, 2 H), 2.93 (apparent q, J = 7.2 Hz, 2 H), 2.01 (s, 3 H), 1.99 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.4, 141.6, 137.9, 136.7, 134.9, 133.3, 129.2, 120.2, 108.4, 48.3, 31.0, 16.5, 15.8; IR (CH_2Cl_2) 2928, 1625, 1576, 1501 cm^{-1}; MS (EI, 20 eV) m/z 227 (M^+, 47), 161 (30), 81 (100); HRMS calcd for $C_{15}H_{17}NO$ 227.1310, found 227.1308.

(±)-2,6-Dimethyl-4-(1,2-dihydropyrrolizin-3-yl)phenol (44). According to the general cyclization procedure, quinone methide **43** (26.8 mg, 0.12 mmol) [$CHCl_3$ (22 mL), $ZnCl_2$ (1.2 mL of a 1.0 M in ether, 1.2 mmol), 0 °C, 5 min; aqueous workup (H_3PO_4 adjusted to pH 3.0, $CHCl_3$, $MgSO_4$)] afforded 22.3 mg of crude product. Flash chromatography (7:1 hexanes/ethyl acetate) afforded **44** as a red viscous liquid (16.5 mg, 62%; purity by GC = 97.3%): ^1H NMR (300 MHz, $CDCl_3$) δ 6.88 (s, 2 H), 6.66 (d, J = 1.0 Hz, 1 H), 6.28 (t, J = 2.7 Hz, 1 H), 5.78 (d, J = 3.1 Hz, 1 H), 4.52 (s, 1 H), 4.24 (t, J = 7.8 Hz, 1 H), 4.13–4.06 (m, 1 H), 3.98–3.90 (m, 1 H), 2.88 (dddd, J = 12.2, 8.1, 7.6, 3.6 Hz, 1 H), 2.36 (dddd, J = 12.6, 8.0, 7.9, 7.9 Hz, 1 H), 2.22 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.8, 140.0, 135.2, 127.5, 123.0, 113.6, 112.2, 99.9, 45.6, 42.8, 39.3, 15.9; IR (CCl_4) 3621, 3532, 2979, 2948, 2929, 1487 cm^{-1}; UV (EtOH) λ_{max} 280, 208 nm; MS (EI, 20 eV) m/z 227 (M^+,100), 226 (53), 212 (42); HRMS calcd for $C_{15}H_{17}NO$ 227.1310, found 227.1309.

2,6-Dimethyl-4-(3-phenyl)propylidene)-2,5-cyclohexadien-1-one (45). According to the general quinone methide preparation, phenol **23a**[15b] (33.5 mg, 0.14 mmol) and Ag_2O [323 mg, 1.39 mmol; $CDCl_3$ (1 mL), 10 min, rt] afforded a solution of **45**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.40–7.20 (m, 6 H), 6.88 (s, 1 H), 6.31 (t, J = 6.0 Hz, 1 H), 2.84 (s, 4 H), 2.02 (s, 3 H), 2.00 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.7, 146.3, 140.4, 138.4, 136.5, 134.8, 132.2, 129.7, 128.5, 128.4, 126.3, 35.3, 30.7, 16.7, 16.0; IR (CCl_4) 3082, 2872, 1629, 1601, 1577, 1496 cm^{-1}; MS (EI, 20 eV) m/z 238 (M^+, 52), 223 (34), 91 (100); HRMS calcd for $C_{17}H_{18}O$ 238.1358, found 238.1362.

(±)-1-(3,5-Dimethyl-4-hydroxyphenyl)-2,3-dihydroindene (46). $TiCl_4$ (0.34 mL, 3.12 mmol) was added to a solution of alcohol **22a**[15b] (200 mg, 0.780 mmol) and CH_2Cl_2 at rt. After 5 min, aqueous workup ($NaHCO_3$, CH_2Cl_2, $MgSO_4$) afforded crude product (170 mg) as a yellow semisolid. Recrystallization (ether/hexanes) afforded **46** (162 mg, 87%; purity by GC = 99.76%, t_R = 13.12 min) as a light yellow solid: mp 107.5–108.0 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.29–7.10 (m, 3 H), 6.95 (d, J = 8.5 Hz, 2 H), 6.80 (s, 1 H), 4.50 (br s, 1 H), 4.20 (t, J = 8.4 Hz, 1 H), 3.07–2.86 (m, 2 H), 2.57–2.47 (m, 1 H), 2.21 (s, 6 H), 2.01–1.85 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.6, 147.3, 144.2, 136.9, 128.1, 126.3, 126.2, 124.9, 124.2, 122.9, 50.9, 36.7, 31.7, 15.9; IR (CCl_4) 3620, 2944, 1489 cm^{-1}; MS (EI, 20 eV) m/z 238 (M^+, 100), 223 (44); HRMS calcd for $C_{17}H_{18}O$ 238.1358, found 238.1363.

(±)-5,7-Dimethyl-1-(3,5-dimethyl-4-hydroxyphenyl)-6-hydroxy-3-(2-phenylethyl)-2-(phenylmethyl)-2,3-dihydroindene (51). According to the general cyclization procedure, quinone methide **45** (26.8 mg, 0.12 mmol; dried by chasing with C_6H_6) [$CHCl_3$ (22 mL), $ZnCl_2$ (1.0 M solution ether, 0.28 mL, 0.28 mmol), −78 °C 5 min then rt 1 h; aqueous workup ($NaHCO_3$, CH_2Cl_2, $MgSO_4$)] afforded 28 mg of crude product. HPLC (2:1 hexanes/ethyl acetate, 0.7 mL/min, t_R = 10.0 min) afforded 24.2 mg (73%) of **51** as a clear oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.38–7.21 (m, 10 H), 6.89 (s, 2 H), 6.32 (s, 1 H), 4.53 (s, 1 H), 4.44 (s, 1 H), 3.95 (d, J = 2.1 Hz, 1 H), 3.28 (q, J = 6.3 Hz, 1 H), 2.94 (dd, J = 5.4, 13.8 Hz, 1 H), 2.84–2.70 (m, 3 h), 2.30 (s, 5 H), 2.12 (s, 6 H), 1.86 (s, 4 H); ^{13}C (75 MHz, $CDCl_3$) δ 160.0, 150.3, 142.6, 142.3, 141.3, 138.2, 135.4, 129.2, 128.3, 128.3, 127.6, 127.5, 125.9, 125.8, 122.9, 122.6, 121.4, 120.4, 54.1, 52.2, 44.4, 34.3, 34.2, 30.8, 16.5, 16.0, 12.13; IR (CCl_4) 3621, 3065, 2855, 1604, 1473 cm^{-1}; MS (EI, 70 eV) m/z 476 (M^+, 48), 371 (26), 280 (60), 91(100).

***(E* and *Z*)-2,6-Dimethyl-4-(7-methoxyhept-1-enylidene]-2,5-cyclohexadien-1-one (52).** According to the general quinone methide preparation, phenol **19** (9.9 mg, 0.0801 mmol) and Ag_2O [190 mg, 0.80 mmol; $CDCl_3$ (1.5 mL), 3 h, rt] afforded a solution of **52**. The pale green reaction mixture was filtered through a plug of Na_2CO_3 ($CDCl_3$), dried over Na_2CO_3, and then used immediately: ^1H NMR (300 MHz, $CDCl_3$) δ 7.31 (s, 1 H), 6.88 (s, 1 H), 6.34–6.26 (m, 2 H), 5.89 (d, J = 6.2 Hz, 1 H), 4.70 (dt, J = 12.6, 7.2 Hz, 1 H), 4.31 (apparent q, J = 7.0 Hz, 1 H), 3.58 (s, 3 H), 3.50 (s, 3 H), 2.49 (apparent q, J = 7.5 Hz, 2 H), 2.04 (s, 3 H), 2.00 (s, 3 H), 1.60–1.38 (m, 4 H).

(1*S,2*S**)- and (1*R**,2*S**)-2-(3,5-Dimethyl-4-hydroxyphenyl)cyclohexanecarboxaldehyde (53 and 54).** According to the general cyclization procedure, quinone methide **52** (from 9.9 mg of **19**, 0.0801 mmol) [$CDCl_3$ (3 mL), $Ti(Oi\text{-}Pr)_3Cl$ (270 μL of a 0.59 M solution in CH_2Cl_2, 0.16 mmol) 4 Å molecular sieves in reaction mixture, −40 °C 1 h and then warm to rt; aqueous workup ($NaHCO_3$, CH_2Cl_2, $MgSO_4$)] afforded crude product (diastereoselectivity >20:1 *trans*/*cis* by ^1H NMR of the crude reaction mixture). Preparative TLC (5:1 hexanes/ethyl acetate) afforded 10.6 mg (58%) of *trans*-**53** as a white solid and 0.3 mg of *cis*-**54** as a colorless oil. *Trans*-diastereomer **53** (1*S**,2*S**): ^1H NMR (300 MHz, C_6D_6) δ 9.33 (d, J = 2.7 Hz, 1 H), 6.65 (s, 2 H), 4.01 (s, 1 H), 2.35 (ddd, J = 11.5, 11.5, 3.5 Hz, 1 H), 2.22 (dddd, J = 11.4, 11.4, 3.1, 3.1 Hz, 1 H) 1.95 (s, 6 H), 1.73–1.52 (m, 8 H); ^{13}C NMR (75 MHz, C_6D_6) δ 203.8, 151.8, 136.4, 123.7, 55.8, 45.1, 35.9, 27.2, 26.8, 25.5, 16.3; IR ($CDCl_3$) 1715 cm^{-1}; MS (EI, 50 eV) m/z 232 (M^+, 82), 161 (92), 135 (100); HRMS calcd for $C_{15}H_{20}O_2$ 232.1463, found 232.1470. *Cis*-diastereomer **54** (1*R**,2*S**): ^1H NMR (300 MHz, $CDCl_3$) δ 9.61 (br s, 1 H), 6.88 (s, 2 H), 4.51 (s, 1 H), 2.97 (ddd, J = 12.0, 4.0, 4.0 Hz, 1 H), 2.78 (m, 1 H) 2.23 (s, 6 H), 1.96–1.28 (m, 8 H).

2,6-Dimethyl-4-[3-[*N*-(benzyloxycarbonyl)-*N*-ethenylamino]propylene]-2,5-cyclohexadien-1-one (55). According to the general quinone methide preparation, phenol **12** (84.8 mg, 0.260 mmol) and Ag_2O [665 mg, 2.87 mmol; $CDCl_3$ (3.0 mL), 2 h, rt, dried over K_2CO_3] afforded a solution of **55**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.34 (s, 5 H), 7.30–6.95 (br m, 2 H), 6.92–6.63 (m, 1 H), 6.36–6.09 (m, 1 H), 5.18 (s, 2 H), 4.49–4.26 (m, 2 H), 3.76 (br m, 2 H), 2.78 (br m, 2 H), 1.98 (s, 6 H).

(±)-1-(Benzyloxycarbonyl)-4-(3,5-dimethyl-4-hydroxyphenyl)-1,4,5,6-tetrahydropyridine (56) and (±)-1-(Benzyloxycarbonyl)-2-hydroxy-4-(3,5-dimethyl-4-hydroxyphenyl)hexahydropyridine (57). According to the general cyclization procedure, quinone methide **55** (from 84.8 mg, 0.260 mmol of phenol **12**) [$CDCl_3$ (3.0 mL), $ZnCl_2$ (5 mg, 0.04 mmol), 8 h, rt)], after aqueous workup ($NaHCO_3$, $CHCl_3$, K_2CO_3), afforded **56** and **57** (85.8 mg, 100% of material 90% pure by ^1H NMR analysis, 17:1 mixture of **56** and **57**). Analytical samples were prepared by HPLC (3:1 hexane/ethyl

acetate, 1.0 mL/min; **56**: t_R = 7.4 min; **57**: t_R = 24.5 min). Compound **56** is a clear oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45–7.31 (m, 5 H), 7.10–6.95 (m, 1 H), 6.82 (s, 2 H), 5.21 (br s, 2 H), 5.05–4.85 (m, 1 H), 4.61 (s, 1 H), 3.77–3.53 (m, 2 H), 3.38 (m, 1 H), 2.23 (s, 6 H), 2.08 (br m, 1 H), 1.77 (br m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, C=O not observed) δ 150.7, 136.5, 136.2, 128.5, 128.2, 127.7, 125.7, 125.2, 123.0, 109.8 (d), 67.6, 67.5, 40.4 (d), 37.3, 37.1, 31.2, 15.9; IR (CCl_4) 3620, 2927, 1711, 1650, 1488 cm^{-1}; MS (CI, NH_3) m/z 338 (MH^+, 64), 91 (100); HRMS calcd for $C_{21}H_{24}NO_3$ (MH^+) 338.1756, found 338.1744. Compound **57** is a clear oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (s, 5 H), 6.82, (s, 2 H), 5.94 (br s, 1 H), 5.17 (s, 2 H), 4.66 (s, 1 H), 4.05 (m, 1 H), 3.32 (m, 1 H), 3.02 (m, 1 H), 2.23 (s, 6 H), 2.05 (br m, 1 H), 1.85 (br m, 1 H), 1.77–1.54 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.6, 137.0, 136.3, 128.6, 128.2, 128.0, 126.8, 123.0, 75.2, 67.4, 39.6, 38.5, 34.4, 32.6, 16.0; IR (CCl_4) 3620, 3471, 1702, 1696 cm^{-1}; MS (CI, NH_3) m/z 356 (MH^+, 4), 91 (100); HRMS calcd for $C_{21}H_{26}NO_4$ (MH^+) 356.1862, found 356.1869.

2,6-Dimethyl-4-[4-[(trimethylsilyl)methyl]-4-pentenylidene]-2,5-cyclohexadien-1-one (58). According to the general quinone methide preparation, phenol **7** (10.6 mg, 0.0383 mmol) and Ag_2O [89 mg, 0.39 mmol; $CDCl_3$ (0.6 mL), 5 min, rt] afforded a solution of **58**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (s, 1 H), 6.90 (s, 1 H), 6.31 (t, J = 7.9 Hz, 1 H), 4.65 (s, 1 H), 4.62 (s, 1 H), 2.66 (apparent q, J = 7.7 Hz, 2 H), 2.18 (t, J = 7.5 Hz, 2 H), 2.06 (s, 3 H), 2.01 (s, 3 H), 1.70 (s, 2 H), 0.05 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.8, 147.5, 145.8, 138.6, 136.4, 134.6, 131.9, 129.8, 108.0, 37.4, 27.2, 26.8, 16.8, 16.0, −1.3; IR (neat) 1639, 1619, 1595, 1570, 1560 cm^{-1}.

(±)-2,6-Dimethyl-4-[3-hydroxy-4-[(trimethylsilyl)-methyl]-4-pentenylidene]-2,5-cyclohexadien-1-one (59). According to the general quinone methide preparation, phenol **10** (29.4 mg, 0.101 mmol) and Ag_2O [117 mg, 0.505 mmol; $CDCl_3$ (1 mL), 10 min, rt] afforded a solution of **59**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (s, 1 H), 6.91 (s, 1 H), 6.38 (t, J = 7.8 Hz, 1 H), 4.99 (br s, 1 H), 4.75 (s, 1 H), 4.16 (m, 1 H), 2.78 (m, 2 H), 2.03 (s, 3 H), 1.98 (s, 3 H), 1.55 (ABq, J = 14.0 Hz, $\Delta\nu$ = 76.2, 2 H), 0.06 (s, 9 H); IR ($CDCl_3$) 3608, 1645, 1620, 1600, 1576, 1566 cm^{-1}.

2,6-Dimethyl-4-[4-[(trimethylsilyl)methyl]-3-[(trimethylsilyl)oxy]-4-pentenylidene]-2,5-cyclohexadien-1-one (60). According to the general quinone methide preparation, phenol **11** (31.5 mg, 0.0864 mmol) and Ag_2O [100 mg, 0.432 mmol; $CDCl_3$ (0.6 mL), 10 min, rt] afforded a solution of **60**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (s, 1 H), 6.90 (s, 1 H), 6.31 (t, J = 8.0 Hz, 1 H), 4.98 (s, 1 H), 4.71 (s, 1 H), 4.11 (t, J = 5.8 Hz, 1 H), 2.70 (m, 2 H), 2.05 (s, 3 H), 2.01 (s, 3 H), 1.50 (ABq, J = 14.4 Hz, $\Delta\nu$ = 70.3 Hz, 2 H), 0.08 (s, 9 H), 0.07 (s, 9 H).

2,6-Dimethyl-4-(3-methylidenecyclopentyl)phenol (61). According to the general cyclization procedure, quinone methide **58** (from 10.6 mg, 0.383 mmol of phenol **7**) [$CDCl_3$ (0.6 mL), $ZnCl_2$ (6.2 mg, 0.0460 mmol), rt, 15 min; aqueous workup (H_2O, CH_2Cl_2, $MgSO_4$)] afforded crude product as a mixture of free phenol and silylated phenol. Treatment of this material with (n-Bu)$_4$NF (0.03 mL of a 1 M solution in THF, 0.03 mmol) in THF (0.2 mL) followed by aqueous workup (H_2O, ether, $MgSO_4$) and preparative TLC (5:1 hexanes/ethyl acetate) afforded **61** (6.4 mg, 83% from **7**) as a clear oil (>99% pure by GC) that crystallized upon storage in the freezer. Recrystallization (hexanes/ethyl acetate) afforded an analytical sample of **61** as white crystals: mp 50.0–51.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.87 (s, 2 H), 4.91 (br s, 1 H), 4.89 (br s, 1 H), 4.49 (s, 1 H), 3.02 (ddt, J = 10.8, 10.7, 6.9 Hz, 1 H), 2.75–2.65 (m, 1 H), 2.58–2.47 (m, 1 H), 2.46–2.30 (m, 2 H), 2.24 (s, 6 H), 2.16–2.04 (m, 1 H), 1.78–1.64 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.3, 150.3, 136.5, 127.0, 122.7, 105.1, 44.8, 41.3, 34.7, 32.6, 15.9; IR (CCl_4) 3635, 1748, 1660, 1492 cm^{-1}; MS (EI, 20 eV) m/z 202 (M^+, 100), 187 (33); HRMS calcd for $C_{14}H_{18}O$ 202.1358, found 202.1358.

(±)-2,6-Dimethyl-4-[4-methylidene-3-[(trimethylsilyl)-oxy]cyclopentyl]phenol (62). According to the general cyclization procedure, quinone methide **60** (26.8 mg, 0.12 mmol) [$CHCl_3$ (22 mL), $ZnCl_2$ (1.2 mL, of a 1.0 M in ether, 1.2 mmol), 0 °C, 5 min; aqueous workup (H_3PO_4 adjusted to pH 3.0, $MgSO_4$)] afforded 32.0 mg of the crude product. Preparative TLC (silica gel, 4:1 hexanes/ethyl acetate) afforded **62** (20.5 mg, 82%) as a clear oil (5:1 mixture of diastereomers, ^{1}H NMR): ^{1}H NMR (300 MHz, $CDCl_3$, major diastereomer) δ 6.85 (s, 2 H), 5.08 (br s, 1 H), 5.01 (s, 1 H) 4.60–4.49 (m, 1 H), 4.50 (s, 1 H), 2.87–2.99 (m, 1 H), 2.79–2.71 (m, 1 H), 2.52–2.42 (m, 1 H), 2.36–2.22 (m, 1 H), 2.23 (s, 6 H), 1.72 (dd, J = 22.4, 12.0 Hz, 1 H), 0.18 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$, major diastereomer) δ 153.1, 150.5, 136.0, 127.0, 122.8, 106.7, 74.8, 43.7, 39.0, 38.7, 15.9, 0.07; IR (CCl_4) 3640, 1670, 1495 cm^{-1}; MS (EI, 20 eV) m/z 290 (M^+, 24), 200 (77), 148 (75), 73 (100); HRMS calcd for $C_{17}H_{26}SiO_2$ 290.1703, found 290.1702.

4-[4,4-Bis(ethoxycarbonyl)-6-[(trimethylsilyl)methyl]-6-heptenylidene]-2,6-dimethyl-2,5-cyclohexadien-1-one (63). According to the general quinone methide preparation, phenol **9** (14.2 mg, 0.0316 mmol) and Ag_2O [73 mg, 0.316 mmol; $CDCl_3$ (0.8 mL), 15 min, rt] afforded a solution of **63**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21 (s, 1 H), 6.90 (s, 1 H), 6.25 (t, J = 8.0 Hz, 1 H), 4.68 (s, 1 H), 4.61 (s, 1 H), 4.20 (m, 4 H), 3.75 (s, 2 H), 2.41 (m, 2 H), 2.10 (m, 2 H), 2.07 (s, 3 H), 1.98 (s, 3 H), 1.42 (s, 2 H), 1.25 (t, J = 7.1 Hz, 6 H), 0.05 (s, 9 H).

(±)-3,3-Bis(ethoxycarbonyl)-6-(3,5-dimethyl-4-hydroxyphenyl)-1-methylenecycloheptane (64). According to the general cyclization procedure, quinone methide **63** (from 14.2 mg, 0.0316 mmol of **9**) [$CDCl_3$ (1.0 mL), $ZnCl_2$ (10 mg, 0.073 mmol), rt, 15 min; aqueous workup (H_2O, CH_2Cl_2, $MgSO_4$)] afforded crude product as a mixture of silylated phenol and free phenol. Treatment of the crude product with (n-Bu)$_4$NF (0.03 mL of a 1 M solution in THF, 0.03 mmol) in THF (0.5 mL) followed by aqueous workup (H_2O, ether, $MgSO_4$) and flash chromatography (10:1 hexanes/ethyl acetate) afforded **64** (11.6 mg, 98%) as a clear oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.79 (s, 2 H), 4.89 (s, 1 H), 4.84 (s, 1 H), 4.48 (s, 1 H), 4.20 (m, 4 H), 2.90 (ABq, J = 14.1 Hz, $\Delta\nu$ = 21.0 Hz, 2 H), 2.58 (m, 2 H), 2.40 (m, 1 H), 2.23 (s, 6 H), 1.85 (m, 4 H), 1.26 (t, J = 7 Hz, 3 H), 1.25 (t, J = 7 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.2, 171.9, 150.3, 144.3, 139.4, 126.7, 122.9, 115.6, 57.4, 46.4, 46.2, 39.4, 33.3, 31.8, 29.7, 16.0, 14.1; IR (CCl_4) 3600–3400, 2930, 1735, 1640 cm^{-1}; MS (EI, 20 eV) m/z 374 (M^+, 25), 173 (53), 161 (100); HRMS calcd for $C_{22}H_{30}O_5$ 374.2094, found 374.2096.

2,6-Dimethyl-4-[6-(methoxycarbonyl)-5-oxo-1-hexylidene]-2,5-cyclohexadien-1-one (65) and 3-(3,5-dimethyl-4-hydroxyphenyl)-2-(methoxycarbonyl)-2-cyclohexen-1-one (67). According to the general quinone methide preparation, phenol **15** (19.1 mg, 0.0687 mmol) and Ag_2O [67.5 mg, 0.291 mmol; $CDCl_3$ (0.8 mL), 25 min, rt] afforded cyclized product **67** directly. Monitoring a similar reaction by ^{1}H NMR (3 min reaction time) allowed a spectrum of **65** to be recorded: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (s, 1 H), 6.88 (s, 1 H), 6.25 (t, J = 8.1 Hz, 1 H), 3.74 (s, 3 H), 3.45 (s, 2 H), 2.62 (t, J = 7.0 Hz, 2 H), 2.52 (apparent q, J = 7.7 Hz, 2 H), 2.05 (s, 3 H), 2.00 (s, 3 H), 1.83 (p, J = 7.2 Hz, 2 H). After reaction with Ag_2O, filtration and concentration afforded a yellow oil. Preparative TLC (2:1 hexanes/ethyl acetate) afforded **67** (14.3 mg, 76%) as a clear oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.02 (s, 2 H), 4.97 (br s, 1 H), 3.66 (s 3 H), 2.74 (t, J = 6.0 Hz, 2 H), 2.53 (t, J = 6.5 Hz, 2 H), 2.24 (s, 6 H), 2.15 (p, J = 6.3 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.6, 168.0, 159.8, 153.8, 131.9, 130.6, 127.3, 123.3, 52.1, 37.0, 31.2, 22.0, 15.9; IR (CCl_4) 3580–3250, 2938, 1740, 1670, 1600 cm^{-1}; MS (EI, 20 eV) m/z 274 (M^+, 100), 246 (16); HRMS calcd for $C_{16}H_{18}O_4$ 274.1205, found 274.1205.

2,6-Dimethoxy-4-[6-(methoxycarbonyl)-5-oxo-1-hexylidene]-2,5-cyclohexadien-1-one (66). According to the general quinone methide preparation, phenol **16** (12.0 mg, 0.0387 mmol) and Ag_2O [179 mg, 0.773 mmol; $CDCl_3$ (0.6 mL), 10 min, rt] afforded a solution of **66**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.60 (s, 1 H), 6.23 (s, 1 H), 6.21 (apparent t, J = 8.0 Hz, 1 H), 3.88 (s, 3 H), 3.79 (s, 3 H), 3.73 (s, 3 H), 3.45 (s, 2H), 2.64 (t, J = 7.0 Hz, 2 H), 2.57 (apparent q, J = 6.5 Hz, 2 H), 1.85 (p, J = 6.4 Hz, 2 H).

2-(3,5-Dimethoxy-4-hydroxyphenyl)-6-oxo-1-cyclohexene-1-carboxylic Acid, Methyl Ester (68) and (1*S,6*R**)-2-(3,5-Dimethoxy-4-hydroxyphenyl)-6-oxocyclohexane-1-carboxylic Acid, Methyl Ester (72).** According to the general cyclization procedure, quinone methide **66** (from 12.0

mg, 0.387 mmol of **16**) [$CDCl_3$ (0.6 mL), $ZnCl_2$ (13 mg, 0.097 mmol), rt, 10 h; aqueous workup (0.5 N HCl, ether, $MgSO_4$)] afforded a light yellow oil. Preparative TLC (1:5 hexanes/ethyl acetate) gave two fractions. The lower R_f fraction (R_f 0.20) afforded 9.2 mg (78%) of cyclohexene **68** as a clear oil: ^1H NMR (300 MHz, $CDCl_3$) δ 6.64 (s, 2 H), 5.69 (s, 1 H), 3.88 (s, 6 H), 3.65 (s, 3 H), 2.76 (t, J = 5.9 Hz, 2 H), 2.54 (t, J = 6.7 Hz, 2 H), 2.15 (p, J = 6.3 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.3, 167.8, 159.4, 147.0, 136.2, 132.5, 129.9, 103.9, 56.3, 52.3, 37.0, 31.2, 22.0; IR ($CDCl_3$) 3521, 1730, 1663, 1600 cm^{-1}; MS (EI, 20 eV) m/z 306 (M^+, 100), 181 (40); HRMS calcd for $C_{16}H_{18}O_6$ 306.1103, found 306.1103. The higher R_f fraction (R_f 0.38) afforded cyclohexane **72** (2.4 mg, 20%) as a 12:1 mixture (^1H NMR) of diastereomers: ^1H NMR (300 MHz, $CDCl_3$, major diastereomer) δ 6.45 (s, 2 H), 5.42 (s, 1 H), 3.88 (s, 6 H), 3.63 (m, 1 H_2), 3.60 (s, 3 H), 3.31 (dt, J = 11.8, 3.5 Hz, 1 H), 2.61–2.55 (m, 1 H), 2.55–2.35 (m, 1 H) 2.17–2.06 (m, 1 H), 1.90–1.48 (m, 3H); IR (CCl_4) 3554, 1751, 1718, 1654, 1617 cm^{-1}; MS (EI, 20 eV) m/z 308 (M^+, 100), 276 (72), 249 (35); HRMS calcd for $C_{16}H_{20}O_6$ 308.1260, found 308.1260.

(±)-Methyl 7-(3,5-Dimethyl-4-oxo-2,5-cyclohexadien-1-ylidene)-6-methyl-3-oxoheptanoate (69). According to the general quinone methide preparation, phenol **17** (19.9 mg, 0.0681 mmol) and Ag_2O [79.0 mg, 0.340 mmol; $CDCl_3$ (1.0 mL), 10 min, rt] afforded a solution of **69**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.24 (s, 1 H), 6.87 (s, 1 H), 6.00 (d, J = 12 Hz, 1 H), 3.71 (s, 3 H) 3.40 (s, 2 H), 2.98–2.86 (m, 1 H), 2.51 (apparent t, J = 7.5 Hz, 2 H), 2.05 (s, 3 H), 2.00 (s, 3 H), 1.92–1.82 (m, 1 H), 1.71–1.58 (m, 1 H), 1.13 (d, J = 6 Hz, 3 H).

(1*R,2*S**,3*R**)- and (1*S**,2*S**,3*R**)-2-(3,5-Dimethyl-4-hydroxyphenyl)-3-methyl-6-oxocyclohexanecarboxylic Acid, Methyl Ester (70a and 70b, respectively).** Filtration of the silver salts from the preceding reaction mixture of **69** after 15 min afforded a 1:1:1 mixture of diastereomeric cyclohexanone products as observed by 300 MHz ^1H NMR [δ = 1.05, 0.79, and 0.74 (d, J = 6.4 Hz, 3 H each, $CHCH_3$), respectively]. This mixture was treated with freshly fused $ZnCl_2$ (21.2 mg, 0.156 mmol) at rt and stirred for 42 h. Workup according to the general procedure followed by flash chromatography (5:1 hexanes/ethyl acetate) and preparative TLC (5:1 hexanes/ethyl acetate) afforded 14.4 mg (73%) of cyclohexanones **70a** and **70b** as a 12:1 mixture by ^1H NMR. Major diastereomer (1*R**,2*S**,3*R**, **70a**): ^1H NMR (300 MHz, $CDCl_3$) δ 6.77 (s, 2 H), 4.55 (s, 1 H), 3.60 (d, J = 12.4 Hz, 1 H), 3.54 (s, 3 H), 2.81 (apparent t, J = 11.7 Hz, 1 H), 2.58–2.53 (m, 1 H), 2.21 (s, 6 H), 2.20–1.98 (m, 3 H), 1.64–1.52 (m, 1 H), 0.74 (d, J = 6.4 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.6, 169.5, 151.0, 132.8, 127.7, 123.0, 64.1, 53.4, 51.8, 41.3, 36.6, 34.1, 19.3, 16.1; IR (CCl_4) 3639, 3524, 1760, 1728, 1662, 1615 cm^{-1}; MS (EI, 20 eV) m/z 290 (M^+, 100), 258 (29); HRMS calcd for $C_{17}H_{22}O_4$ 290.1519, found 290.1518.

1-(3,5-Dimethyl-4-hydroxyphenyl)-3-hydroxy-4-[(trimethylsilyl)methyl]-1,4-pentadiene (71). (n-Bu)$_4$NF (120 μL of a 1 M solution in THF, 0.12 mmol) was added to a solution of quinone methide **59** (from **10**; 29.4 mg) in $CDCl_3$ (3 mL) . The resulting solution was stirred for 10 min. Aqueous workup (H_2O, CH_2Cl_2, Na_2SO_4) afforded a yellow oil which rapidly decomposed upon standing. Flash chromatography (silica gel pretreated with the eluting solvent), 3:1:0.1 hexanes/ethyl acetate/triethylamine) afforded unstable dienol **71** (18.8 mg, 64%) as a clear oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.03 (s, 2 H), 6.48 (d, J = 15.9 Hz, 1 H), 5.99 (dd, J = 15.8, 7.1 Hz, 1 H), 5.05 (d, J = 1.1 Hz, 1 H), 4.73 (s, 1 H), 4.64 (s, 1 H), 4.54 (br d, J = 6.8 Hz, 1 H), 2.23 (s, 6 H), 1.56 (ABq, J = 13.7 Hz, $\Delta\nu$ = 44.2 Hz, 2 H), 0.04 (s, 9 H); IR ($CDCl_3$) 3608, 1604, 1598, 1573, 1534, 1489 cm^{-1}; MS (EI, 20 eV) m/z 290 (M^+, 16), 177 (66), 135 (55), 73 (100).

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Supplementary Material Available: Copies of NMR spectra for compounds **3–17**, **19**, **23b**, **24–46**, **48**, and **51–70** (109 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.