Use of Conjugated Dienones in Cyclialkylations: Total Syntheses of Arucadiol, 1,2-Didehydromiltirone, (±)-Hinokione, (±)-Nimbidiol, Sageone, and Miltirone†

George Majetich,* Shuang Liu, Jing Fang, David Siesel, and Yong Zhang

Department of Chemistry, The University of Georgia, Athens, Georgia 30602

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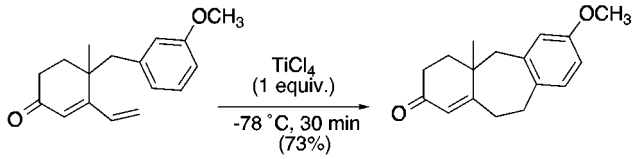
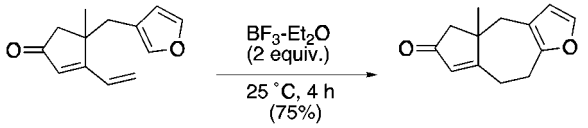
Functionalized hydrophenanthrenes can be prepared using a cyclialkylation-based strategy. These annulations are highly dependent on the directing effects of the arene substitutents and on conformational considerations. The utility of this methodology was featured in the syntheses of six diterpenoids.

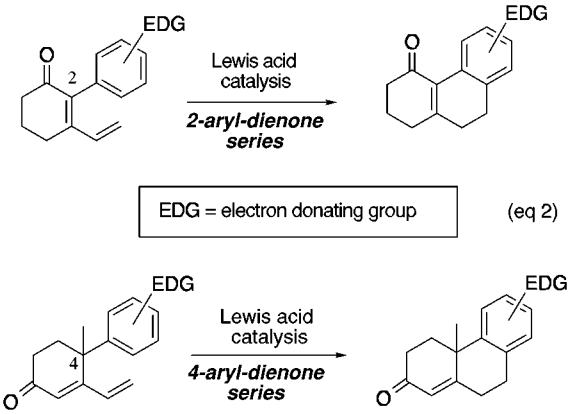
We have found that intramolecular Friedel−Crafts alkylations of conjugated dienones are useful for the preparation of tricyclic compounds with a central seven-membered ring fused to either an arene[1] or furan ring[2] (eq 1).



(eq 1)



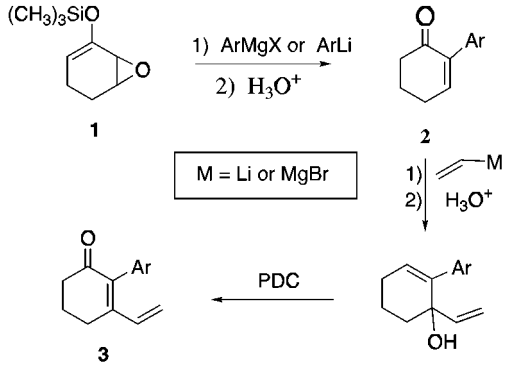
This cyclialkylation-based strategy[3] can also be used for the preparation of functionalized hydrophenanthrenes, as generalized by the two series of aryl dienone cyclizations presented in eq 2.[4,5] Since this new annulation procedure represents an attractive strategy for the synthesis of a 6,6,6-fused subunit, we sought to determine its scope and limitations and to demonstrate its synthetic utility through the synthesis of several diterpenes. This paper details this study.[6]



Preparation of Substrates

Coupling our own methodology with research developed by Wender and co-workers[7] allowed us to devise a three-step sequence for the preparation of all the 2-aryl dienones in this study (Scheme 1). Previously, we have found that 3-vinyl-2-cycloalkenones (cf. **3**) can be prepared from 2-cycloalkenones in good yield by oxidizing the appropriate bis-allylic tertiary alcohol with pyridinium dichromate (PDC).[8] Treating epoxide **1** with either aryl Grignard reagents or aryllithium reagents gave 2-aryl-2-cyclohexenones in high yield (cf. **2**), which were treated with either vinyllithium or vinylmagnesium bromide to give the desired 1-vinyl-2-cycloalken-3-ols for oxidation.

Scheme 1



The preparation of the 4-aryl dienones was more problematic. Wender reported that treatment of epoxide **1** with lithium dimethylcuprate gives 6-methyl-2-cyclohexenone in 55% yield. In theory, the reaction of lithium diarylcuprates with **1** would allow us to prepare 6-aryl-2-cyclohexenones (cf. **4**, Scheme 2), which could be converted to functionalized cyclohexenone **5** using the transformations shown. However, we found that the cuprate reagents derived from oxygenated arenes were often unstable and gave low yields of the adduct. These

† Taken in part from the Ph.D. Dissertation of Shuang Liu, University of Georgia, 1997.

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(1) Majetich, G.; Zhang, Y.; Feltman, T. L.; Belfoure, V. *Tetrahedron Lett.* **1993**, *34*, 441.
(2) Majetich, G.; Zhang, Y.; Liu, S. *Tetrahedron Lett.* **1994**, *35*, 4887.
(3) Brunson, H. A.; Kroeger, J. W. *J. Am. Chem. Soc.* **1940**, *62*, 36.
(4) For a review of perhydrophenanthrene syntheses prior to 1987, see: Ho, T.-L. In *Carbocycle Construction in Terpenes Synthesis*; VCH Publishers: New York, 1988.
(5) For recent perhydrophenanthrene syntheses, see: (a) Chiu, C. K.-F.; Govindan, S. U.; Fuchs, P. L. *J. Org. Chem.* **1994**, *59*, 311. (b) Spino, C.; Crawford, J.; Bishop, J. *J. Org. Chem.* **1995**, *60*, 844. (c) Kondo, K.; Sodeoka, M.; Shibasaki, M. *J. Org. Chem.* **1995**, *60*, 4322.
(6) For a preliminary account of this work, see: Majetich, G.; Liu, S.; Siesel, D.; Zhang, Y. *Tetrahedron Lett.* **1995**, *36*, 4749.
(7) Wender, P. A.; Erhardt, J. M.; Letendre, L. J. *J. Am. Chem. Soc.* **1981**, *103*, 2114.
(8) Majetich, G.; Condon, S.; Hull, K.; Ahmad, S. *Tetrahedron Lett.* **1989**, *30*, 1033.

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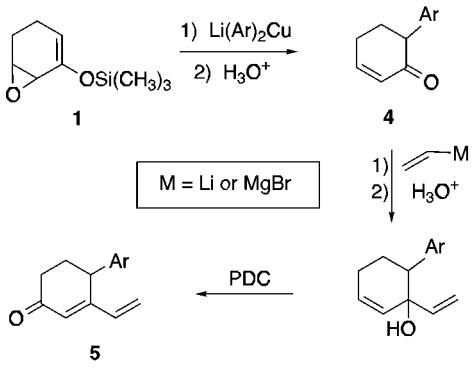
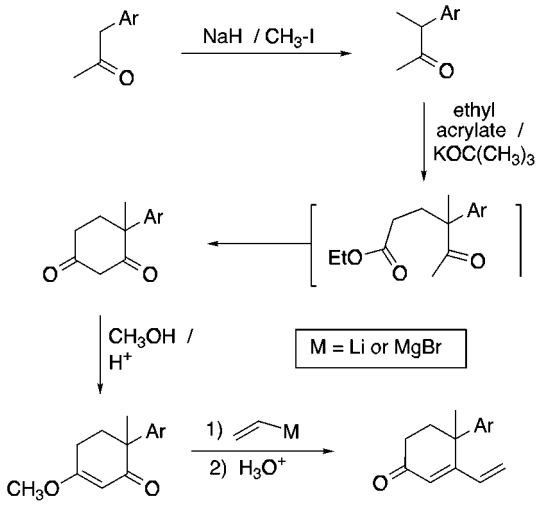
Scheme 2



1 4 5

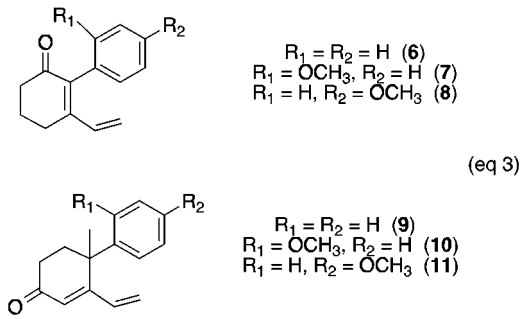
difficulties were also encountered if a "higher order" aryl cuprate was used.[9] Instead a more classical approach for the preparation of 4-aryl diones was used, as generalized in Scheme 3. Here a functionalized arylacetone derivative is alkylated with iodomethane, followed by a Michael addition/mixed Claisen condensation sequence[10] to produce a 4-methyl-4-arylcyclohexane-1,3-dione. This cyclic 1,3-diketone can be converted to the desired 4-aryl dienone by treating it with acidic methanol to produce a 3-methoxycycloalkenone followed by the addition of vinylmagnesium bromide (or vinyllithium) and subsequent acid hydrolysis.

Scheme 3



Results and Discussion

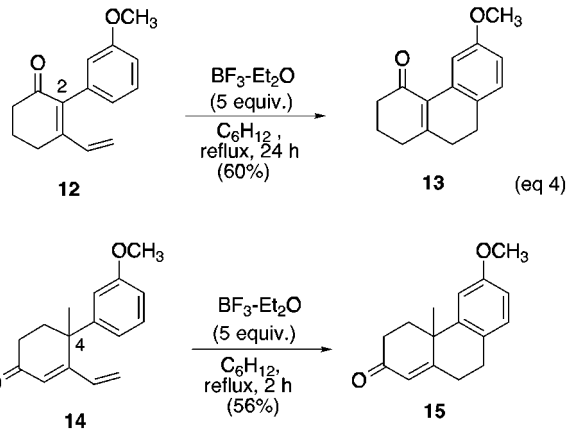
Simple aryl dienones, such as **6** and **9**, are not sufficiently electron-rich to cyclize (eq 3). Alternatively, the



(eq 3)

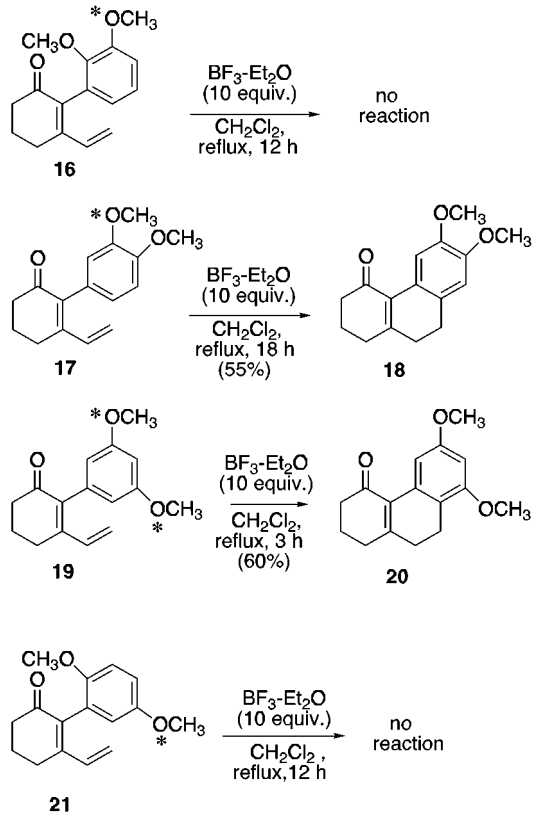
directing nature of the methoxy group prevents the precursors **7**, **8**, **10**, and **11** from cyclizing. In substrate **7**, for example, the methoxy substituent activates positions which are geometrically precluded from intramolecular reaction with the Lewis acid-activated conjugated dienone.

In contrast, treating of 2-aryl dienone **12** with boron trifluoride etherate in refluxing cyclohexane (81 °C) produces enone **13** in 60% yield within 2 h (eq 4). 4-Aryl dienone **14** also cyclizes under similar conditions and in comparable yield.



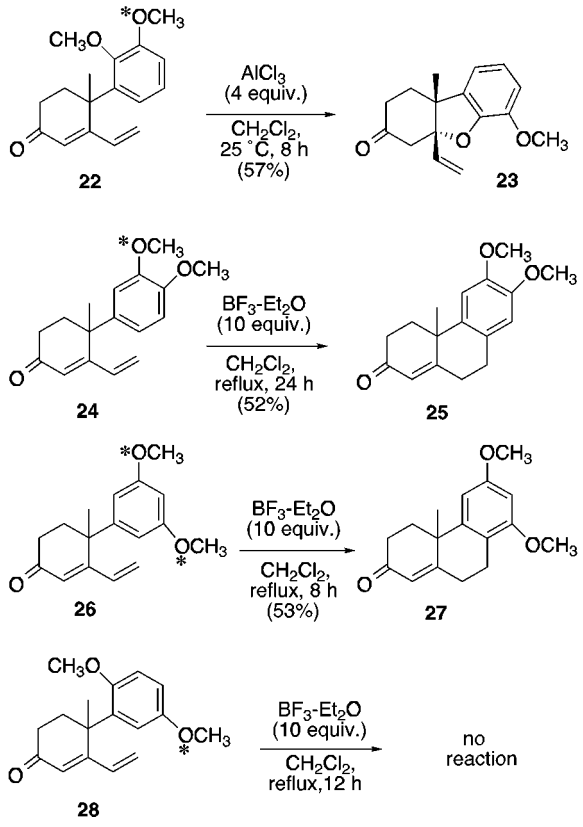
Four 2-aryl dienones with two methoxy groups were prepared using the Grignard-based protocol presented earlier (cf. **1** → **2** → **3**). Each of the substrates in Chart 1 was expected to cyclize because of the favorable directing effects of the indicated (*) substituent(s); however, two substrates did not. Four analogous 4-aryl dienones were also synthesized, and once again, two of the cyclialkylations failed despite the favorable directing effects of the methoxy substituents (Chart 2). Note that in the case of dienone **22**, demethylation of one of the

Chart 1



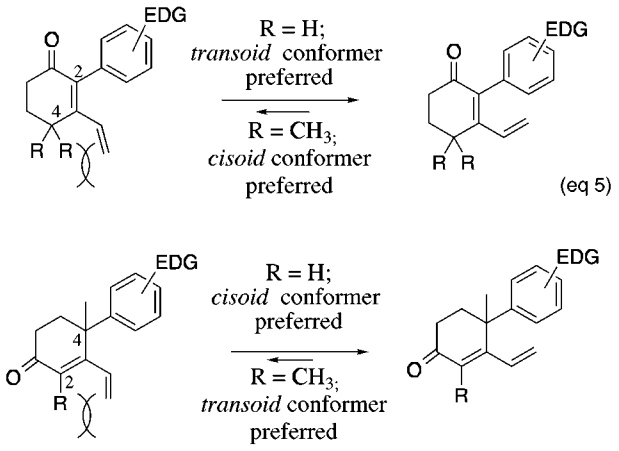
(9) Marino, J. P. ; Jaen, J. C. *J. Am. Chem. Soc.* **1982**, *104*, 3165.
(10) Zimmerman, H. E.; Pasteris, R. J. *J. Org. Chem.* **1980**, *45*, 4876.

Chart 2



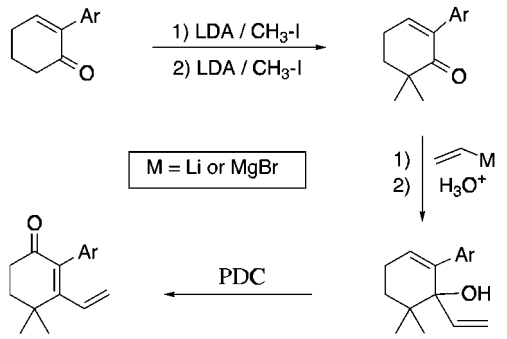
ethers occurred, followed by ring closure to give a benzofuran in 57% yield.

We reasoned that the four unsuccessful reactions listed in Charts 1 and 2 failed because these substrates preferred a diene conformation which precludes cyclization. This suggested that the introduction of steric hindrance at either the 4-position of a 2-aryl dienone or at the 2-position of a 4-aryl dienone would favor a dienone orientation leading to ring closure (eq 5).



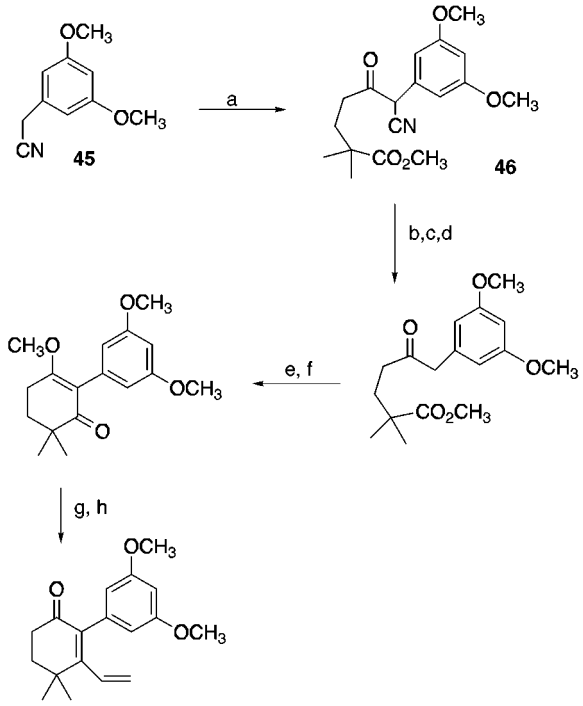
Toward this end substrates with additional alkyl substituents analogous to those shown in Charts 1 and 2 were prepared. The preparation of dienones **29**, **31**, and **35** again features Wender's synthesis of 2-aryl-2-cyclohexenones and is generalized in Scheme 4. Unfortunately, this approach could not be used to prepare substrate **33** because the lithium anion derived from the requisite 1-bromo-3,5-dimethoxybenzene undergoes rapid intermolecular proton abstraction to generate the 2-lithio

Scheme 4



anion of resorcinol dimethyl ether instead of reacting with epoxide **1**.[11] Dienone **33** was prepared from nitrile **45** using the seven-step sequence shown in Scheme 5.[12]

Scheme 5[a]



[a] (a) dimethyl glutarate/NaH; (b) H^+/heat; (c) CH_3OH/H^+; (d) $KHCO_3/(CH_3O)_2SO_2$; (e) NaH; (f) CH_3OH/H^+; (g) vinylmagnesium bromide; (h) H_3O^+.

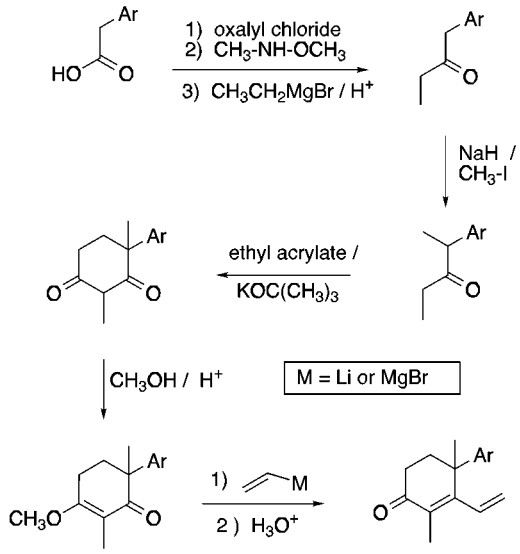
The synthesis of the 2,4-dimethyl-4-aryl dienones exploits the strategy presented in Scheme 3. Although it is conceptually feasible to methylate the functionalized cyclohexane-1,3-dione, this alkylation is troublesome. Instead, we chose to introduce the methyl group prior to assembling the functionalized cyclohexane-1,3-dione using the cyclohexane annulation developed by Zimmerman and Pasteris[10] (Scheme 6). Our first way to prepare functionalized 2-arylpentan-3-ones exploits the Nahm–Weinreb protocol to homologate phenylacetic acid derivatives (Scheme 6). Since several of the required oxygenated phenylacetic acid derivatives are not commerically available, the requisite 2-arylpentanones were readily prepared by reacting 1,2-epoxybutane with the ap-

(11) For reviews, see: (a) Wakefield, B. J. *The Chemistry of Organolithium Compounds*; Pergamon Press: Elmsford, New York, 1974. (b) Slocum, D. W.; Sugarman, D. I. *Adv. Chem. Ser.* **1974**, *130*, 222.

(12) Born, H.; Pappo, R.; Szmuszkovicz, J. *J. Chem. Soc.* **1953**, 1779.

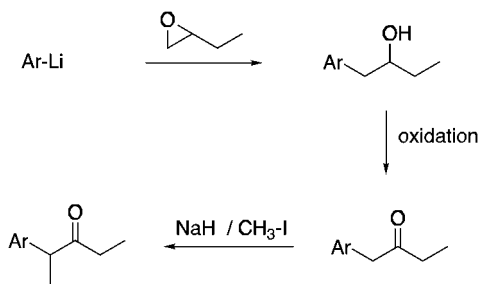
(13) Nahm, S.; Weinreb, S. M. *Tetrahedron Lett.* **1981**, *22*, 3815.

Scheme 6



propriately functionalized aryllithium, followed by an oxidation (Scheme 7). Subjecting these arylated pentanones to the tandem Michael addition/mixed Claisen condensation permitted the preparation of 4-aryl dienones with a methyl group at the α-position of the conjugated dienone. This epoxide-based route was used when convenient to prepare other 4-aryl dienones.

Scheme 7



The results presented in Charts 3 and 4 clearly affirm our conjecture that sluggish cyclialkylations can be attributed to conformational preferences. Moreover, the seven successful cyclialkylations required less Lewis acid and shorter reaction times than their less alkylated counterparts (cf. Charts 1 and 2). Several of these cyclizations are particularly noteworthy. For example, recall that substrates **16** and **22** which lack these steric influences failed to cyclize. Surprisingly, substrate **35** not only gave a 41% yield of **36**, the normal cyclialkylation product, but also a 56% yield of naphthalene **37**, an unexpected product. Scheme 8 offers our explanation for the formation of both tricycles **36** and **37**. These products arise from conformers **i** or **ii**, respectively, with the cyclialkylation controlled by the indicated (*) substituent.

An alternative strategy for manipulating the population of the diene conformers is illustrated in eq 6. Inspec-

(14) A related silicon-mediated conformational biasing has been used to achieve the following annulation process, see: Narasaka, K.; Hayashi, Y.; Shimada, S.; Yamada, J. *Israel J. Chem.* **1991**, *31*, 261.

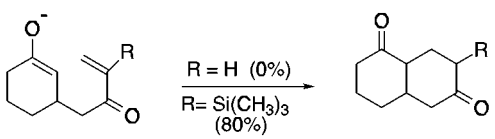
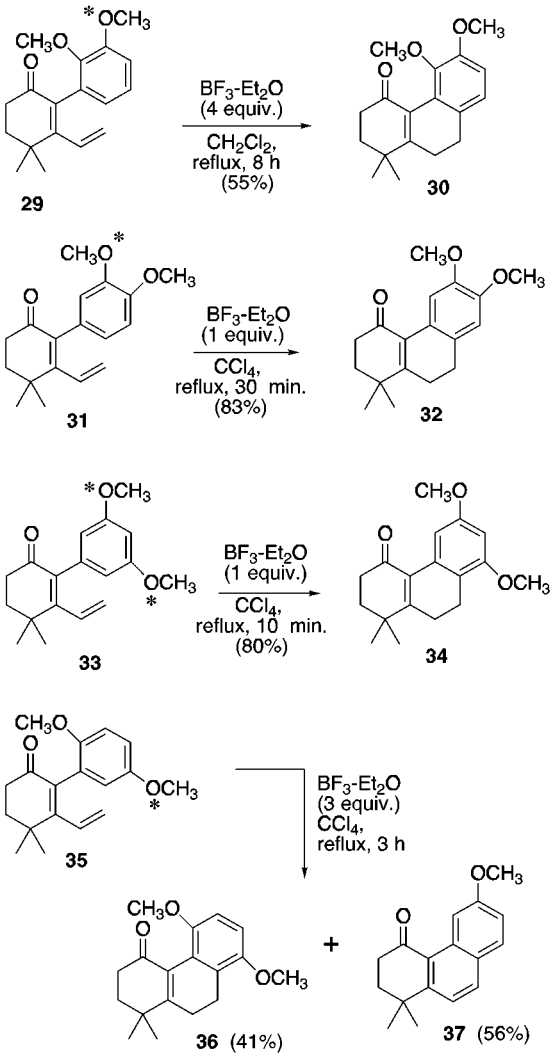
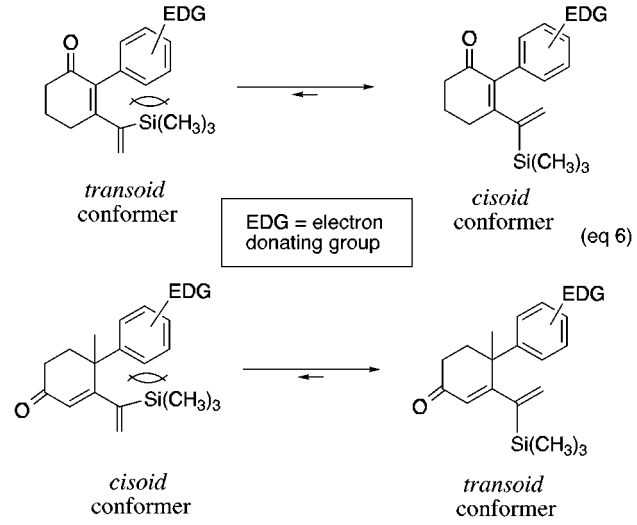


Chart 3

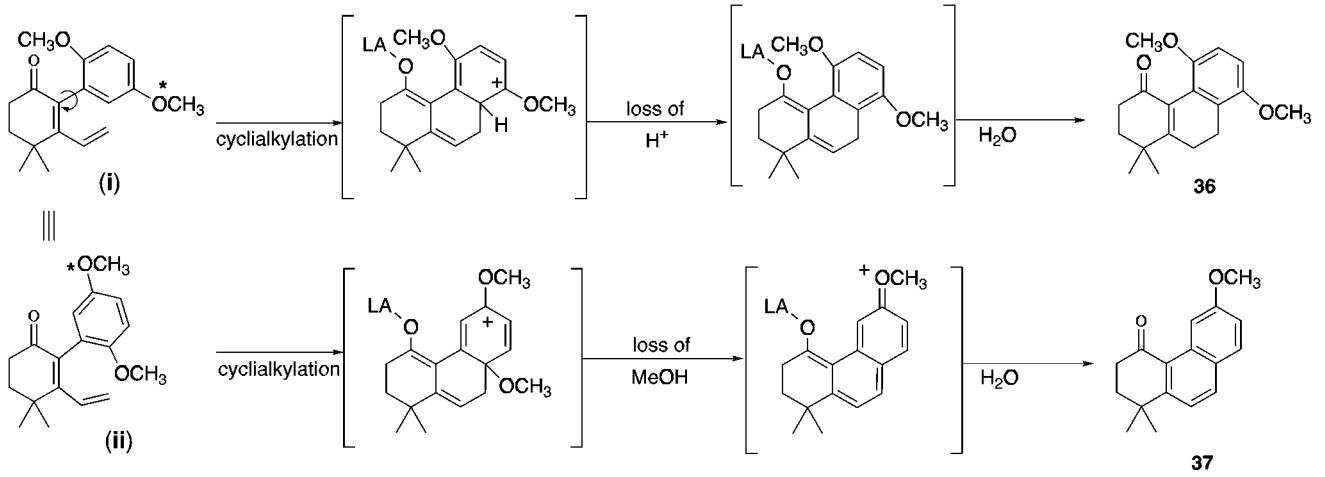


tion of Drieding stereomodels suggests that the presence of a bulky trimethylsilyl group at the γ-position of the conjugated dienone system favors the *cisoid* conformation needed for cyclialkylation of the 2-aryl dienone series substrates and the *transoid* conformation required for cyclialkylation of the 4-aryl dienone precursors.[14]



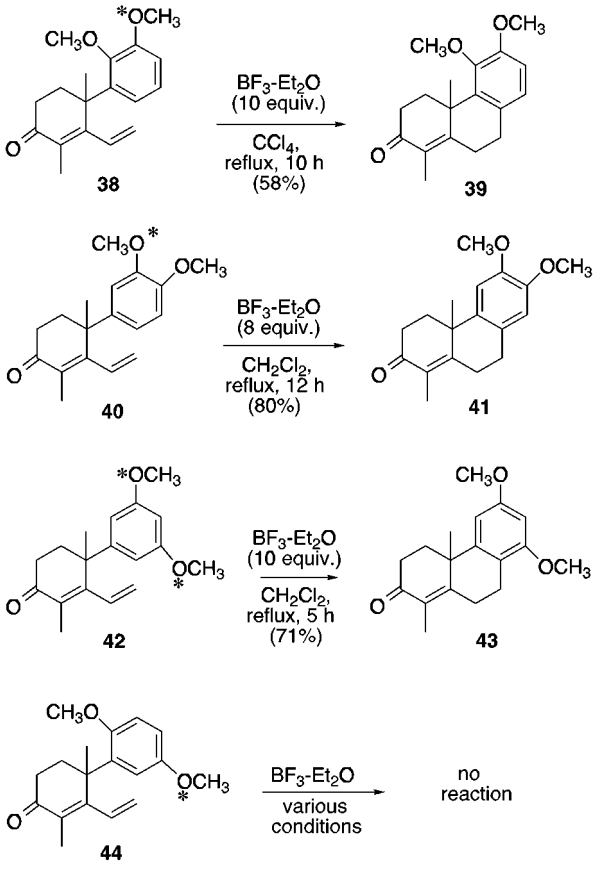
These silylated substrates were readily prepared by treating the appropriately functionalized cyclohexenone

Scheme 8



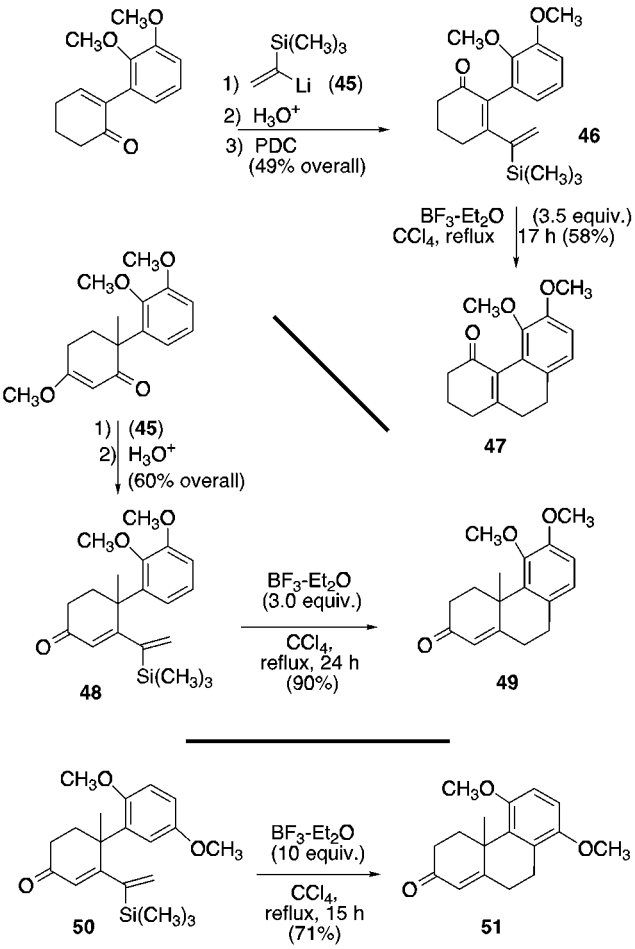
with organolithium reagent **45**. Treatment of aryl dienones **46**, **48**, and **50** with boron trifluoride etherate in refluxing CCl_4 resulted in facile cyclialkylation (Scheme 9). These results contrast sharply with those of the nonsilylated aryl dienones **16** (cf. Chart 1) and **28** (cf. Chart 2) which did not react or with aryl dienone **22** (cf. Chart 2) which produced a dihydrofuran. Note that the trimethylsilyl group can be lost only after annulation occurs. Hindsight suggests that the cyclialkylations in Charts 1 and 2 which gave only modest yields would be improved by cyclizing the appropriate aryl γ-silyl dienones.

Chart 4



These dramatic results prompted us to prepare silylated analogues of those substrates (cf. **7**, **8**, **10**, and **11**) which had failed to cyclize, undoubtedly due to the unfavorable directing effects of the substituents (cf. eq 3). While silylated 4-aryl dienones **56** and **58** cyclized (eq 8), the 2-aryl dienone analogues resisted cyclization (eq 7).

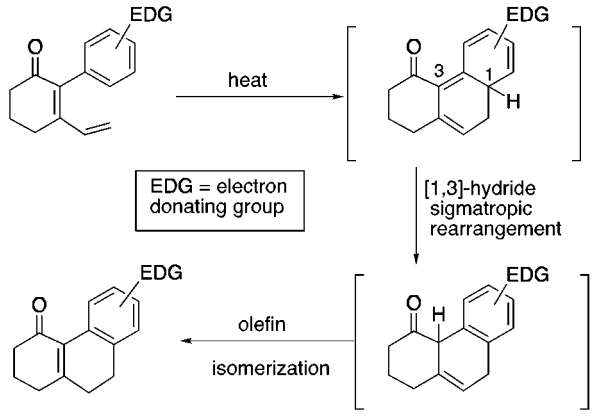
Scheme 9



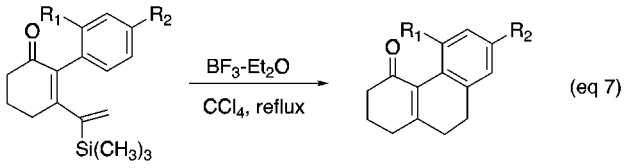
Given that all of these cyclialkylations required reaction temperatures between 40 and 77 °C, it could be argued that the 2-aryl dienone annulations occurred via a thermal six-electron cyclization, analogous to the *cis*-hexatriene−cyclohexadiene interconversion,[15] instead of by a Friedel−Crafts mechanism (cf. Scheme 10). An

(15) Lewis, K. E.; Steiner, H. *J. Chem. Soc.* **1964**, 3080.

Scheme 10



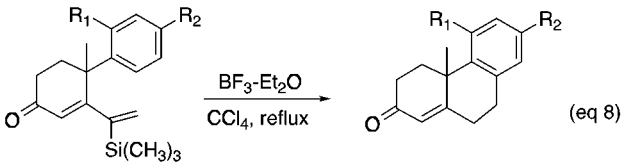
electrocyclic, pericyclic pathway can not be used to explain the 4-aryl dienone cyclizations.



$R_1 = OCH_3$, $R_2 = H$ (**52**)
$R_1 = H$, $R_2 = OCH_3$ (**54**)

$R_1 = OCH_3$, $R_2 = H$ (**53**) (0%)
$R_1 = H$, $R_2 = OCH_3$ (**55**) (< 5%)

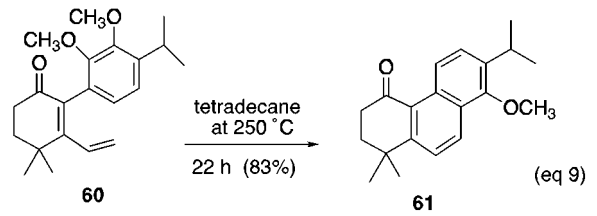
While certain electrocyclizations occur at room temperature,[16] the participation of an aromatic ring bond in the electrocyclization retards the cyclization so that retroelectrocyclization is often favored.[17] Indeed, elec-



$R_1 = OCH_3$, $R_2 = H$ (**56**)
$R_1 = H$, $R_2 = OCH_3$ (**58**)

$R_1 = OCH_3$, $R_2 = H$ (**57**) (43%)
$R_1 = H$, $R_2 = OCH_3$ (**59**) (45%)

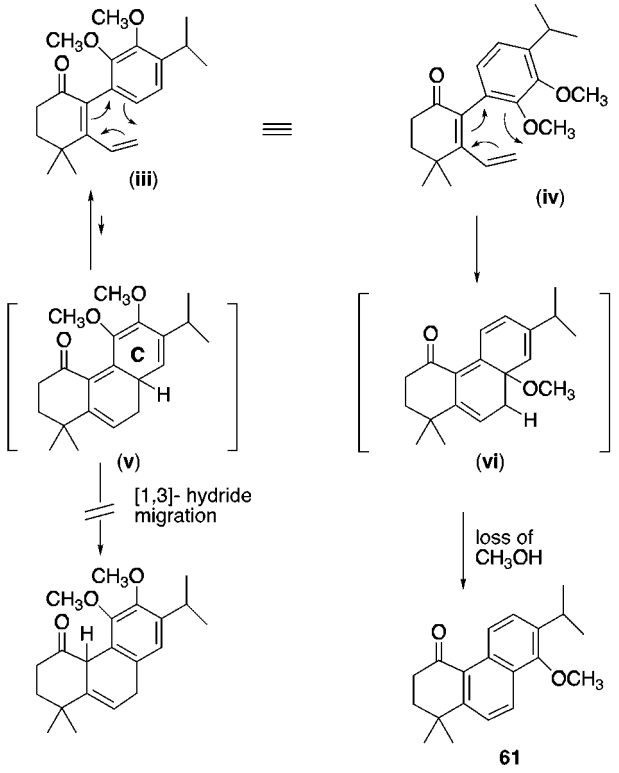
trocyclization was not observed when 2-aryl dienone **60** was either heated in solvents at temperatures <250 °C or heated neat at 250 °C for a period of 10 h. However, heating **60** at 250 °C in tetradecane, an inert, high-boiling solvent, for 24 h produced naphthalene derivative **61** in 83% yield, along with a 15% yield of unreacted **60** (eq 9).



60 **61**

The formation of naphthalene derivative **61** confirms that the Lewis acid-promoted cyclialkylations proceed via a cationic-based mechanism rather than a pericyclic, sigmatropic process. A six electron−six atom reaction

Scheme 11



of rotomer **iii** generates intermediate **v**, which undergoes retroelectrocyclization instead of the expected [1,3]-hydride rearrangement because of the unfavorable loss of aromaticity within the C ring (Scheme 11). In contrast, electrocyclization of rotomer **iv** not only involves the participation of the more electron-rich aromatic ring bond but results in the formation of cyclohexadiene **vi** which can lose methanol to produce a more stable naphthalene system.

Synthetic Applications

In order to demonstrate how practical this new annulation strategy is for the preparation of hydrophenanthrenes, six diterpenes were synthesized using either a 2- or a 4-aryl dienone cyclialkylation strategy (Figure 1). Each synthesis will be discussed separately.

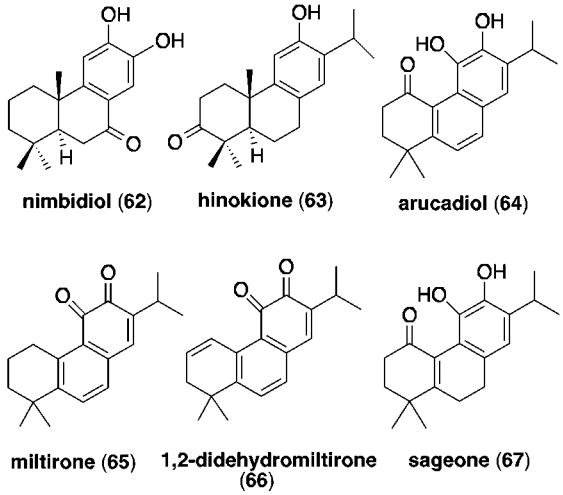
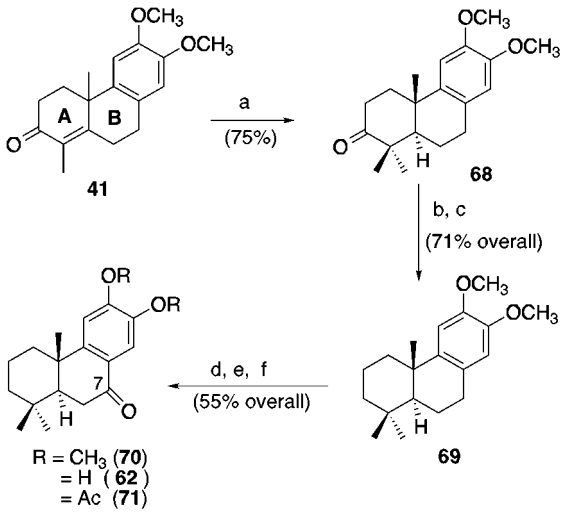


Figure 1.

(16) Sieber, W.; Heimgartner, M.; Hansen, H.-J.; Schmid, H. *Helv. Chim. Acta* **1972**, *55*, 3005.
(17) (a) Heimgartner, H.; Hansen, H.-J.; Schmid, H. *Helv. Chim. Acta.* **1972**, *55*, 1385. (b) Darcy, P. J.; Hart, R. J.; Heller, H. G. *J. Chem. Soc., Perkin Trans. 1* **1978**, 571. (c) Crescente, O.; Heller, H. G.; Oliver, S. *J. Chem. Soc., Perkin Trans. 1* **1979**, 150. (d) Heller, H. G.; Oliver, S.; Shawe, S. *J. Chem. Soc., Perkin Trans. 1* **1979**, 154.

Scheme 12[a]

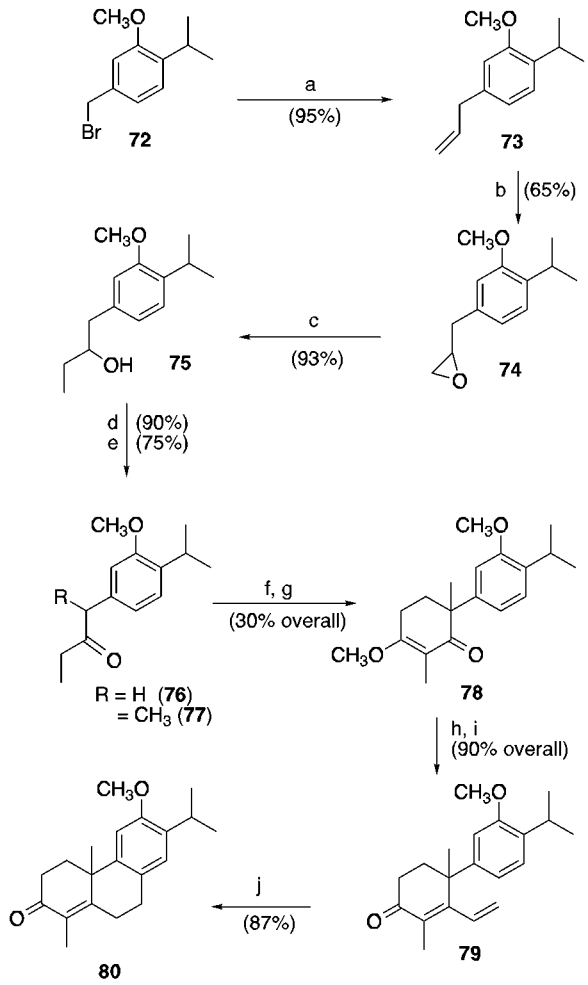


[a] (a) Li, NH_3, *t*-BuOH, CH_3I; (b) ethanedithiol/H^+; (c) Raney nickel; (d) PCC; (e) BBr_3; (f) Ac_2O.

Total Synthesis of (±)-Nimbidiol. Our stereoselective synthesis of the diterpene nimbidiol (**62**),[18] isolated from the root bark of *Azadirachta indica*,[19] utilizes tricycle **41** (cf. Chart 4) as the key synthetic intermediate (Scheme 12). Reductive alkylation,[26] followed by removal of the C(3) carbonyl moiety using a thioketal/reduction sequence,[21] completed the functionalization of the A ring (cf. **69**). Benzylic oxidation introduced the C(7) carbonyl moiety and deprotection using boron tribromide furnished nimbidiol on the basis of ^{1}NMR analysis. Our racemic material was acetylated prior to obtaining its ^{13}C NMR, IR, and mass spectra.[22] This data was indistinguishable from that reported for nimbidiol acetate (**71**) derived from natural material.

Formal Synthesis of (±)-Hinokione. The phenolic diterpene ketone hinokione was isolated as a congener of hinokiol from the heartwood of *Chamaecyparis obtusa* ("hinoki") by Yoshiki and Ishiguro.[23] The first synthesis of hinokione methyl ether, and by extension hinokione, was carried out by Chow.[24] Our synthetic route required the preparation of the functionalized phenyl acetone derivative **76** (Scheme 13) from bromide **72**.[25] Vinylmagnesium bromide was coupled with bromide **72** to give olefin **73** in high yield. Olefin **73** was converted into ketone **77** by using four standard transformations: epoxidation, nucleophilic epoxide opening, oxidation, and alkylation. The remaining steps used to prepare the conjugated dienone **79** have been discussed earlier. Cyclialkylation of **79** to tricycle **80** occurred in high yield under mild conditions. Watt and co-workers have shown that compound **80** can be converted to hinokione in two steps.[26]

Scheme 13[a]

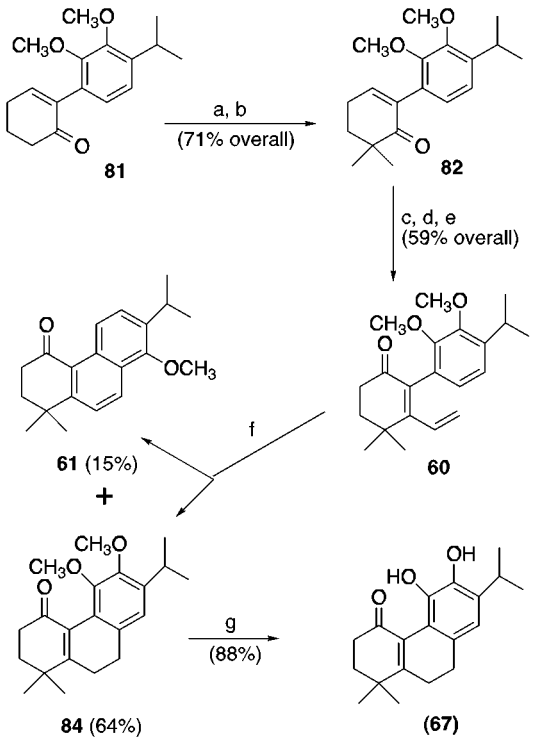


[a] (a) vinylmagnesium bromide/10% CuI; (b) *m*-CPBA; (c) CH_3MgBr/10% CuI; (d) Jones reagent; (e) NaH/CH_3I; (f) methyl acrylate/$KOC(CH_3)_3$; (g) CH_3OH/H^+; (h) vinyllithium; (i) H_3O^+; (j) $BF_3{\cdot}Et_2O$, CH_2Cl_2; reflux, 8 h.

Total Syntheses of Arucadiol, 1,2-Didehydromiltirone, Miltirone, and Sageone. The wild herb Tanshen (*Salvia miltiorrhiza* Bunge) has been used in traditional Chinese medicine because of its sedative and tranquilizing effects[27] and is also being used to treat coronary heart disease and insomnia.[28] A wide range of diterpenoid quinones have been isolated from Tanshen,[29] including miltirone (**65**) which is also known as rosmariquinone, one of the antioxidant components of rosemary.[30] We recognized that many of the cyclization products presented in Charts 3 and 4 possess most of the salient features of the diterpene quinone pigments. Having utilized 4-aryl dienone cyclialkylations to facilitiate the syntheses of nimbidiol and hinokione, we chose to illustrate the utility of 2-aryl dienone cyclialkylation through the total syntheses of miltirone (**65**) and three closely related diterpenoids: arucadiol (**64**),[31] 1,2-didehydromiltirone (**66**),[32] and sageone (**67**).[33]

(18) Majetich, G.; Siesel, D. *Synlett.* **1995**, 559.
(19) Majumder, P. L.; Maiti, D. C.; Kraus, W.; Bokel, M. *Phytochemistry* **1987**, *26*, 3021.
(20) ApSimon, J. W.; Baker, P.; Buccini, J.; Hooper, J. W.; Macauley, S. *Can. J. Chem.* **1972**, *50*, 1944.
(21) (a) Hatch, R. P.; Shringarpure, J.; Weinreb, S. M. *J. Org. Chem.* **1978**, *43*, 4172. (b) Matsumoto, T.; Tachibana, Y.; Uchida, J.; Fukui, K. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 2766.
(22) Harring, S. R.; Livinghouse, T. *Tetrahedron Lett.* **1989**, *30*, 1499.
(23) For the isolation of hinokione, see: Yoshiki, Y.; Ishiguro, T. *J. Pharm. Soc. Jpn.* **1913**, *53*, 1.
(24) Chow, Y.-L. *Acta Chem. Scand.* **1960**, *14*, 1671.
(25) Majetich, G.; Hicks, R.; Zhang, Y.; Tian, X.; Feltman, T. L.; Fang, J.; Duncan, S., Jr. *J. Org. Chem.* **1996**, *61*, 8169.
(26) Snitman, D. L.; Himmelsbach, R. J.; Watt, D. S. *J. Org. Chem.* **1978**, *43*, 4758.
(27) Fang, C.-N.; Chang, P.-L.; Hsu, T.-P. *Acta Chim. Sin.* **1976**, *34*, 197.
(28) *Pharmacology and Applications of Chinese Materia Medica*; Chang, H. M., But, P., Eds.; World Scientific Publishing Co.: Singapore, 1986; Vol. 1, pp 255−268.
(29) Chang, H. M.; Cheng, K. P.; Choang, T. F.; Chow, H. F.; Chui, K. Y.; Hon, P. M.; Tan, F. W. L.; Yang, Y.; Zhong, Z. P. *J. Org. Chem.* **1990**, *55*, 3537.
(30) For the isolation of Miltirone [also known as rosmariquinone], see: (a) Gordon, M. H.; Weng, X. C. *J. Agric. Food Chem.* **1992**, *40*, 1331. (b) Ikeshiro, Y.; Mase, I.; Tomita, Y. *Phytochemistry* **1989**, *28*, 3139.

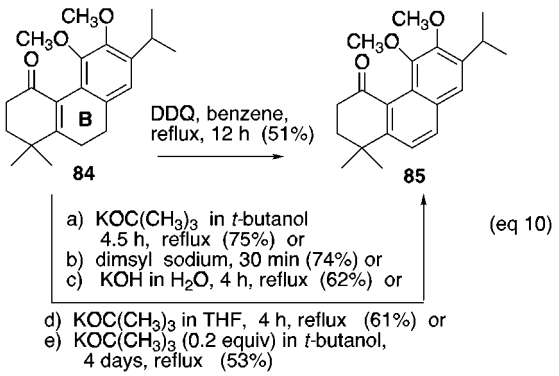
Scheme 14[a]



[a] (a) LDA/CH_3I; (b) LDA/CH_3I; (c) vinyllithium; (d) H_3O^+ to give **83**; (e) PDC; (f) $BF_3{\cdot}Et_2O$, CCl_4, 6 h, reflux; (g) BBr_3.

The organolithium species derived from isopropylveratrole[34] was used to prepare cyclohexenone **81** using Wender's methodology[7] (Scheme 14). The route used in the conversion of **81** to conjugated dienone **60** has been discussed earlier (cf. Scheme 4). Cyclialkylation using excess boron trifluoride etherate in refluxing CCl_4 gave the expected cyclization product **84** in 64% yield along with naphthalene **61** in 15% yield, undoubtedly via the Lewis acid-promoted cyclization of rotomer **iv** (cf. Scheme 11).

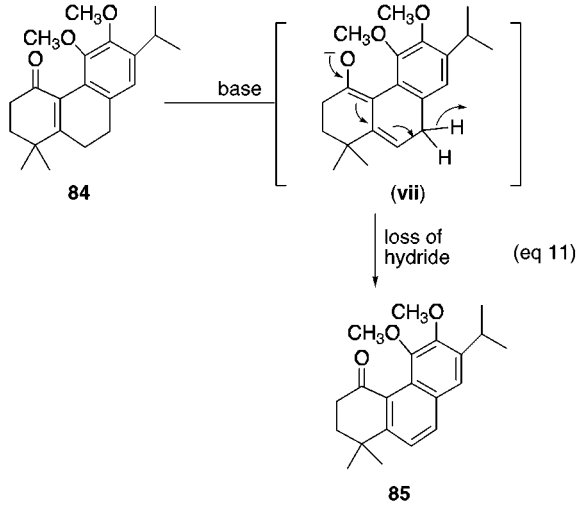
Enone **84** serves as the common intermediate for each of the following syntheses. For example, treating **84** with



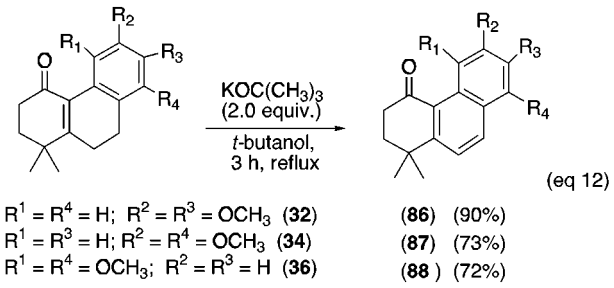
boron tribromide at −78 °C and then allowing the reaction mixture to warm to −10 °C over a 2 h period furnished sageone (**67**), a diterpenoid which possesses significant antiviral activity,[33] in 88% yield.

Arucadiol, miltirone, and 1,2-didehydromiltrone have an aromatic "B" ring. Although DDQ can be used to aromatize the B ring of **84**, this dehydrogenative aromatization could also be achieved by heating this cyclialkylation product with various bases in protic media (eq 10); however, no oxidation was observed at room temperature.

The first step in the probable mechanism is the *in situ* formation of dienolate **vii** (eq 11). Loss of a hydride from

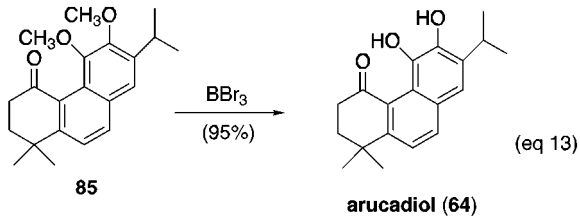


vii generates the more stable aromatic system. Furthermore the hydride regenerates the base, making this process catalytic. The ease of aromatization of these hydrophenanthrenes is undoubtedly the driving force behind this oxidation.[35] Three additional examples of this process are summarized in eq 12.



$R^1 = R^4 = H$; $R^2 = R^3 = OCH_3$ (**32**) (**86**) (90%)
$R^1 = R^3 = H$; $R^2 = R^4 = OCH_3$ (**34**) (**87**) (73%)
$R^1 = R^4 = OCH_3$; $R^2 = R^3 = H$ (**36**) (**88**) (72%)

With ketone **85** in hand, only demethylation of the ethers was required to complete a synthesis of arucadiol (**64**). This transformation was accomplished in 97% yield



using boron tribromide in methylene chloride at −78 °C (eq 13). Our synthetic arcudiol was spectrally identical with both the natural[32] and the synthetic material.[29]

(31) Arucadiol has been isolated from the root of *Salvia argentea* [Michavila, A.; de la Torre, M. C.; Rodgriguez, B. *Phytochemistry* **1986**, *25*, 1935] and Tanshen.[29]

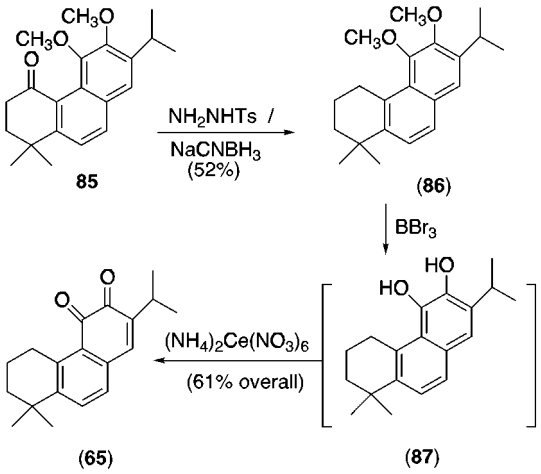
(32) For the isolation of 1,2-didehydromiltirone, see: Luo, H.-W.; Hu, X.-J.; Wang, N.; Ji, J. *Acta Pharm. Sin.* **1988**, *23*, 830. The first synthesis of **66** was achieved by Chui and co-workers.[29]

(33) For the isolation of sageone, see: Tada, M.; Okuno, K.; Chiba, K.; Ohnishi, E.; Yoshi, T. *Phytochemistry* **1994**, *35*, 539.

(34) Isopropylveratrole is no longer commerically available. For an efficient, two-step preparation, see: Majetich, G.; Liu, S. *Synth. Commun.* **1993**, *23*, 2331.

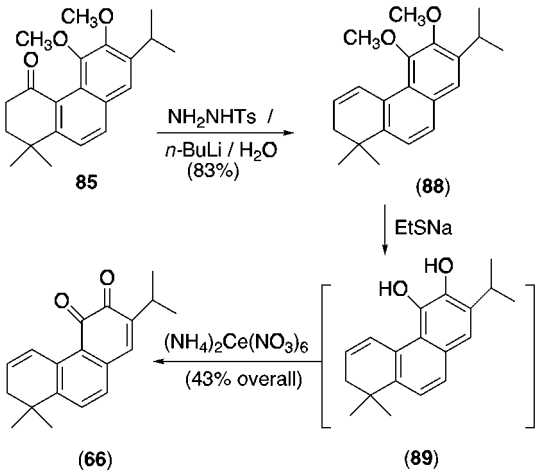
(35) The loss of a hydride to form a more stable aromatic system occurs during the condensation of an aliphatic aldehyde with ammonia to produce pyridine derivatives (a Chichibabin pyridine synthesis). See: (a) Chichibabin, A. E. *J. Prakt. Chem.* **1924**, *107*, 122. (b) Farley, C. P.; Eliel, E. L. *J. Am. Chem. Soc.* **1956**, *78*, 3477.

Scheme 15



Ketone **85** also serves as a precursor for both miltirone (**65**) and 1,2-didehydromiltirone (**66**). The sequence used to complete a synthesis of **65** is shown in Scheme 15 and consisted of first a modified Wolff−Kishner reduction[36] to convert the C(5) carbonyl moiety into a methylene followed by deprotection of the aryl methyl ethers and oxidation to an *o*-quinone using ceric ammonium nitrate. The transformations used to convert ketone **85** into 1,2-didehydromiltirone were straightforward (Scheme 16). The physical and spectroscopic data of our synthetic **65** and **66** are identical with those reported for the natural products.

Scheme 16



Conclusions

This study demonstrates that a cyclialkylation-based strategy can be used to prepare a wide variety of functionalized hydrophenanthrenes. In general, these annulations occur in synthetically useful yields with electron-rich arenes and substrates in which either a conformational or a steric bias leads to cyclialkylation.

Experimental Section

General Procedures. All reactions were run under an atmosphere of nitrogen and monitored by TLC analysis until the starting material was completely consumed. Unless otherwise indicated, all ethereal workups consisted of the following procedure: the reaction was quenched at rt with saturated aqueous ammonium chloride. The organic solvent was removed under reduced pressure on a rotary evaporator, and the residue was taken up in ether, washed with brine, and dried over anhydrous $MgSO_4$. Filtration, followed by concentration at reduced pressure on a rotary evaporator and at 1 Torr to constant weight, afforded a crude residue which was purified by flash chromatography using NM silica gel 60 (230−400 mesh ASTM) and distilled reagent grade solvents (hexanes and ether). Microanalysis was performed by Atlantic Microlab, Inc., Atlanta, GA. All spectra were obtained in $CDCl_3$. Proton NMR spectra were calibrated using trace $CHCl_3$ present (δ 7.27) as an internal reference.

The following abbreviations are used throughout this section: hexanes (H) and diethyl ether (E).

The following procedures were used repeatedly during the course of this study:

(A) 2-Phenylcyclohex-2-enone. To solution of phenyllithium [12 mL of a 2 M solution in cyclohexane, Aldrich, 24.00 mmol] at 0 °C was added epoxide **1** (1.84 g, 10.00 mmol) in 5 mL of THF. The resulting mixture was warmed to rt and stirred at rt for 5 h. After standard ethereal workup, the crude residue was refluxed in a 1:1 mixture of ethanol and 2% HCl for 1 h. Standard ethereal workup, followed by chromatography (elution with H:E, 5:1), gave 600 mg of 2-phenylcyclohex-2-enone (37%) [4556-09-6] (Registry numbers supplied by author) which was homogeneous by TLC analysis [H:E, 1:1, R_f(enone) = 0.38]: ^{1}H NMR (250 MHz) δ 2.10 (pentet, 2 H, J = 6 Hz), 2.47−2.68 (m, 4 H), 7.02 (t, 1 H, J = 4.0 Hz), 7.21−7.41 (m, 5 H).

(B) 2-Phenyl-1-vinylcyclohex-2-en-1-ol. A solution of 216 mg (1.30 mmol) of 2-phenylcyclohex-2-enone in THF (5 mL) at 0 °C was treated dropwise with 4.0 mL (4.00 mmol) of vinylmagnesium bromide (1.0 M solution in THF) over a 5-min period. The reaction mixture was stirred at rt for 1 h. The reaction mixture was quenched with ice and then diluted with ether (20 mL). After standard ethereal workup, the crude bisallylic tertiary alcohol was used directly in the next reaction without purification or characterization.

(C) Preparation of Vinyllithium.[37] To a solution of vinyl bromide (0.94 mL, 10.16 mmol) in anhydrous ether (6 mL) at −78 °C was added 12 mL of *tert*-butyllithium (1.7 M solution in pentane). The resulting mixture was stirred at −78 °C for 2 h and then slowly warmed to 0 °C. Titration of the resulting solution of organolithium reagent indicated a molarity of 0.54 M.

(D) 2-Phenyl-3-vinylcyclohex-2-enone (6). PDC (990 mg, 2.60 mmol) was added to a solution of crude 2-pheny-1-vinylcyclohex-2-en-1-ol [the preparation of which is described in general procedure B] in CH_2Cl_2 (5 mL). After being stirred for a 5-h period, the reaction mixture was diluted with ether (20 mL) and the resulting mixture was filtered through a short pad of silica gel. Removal of the volatiles, followed by chromatography (elution with H:E, 5:1), afforded 160 mg of conjugated dienone **6** in 65% yield as a yellow oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(**6**) = 0.40]: ^{1}H NMR (250 MHz) δ 2.14 (pentet, 2 H, J = 6.4 Hz), 2.59 (t, 2 H, J = 6.5 Hz), 2.67 (t, 2 H, J = 6.0 Hz), 5.33 (d, 1 H, J = 11.0 Hz), 5.67 (d, 1 H, J = 17.5 Hz), 6.46 (dd, 1 H, J = 17.5 Hz, 11.0 Hz), 7.05−7.08 (m, 2 H), 7.31−7.40 (m, 3 H); ^{13}C NMR (62.7 MHz) 198.8 (s), 151.1 (s), 138.5 (s), 136.2 (d), 134.9 (s), 130.4 (d), 127.8 (d), 127.3 (d), 120.4 (t), 38.2 (t), 25.2 (t), 21.7 (t) ppm; IR (film) 1665 cm^{-1}.

(E) 1-[2′,3′-Dimethoxyphenyl]propan-2-ol. To a solution of veratrole (6.90 g, 50.00 mmol) in 25 mL of THF at 0 °C was added 20 mL of *n*-butyllithium (2.5 M solution in hexanes). The resulting mixture was stirred at 0 °C for 3 h. Propene oxide (2.90 g, 50.00 mmol) was added dropwise to the reaction mixture. The resulting mixture was allowed to warm to rt and stirred at rt for 8 h. Standard ethereal workup, followed by chromatography (elution with H:E, 1:1), gave 2.27 g of recovered veratrole (33%) and 5.03 g (51%) of 1-[2′,3′-dimethoxyphenyl]propan-2-ol as a light oil which was homogeneous by TLC analysis [H:E, 2:3, R_f(propanol) = 0.38]: ^{1}H NMR (300 MHz) δ 1.24 (d, 3 H, J = 6.1 Hz), 2.22 (d, 1 H, J = 3.8 Hz), 2.70−2.95 (m, 2 H), 3.85 (s, 3 H), 3.88 (s, 3 H), 3.95−

(36) Hutchins, R. O.; Milewski, C. A.; Maryanoff, B. E. *J. Am. Chem. Soc.* **1973**, *95*, 3662.

(37) Neumann, H.; Seebach, D. *Tetrahedron Lett.* **1976**, 4839.

4.16 (m, 1 H), 6.69 (d, 1 H, J = 7.8 Hz), 6.84 (d, 1 H, J = 7.8 Hz), 7.02 (t, 1 H, J = 8.0 Hz).

(F) 1-[2′,3′-Dimethoxyphenyl]propan-2-one. To a solution of 1-[2′,3′-dimethoxyphenyl]propan-2-ol (4.23 g, 21.58 mmol) in acetone (120 mL) at 0 °C was added 9.0 mL of Jones reagent (2.7 M solution) dropwise. The mixture was stirred at 0 °C for 1 h. Excess oxidant was destroyed by dropwise addition of 2-propanol (3 mL). The volatiles were evaporated, and the crude ketone was isolated via standard ethereal workup. Chromatography (elution with H:E, 4:1) gave 2.45 g (60%) of 1-[2′,3′-dimethoxyphenyl]propan-2-one as a light oil which was homogeneous by TLC analysis [H:E, 3:1, R_f(propanone) = 0.30]: ^{1}H NMR (300 MHz) δ 2.18 (s, 3 H), 3.72 (s, 2 H), 3.80 (s, 3 H), 3.88 (s, 3 H), 6.75 (d, 1 H, J = 7.8 Hz), 6.86 (d, 1 H, J = 7.8 Hz), 7.02 (t, 1 H, J = 7.9 Hz); ^{13}C NMR (75.5 MHz) 206.7 (s), 152.7 (s), 147.1 (s), 128.8 (s), 124.1 (d), 122.7 (d), 111.6 (d), 60.4 (q), 55.7 (q), 45.3 (t), 29.4 (q) ppm; IR (film) 1714, 1474, 1272, 1075 cm^{-1}.

(G) 3-[2′,3′-Dimethoxyphenyl]butan-2-one. To a suspension of NaH (60% suspension in mineral oil, 510 mg, 12.8 mmol) in 15 mL of THF at 0 °C was added 1-[2′,3′-dimethoxyphenyl]propan-2-one (2.37 g, 12.20 mmol) in 10 mL of THF. The resulting mixture was warmed to rt over a period of 30 min. The reaction mixture was cooled to 0 °C, and 2.70 g of iodomethane (19.10 mmol) was added. The resulting mixture was stirred at 0 °C for 1 h and rt for 4 h. Standard ethereal workup, followed by chromatography (elution with H:E, 4:1), gave 2.30 g (91%) of 3-[2′,3′-dimethoxyphenyl]butan-2-one as a light oil which was homogeneous by TLC analysis [H:E, 3:1, R_f(butanone) = 0.35]: ^{1}H NMR (250 MHz) δ 1.35 (d, 3 H, J = 7.3 Hz), 2.05 (s, 3 H), 3.85 (s, 3 H), 3.88 (s, 3 H), 4.12 (q, 1 H, J = 7.2 Hz), 6.69 (d, 1 H, J = 7.8 Hz), 6.84 (d, 1 H, J = 7.8 Hz), 7.04 (t, 1 H, J = 7.7 Hz); ^{13}C (62.7 MHz), 209.2 (s), 152.8 (s), 146.5 (s), 134.8 (s), 124.4 (d), 119.9 (d), 111.1 (d), 60.8 (q), 55.7 (q), 46.8 (q), 28.4 (t), 16.7 (q) ppm; IR (film) 1708, 1583, 1474, 1272 cm^{-1}.

(H) 1-[3′,5′-Dimethoxyphenyl]butan-2-one. To a solution of (3,5-dimethoxyphenyl)acetic acid (2.05 g, 10.40 mmol) in 25 mL of benzene at 0 °C was added oxalyl chloride (2.10 mL, 24.00 mmol). The resulting solution was stirred at rt for 17 h. The benzene was removed *in vacuo*, the crude residue was dissolved in CH_2Cl_2 (25 mL), and cooled to 0 °C, and (MeO)MeNH−HCl (1.22 g, 12.50 mmol) was added. To this mixture was added dropwise pyridine (2.0 mL, 25.00 mmol). The mixture was stirred at rt for 2 h. Standard ethereal workup, followed by chromatography (elution with ether), afforded 2.46 g of *N*-methyl-*N*-methoxy-2-[3′,5′-dimethoxyphenyl]ethanamide (99%) as an oil which was homogeneous by TLC analysis [ether, R_f(amide) = 0.31]: ^{1}H NMR (300 MHz) δ 3.20 (s, 3 H), 3.62 (s, 2 H), 3.77 (s, 6 H), 3.81 (s, 3 H), 6.35 (t, 1 H, J = 2.2 Hz), 6.45 (d, 2 H, J = 2.3 Hz).

The above amide (2.46 g, 10.30 mmol) was dissolved in 20 mL of THF, and 10.30 mL of a 3 M solution of ethylmagnesium bromide in Et_2O (30.90 mmol) was added at 0 °C. The resulting mixture was stirred at 0 °C for 1 h and then stirred for 1 h at rt. Standard ethereal workup, followed by chromatography (elution with H:E, 4:1), gave 670 mg of 1-[3′,5′-dimethoxyphenyl]butan-2-one (31%) which was homogeneous by TLC analysis [H:E, 4:1, R_f(ketone) = 0.23]: ^{1}H NMR (250 MHz) δ 1.01 (t, 3 H, J = 7.3 Hz), 2.47 (q, 2 H, J = 7.3 Hz), 3.59 (s, 2 H), 3.76 (s, 6 H), 6.35 (s, 3 H); ^{13}C NMR (62.7 MHz) 208.8 (s), 160.8 (s), 136.5 (s), 107.3 (d), 98.8 (d), 55.2 (q), 50.0 (t), 34.9 (t), 7.7 (q) ppm; IR (film) 1712, 1596, 1205 cm^{-1}.

(I) 6-[2′,3′-Dimethoxyphenyl]-2,6-dimethylcyclohexane-1,3-dione. A solution of 2-[2′,3′-dimethoxyphenyl]pentan-3-one [cf. the preparation of **38**, 1.25 g, 5.63 mmol] in THF (15 mL) was added to KO-*t*-Bu (694 mg, 6.19 mmol) in 5 mL of THF. After 30 min, methyl acrylate (526 mg, 6.19 mmol) dissolved in 2 mL of THF was added. After 3 days, the reaction mixture was diluted with water (100 mL). The aqueous layer was extracted with ether (3 × 30 mL), and the combined ethereal extracts were dried over anhydrous $MgSO_4$ and concentrated to provide 800 mg (64%) of the unreacted pentanone. Acidifying the aqueous phase to pH = 1, followed by standard ethereal workup, gave 350 mg of 6-[2′,3′-dimethoxyphenyl]-2,6-dimethylcyclohexane-1,3-dione which was used immediately without purification and characterization.

(J) 6-[2′,3′-Dimethoxyphenyl]-2,6-dimethyl-3-methoxycyclohex-2-enone. The crude 6-[2′,3′-dimethoxyphenyl]-2,6-dimethylcyclohexane-1,3-dione was dissolved in 40 mL of methanol, and *p*-TsOH (38 mg, 0.20 mmol) was added. The solution was refluxed for 2 h. Standard ethereal workup, followed by chromatography (elution with H:E, 1:1), gave 350 mg (22% for two steps, 88% based on recovered starting pentanone) of 6-[2′,3′-dimethoxyphenyl]-2,6-dimethyl-3-methoxycyclohex-2-enone as a light yellow solid which was homogeneous by TLC analysis [H:E, 1:1, R_f(enone) = 0.30]: mp 70−73 °C; ^{1}H NMR (300 MHz) δ 1.48 (s, 3 H), 1.69−1.76 (m, 1 H), 1.78 (s, 3 H), 2.49−2.58 (m, 2 H), 2.63−2.73 (m, 1 H), 3.67 (s, 3 H), 3.78 (s, 3 H), 3.84 (s, 3 H), 6.82−6.85 (m, 2 H), 6.99 (t, 1 H, J = 8.0 Hz); ^{13}C NMR (75.5 MHz) 201.5 (s), 168.2 (s), 152.8 (s), 146.6 (s), 139.3 (s), 123.2 (d), 119.4 (d), 113.1 (s), 111.3 (d), 59.7 (q), 55.6 (q), 54.7 (q), 46.9 (s), 33.8 (t), 22.4 (q), 22.2 (t), 8.0 (q) ppm; IR (film) 1767, 1723, 1615 cm^{-1}; MS, m/z 290 (M$^+$). Anal. Calcd for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.07; H, 7.74.

(K) 4-[3′,4′-Dimethoxyphenyl]-4-methyl-3-vinylcyclohex-2-enone (24). A solution of 220 mg (0.80 mmol) of 6-[3′,4′-dimethoxyphenyl]-6-methyl-3-methoxycyclohex-2-enone [cf. the preparation of **24**] in 2 mL of THF which contained cerium chloride (20 mg, 0.080 mmol) at 0 °C was treated dropwise with 3.2 mL (3.20 mmol) of vinylmagnesium bromide (1.0 M solution in THF) over a 5-min period. The reaction mixture was stirred at rt for 4 h. The reaction mixture was quenched with ice and then diluted with ether (70 mL). The organic layer was shaken with 2% aqueous HCl (15 mL) for a 20-min period. Standard ethereal workup, followed by chromatography (elution with H:E, 4:1), gave 196 mg of 4-[3′,4′-dimethoxyphenyl]-4-methyl-3-vinylcyclohex-2-enone (**24**) (96%) which was homogeneous by TLC analysis [H:E, 4:1, R_f(**24**) = 0.47]: ^{1}H NMR (250 MHz) δ 1.62 (s, 3 H), 2.08−2.19 (m, 2 H), 2.34−2.43 (m, 2 H), 3.85 (s, 3 H), 3.87 (s, 3 H), 5.29 (d, 1 H, J = 11.0 Hz), 5.63 (d, 1 H, J = 17.5 Hz), 6.10 (dd, 1 H, J = 17.5 Hz, 11.0 Hz), 6.34 (s, 1 H), 6.75 (s, 1 H), 6.82 (s, 2 H); ^{13}C NMR (62.5 MHz) 199.7 (s), 163.6 (s), 148.9 (s), 147.7 (s), 137.5 (s), 135.0 (d), 124.8 (d), 120.8 (t), 118.8 (d), 110.8 (d), 110.2 (d), 55.9 (q), 55.8 (q), 42.6 (s), 40.1 (t), 34.4 (t), 25.0 (q) ppm. Anal. Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 75.20; H, 7.39.

(L) 2-[2′,3′-Dimethoxy-4-isopropylphenyl]-6-methylcyclohex-2-enone. To a solution of LDA, prepared from diisopropylamine (3.9 mL, 27.88 mmol) in 20 mL of THF and 11 mL (22.50 mmol) of *n*-butyllithium (2.5 M solution in hexanes), at −78 °C was added a solution of 1.90 g (6.93 mmol) of 2-[2′,3′-dimethoxy-4′-isopropylphenyl]cyclohex-2-enone (**81**) in 5 mL of THF over a 5-min period. After an additional 1 h at −78 °C, 3.88 g of iodomethane (27.52 mmol) was added and the reaction mixture was warmed to rt over a 4-h period. Standard ethereal workup, followed by chromatography (elution with H:E, 2:1), gave 1.52 g of 2-[2′,3′-dimethoxy-4-isopropylphenyl]-6-methylcyclohex-2-enone (75%) as a yellow oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(**81**) = 0.51, R_f(alkylated enone) = 0.78]: ^{1}H NMR (250 MHz) δ 1.17−1.27 (m, 9 H), 1.80−1.97 (m, 1 H), 2.11−2.22 (m, 1 H), 2.51−2.69 (m, 3 H), 3.31 (septet, 1 H, J = 7.0 Hz), 3.74 (s, 3 H), 3.83 (s, 3 H), 6.82 (t, 1 H, J = 4.1 Hz), 6.85 (ABq, 2 H, $\Delta\nu_{AB}$ = 40.0 Hz, J_{AB} = 8.0 Hz); ^{13}C NMR (62.7 MHz) 200.6 (s), 149.9 (s), 146.7 (d), 142.7 (s), 138.1 (d), 129.5 (s), 125.2 (d), 120.9 (d), 115.2 (s), 60.4 (q), 60.0 (q), 41.8 (d), 30.8 (t), 26.7 (d), 25.4 (t), 23.5 (q), 15.2 (q) ppm; IR (film) 1680, 1454, 1405, 1267 cm^{-1}; MS, m/z 288 (M$^+$). Anal. Calcd for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39. Found: C, 74.79; H, 8.47.

2-[2′-Methoxyphenyl]-3-vinylcyclohex-2-enone (7). To a solution of 1-bromo-2-methoxybenzene (1.87 g, 10.00 mmol) dissolved in 20 mL of dry THF was added 12 mL of *n*-butyllithium (1.7 M solution in pentane), and the mixture was stirred for 1 h at −78 °C.

The above solution of organolithium reagent was treated with epoxide **1** (920 mg, 5.00 mmol) using procedure A to give 313 mg of 2-[2′-methoxyphenyl]cyclohex-2-enone (30%) which was homogeneous by TLC analysis [H:E, 3:2, R_f(enone) = 0.29]: ^{1}H NMR (250 MHz) δ 2.13 (pentet, 2 H, J = 6.5 Hz), 2.49−2.62 (m, 4 H), 3.76 (s, 3 H), 6.88−6.97 (m, 3 H), 7.04−7.08 (m, 1 H), 7.29 (t, 1 H, J = 7.5 Hz); ^{13}C NMR (62.7 MHz) 197.5(s),

156.9 (s), 147.9 (d), 139.0 (s), 130.5 (d), 129.1 (d), 126.6 (s), 120.4 (d), 110.9 (d), 55.6 (q), 38.6 (t), 26.3 (t), 23.0 (t) ppm; MS, *m/z* 202 (M^+), 131 (base).

The above enone (268 mg, 1.33 mmol) was treated with 3.0 equiv of vinylmagnesium bromide using procedure B to provide 192 mg of a bis-allylic tertiary alcohol (64%) which was homogeneous by TLC analysis [H:E, 3:2, R_f(enone) = 0.29, R_f(alcohol) = 0.46]: ^{1}H NMR (250 MHz) δ 1.62−1.90 (m, 3 H), 2.00−2.40 (m, 3 H), 3.84 (s, 3 H), 4.45 (br s, 1 H), 4.84 (d, 1 H, J = 10.8 Hz), 5.24 (d, 1 H, J = 16.2 Hz), 5.71 (dd, 1 H, J = 16.2 Hz, 10.8 Hz), 5.84 (t, 1 H, J = 4.0 Hz), 6.85 (d, 1 H, J = 8.1 Hz), 6.93 (t, 1 H, J = 7.7 Hz), 7.03 (d, 1 H, J = 7.3 Hz), 7.23 (t, 1 H, J = 7.7 Hz); ^{13}C NMR (62.7 MHz) 155.6 (s), 144.5 (d), 140.2 (s), 132.1 (d), 131.9 (d), 131.5 (s), 128.2 (d), 121.2 (d), 111.3 (t), 110.3 (d), 71.6 (s), 55.5 (q), 36.7 (t), 26.1 (t), 17.8 (t) ppm.

The above tertiary alcohol (146 mg, 0.64 mmol) was oxidized using procedure D and 482 mg of PDC (1.28 mmol) to furnish 51 mg of dienone **7** (35%) which was homogeneous by TLC analysis [H:E, 3:1, R_f(alcohol) = 0.31, R_f(**7**) = 0.24]: ^{1}H NMR (250 MHz) δ 2.05−2.22 (m, 2 H), 2.56−2.70 (m, 4 H), 3.73 (s, 3 H), 5.29 (d, 1 H, J = 12.5 Hz), 5.64 (d, 1 H, J = 17.5 Hz), 6.39 (dd, 1 H, J = 17.5 Hz, 12.5 Hz), 6.90−6.98 (m, 3 H), 7.28−7.34 (m, 1 H); ^{13}C NMR (75.5 MHz) 198.4 (s), 157.4 (s), 151.2 (s), 136.3 (d), 136.1 (s), 131.7 (d), 129.1 (d), 124.5 (s), 120.3 (d), 119.9 (t), 110.9 (d), 55.6 (q), 38.2 (t), 25.1 (t), 21.9 (t) ppm. Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 79.27; H, 7.26.

2-[4′-Methoxyphenyl]-3-vinylcyclohex-2-enone (8). To a solution of 1-bromo-4-methoxybenzene (1.87 g, 10.00 mmol) dissolved in 2.0 mL of dry THF was added 12 mL of *tert*-butyllithium (1.7 M solution in pentane), and the mixture was stirred for 1 h at −78 °C.

The above solution of organolithium reagent was treated with epoxide **1** (920 mg, 5.0 mmol) using procedure A to give 475 mg of 2-[4′-methoxyphenyl]cyclohex-2-enone (47%) which was homogeneous by TLC analysis [H:E, 3:2, R_f(enone) = 0.34]: ^{1}H NMR (250 MHz) δ 2.09 (pentet, 2 H, J = 6.5 Hz), 2.49−2.61 (m, 4 H), 3.80 (s, 3 H), 6.99 (t, 1 H, J = 4.3 Hz), 7.07 (ABq, 2 H, $\Delta\nu_{AB}$ = 93.7 Hz, J_{AB} = 9.7 Hz); ^{13}C NMR (62.9 MHz) 198.6 (s), 159.0 (s), 147.2 (d), 139.6 (s), 129.7 (d), 128.9 (s), 113.3 (d), 55.2 (q), 39.0 (t), 26.5 (t), 22.8 (t) ppm; IR (film) 1672, 1509, 1249 cm^{-1}; MS, *m/z* 202 (M^+). Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.02; H, 6.93.

The above enone (400 mg, 1.98 mmol) was treated with 3.0 equiv of vinylmagnesium bromide using procedure B to provide 325 mg of a bis-allylic tertiary alcohol (71%) which was homogeneous by TLC analysis [H:E, 3:2, R_f(enone) = 0.34, R_f(alcohol) = 0.42]: ^{1}H NMR (250 MHz) δ 1.73−1.89 (m, 4 H), 2.18−2.26 (m, 2 H), 3.79 (s, 3 H), 5.15 (d, 1 H, J = 10.4 Hz), 5.24 (d, 1 H, J = 16.6 Hz), 5.93 (t, 1 H, J = 3.7 Hz), 6.03 (dd, 1 H, J = 16.6 Hz, 10.6 Hz), 7.08 (ABq, 4 H, $\Delta\nu_{AB}$ = 130.0 Hz, J_{AB} = 8.8 Hz); ^{13}C NMR (62.5 MHz) 158.5 (s), 144.2 (d), 140.6 (s), 132.5 (s), 129.5 (d), 128.8 (d), 113.8 (t), 113.2 (d), 73.9 (s), 55.1 (q), 38.0 (t), 25.7 (t), 18.7 (t) ppm; MS, *m/z* 230 (M^+).

The above tertiary alcohol (285 mg, 1.24 mmol) was oxidized using procedure D and 932 mg of PDC (2.48 mmol) to furnish 127 mg of dienone **8** (45%) which was homogeneous by TLC analysis [H:E, 3:2, R_f(alcohol) = 0.42, R_f(**8**) = 0.29]: ^{1}H NMR (250 MHz) δ 2.13 (pentet, 2 H, J = 6.5 Hz), 2.59 (t, 2 H, J = 6.5 Hz), 2.67 (t, 2 H, J = 6.0 Hz), 3.82 (s, 3 H), 5.33 (d, 1 H, J = 11.2 Hz), 5.65 (d, 1 H, J = 17.7 Hz), 6.51 (dd, 1 H, J = 17.7 Hz, 11.2 Hz), 6.96 (ABq, 4 H, $\Delta\nu_{AB}$ = 30.0 Hz, J_{AB} = 8.8 Hz); ^{13}C NMR (62.5 MHz) 199.0 (s), 158.9 (s), 151.2 (s), 137.9 (s), 136.5 (d), 131.7 (d), 127.2 (s), 120.1 (t), 113.4 (d), 55.2 (q), 38.4 (t), 25.4 (t), 21.8 (t) ppm; MS, *m/z* 228 (M^+). Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 79.27; H, 7.26.

4-Methyl-4-phenyl-3-vinylcyclohex-2-enone (9). Phenylacetone (690 mg, 5.15 mmol) was treated with NaH (60% suspension in mineral oil, 216 mg, 5.47 mmol) and iodomethane (726 mg, 5.15 mmol) using procedure G to give 720 mg of 3-phenylbutan-2-one (95%) which was homogeneous by TLC analysis [H:E, 1:1, R_f(butanone) = 0.80]: ^{1}H NMR (250 MHz) δ 1.39 (d, 3 H, J = 7.0 Hz), 2.04 (s, 3 H), 3.70−3.80 (m, 1 H), 7.20−7.34 (m, 5 H).

The above butanone (326 mg, 2.20 mmol) was treated with KO-*t*-Bu (246 mg, 2.20 mmol) and methyl acrylate (190 mg, 2.20 mmol) using procedure I to give 195 mg of recovered butanone (60%) and 115 mg of the crude cyclohexane-1,3-dione which was converted, using procedure J, to 120 mg of 3-methoxy-6-methyl-6-phenylcyclohex-2-enone (25% for two steps, 85% based on recovered starting butanone) as a light oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(enone) = 0.35]: ^{1}H NMR (300 MHz) δ 1.42 (s, 3 H), 2.00−2.15 (m, 1 H), 2.25−2.32 (m, 2 H), 2.39−2.49 (m, 1 H), 3.65 (s, 3 H), 5.46 (s, 1 H), 7.15−7.33 (m, 5 H); ^{13}C NMR (75.5 MHz) 202.1 (s), 177.2 (s), 142.6 (s), 128.3 (d), 126.4 (d), 126.0 (d), 102.0 (d), 55.6 (q), 48.8 (s), 34.5 (t), 26.4 (t), 26.4 (q) ppm; IR (film) 1657, 1197 cm^{-1}; MS, *m/z* 216 (M^+). Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.55; H, 7.50.

The above enone (40 mg, 0.17 mmol) was treated with 8.0 equiv of vinylmagnesium bromide and cerium chloride (5 mg, 0.02 mmol) using procedure K to give 36 mg of dienone **9** (98%) which was homogeneous by TLC analysis [H:E, 1:1, R_f(**9**) = 0.60]: ^{1}H NMR (300 MHz) δ 1.67 (s, 3 H), 2.10−2.50 (m, 4 H), 5.30 (d, 1 H, J = 11.0 Hz), 5.63 (d, 1 H, J = 18.0 Hz), 6.12 (dd, 1 H, J = 18.0 Hz, 11.0 Hz), 6.48 (s, 1 H), 7.20−7.40 (m, 5 H); ^{13}C NMR (75.5 MHz) 199.7 (s), 163.4 (s), 144.9 (s), 135.0 (d), 128.5 (d), 126.7 (d) (the preceding signals overlap), 125.2 (d), 120.9 (t), 42.9 (s), 40.2 (t), 34.3 (t), 25.1 (q) ppm; IR (film) 1668 cm^{-1}; MS, *m/z* 212 (M^+).

4-[2′-Methoxyphenyl]-4-methyl-3-vinylcyclohex-2-enone (10). (2′-Methoxyphenyl)acetone (3.28 g, 20.00 mmol) was treated with NaH (60% suspended in mineral oil, 840 mg, 21.00 mmol) and iodomethane (2.96 g, 21.00 mmol) using procedure G to give 3.22 g of 3-(2′-methoxyphenyl)butan-2-one (92%) which was homogeneous by TLC analysis [H:E, 1:1, R_f(butanone) = 0.75]: ^{1}H NMR (300 MHz) δ 1.35 (d, 3 H, J = 7.0 Hz), 2.02 (s, 3 H), 3.84 (s, 3 H), 4.04 (q, 1 H, J = 7.0 Hz), 6.88−6.96 (m, 2 H), 7.12 (d, 1 H, J = 8.3 Hz), 7.21−7.28 (m, 1 H).

The above butanone (780 mg, 4.40 mmol) was treated with KO-*t*-Bu (492 mg, 4.40 mmol) and methyl acrylate (380 mg, 4.40 mmol) using procedure I to give 220 mg of unreacted butanone (28%) and 333 mg of the crude cyclohexane-1,3-dione which was converted, using procedure J, to 345 mg of 3-methoxy-6-(2′-methoxyphenyl)-6-methylcyclohex-2-enone (32% for two steps, 60% based on recovered butanone) which was homogeneous by TLC analysis [H:E, 1:1, R_f(enone) = 0.28]: mp 58−59 °C; ^{1}H NMR (300 MHz) δ 1.52 (s, 3 H), 1.59−1.70 (m, 1 H), 2.25−2.37 (m, 1 H), 2.50−2.79 (m, 2 H), 3.72 (s, 3 H), 3.79 (s, 3 H), 5.43 (s, 1 H), 6.87−7.01 (m, 2 H), 7.20−7.30 (m, 2 H); ^{13}C NMR (75.5 MHz) 202.8 (s), 175.3 (s), 156.6 (s), 133.8 (s), 128.0 (d), 127.3 (d), 120.7 (d), 119.9 (d), 100.8 (d), 55.4 (q), 55.3 (q), 47.3 (s), 33.2 (t), 26.3 (t), 21.1 (q) ppm; IR (film) 1656 cm^{-1}; MS, *m/z* 246 (M^+), 148 (32), 73 (base). Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.13; H, 7.37. Found: C, 72.88; H, 7.46.

The above enone (60 mg, 0.24 mmol) was treated with 8.0 equiv of vinylmagnesium bromide and cerium chloride (10 mg, 0.04 mmol) using procedure K to give 52 mg of conjugated dienone **10** (88%) which was homogeneous by TLC analysis [H:E, 1:1, R_f(**10**) = 0.70]: ^{1}H NMR (300 MHz) δ 1.66 (s, 3 H), 1.72−1.83 (m, 1 H), 2.38−2.48 (m, 1 H), 2.54−2.68 (m, 1 H), 2.75−2.87 (m, 1 H), 3.76 (s, 3 H), 5.14 (d, 1 H, J = 11.0 Hz), 5.53 (d, 1 H, J = 18.0 Hz), 6.00 (dd, 1 H, J = 18.0 Hz, 11.0 Hz), 6.20 (s, 1 H), 6.86 (d, 1 H, J = 8.0 Hz), 6.95 (t, 1 H, J = 7.6 Hz), 7.20−7.34 (m, 2 H); ^{13}C NMR (75.5 MHz) 199.9 (s), 167.1 (s), 157.2 (s), 135.3 (d), 133.9 (s), 128.4 (d), 127.2 (d), 122.3 (d), 120.5 (d), 119.6 (t), 111.4 (d), 54.7 (q), 41.5 (s), 35.4 (t), 34.7 (t), 24.0 (q) ppm; IR (film) 1661, 1244 cm^{-1}; MS, *m/z* 242 (M^+).

4-[4′-Methoxyphenyl]-4-methyl-3-vinylcyclohex-2-enone (11). (4′-Methoxyphenyl)acetone (1.20 g, 7.30 mmol) was treated with NaH (60% suspension in mineral oil, 307 mg, 7.70 mmol) and iodomethane (2.06 g, 14.60 mmol) using procedure G to give 1.18 g of 3-(4′-methoxyphenyl)butan-2-one (90%) which was homogeneous by TLC analysis [H:E, 1:1, R_f(butanone) = 0.65]: ^{1}H NMR (300 MHz) δ 1.36 (d, 3 H, J = 7.0 Hz), 2.05 (s, 3 H), 3.69 (q, 1 H, J = 7.0 Hz), 3.80 (s, 3 H), 7.00 (ABq, 4 H, $\Delta\nu_{AB}$ = 81.0 Hz, J_{AB} = 9.0 Hz).

The above butanone (400 mg, 2.25 mmol) was treated with KO-*t*-Bu (252 mg, 2.25 mmol) and methyl acrylate (193 mg, 2.25 mmol) using procedure I to give 160 mg of unreacted

butanone (40%) and 132 mg of the crude cyclohexane-1,3-dione which was converted, using procedure J, to 145 mg of 3-methoxy-6-(4′-methoxyphenyl)-6-methylcyclohex-2-enone (27% for two steps, 67% based on recovered butanone) as a light solid which was homogeneous by TLC analysis [H:E, 1:1, R_f(enone) = 0.35]: mp 105−107 °C; ^{1}H NMR (250 MHz) δ 1.38 (s, 3 H), 2.00−2.11 (m, 1 H), 2.26−2.33 (m, 2 H), 2.34−2.75 (m, 1 H), 3.64 (s, 3 H), 3.78 (s, 3 H), 5.56 (s, 1 H), 7.01 (ABq, 4 H, $\Delta\nu_{AB}$ = 85.0 Hz, J_{AB} = 8.8 Hz); ^{13}C NMR (62.5 MHz) 202.2 (s), 177.2 (s), 158.1 (s), 134.6 (s), 127.1 (d), 113.8 (d), 102.0 (d), 55.7 (q), 55.2 (q), 48.3 (s), 34.7 (t), 26.7 (t), 26.5 (q) ppm; MS, *m*/*z* 246 (M^+), 148 (base). Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.22; H, 7.43.

The above enone (63 mg, 0.26 mmol) was treated with 9.0 equiv of vinylmagnesium bromide and cerium chloride (10 mg, 0.04 mmol) using procedure K to give 58 mg of dienone **11** (93%) which was homogeneous by TLC analysis [H:E, 1:1, R_f(**11**) = 0.65]: ^{1}H NMR (250 MHz) δ 1.60 (s, 3 H), 2.05−2.15 (m, 2 H), 2.28−2.40 (m, 2 H), 3.77 (s, 3 H), 5.28 (d, 1 H, *J* = 12.0 Hz), 5.61 (d, 1 H, *J* = 18.0 Hz), 6.10 (dd, 1 H, *J* = 18.0 Hz, 12.0 Hz), 6.32 (s, 1 H), 7.02 (ABq, 4 H, $\Delta\nu_{AB}$ = 81.2 Hz, J_{AB} = 10.0 Hz); ^{13}C NMR (62.5 MHz) 199.6 (s), 163.6 (s), 158.1 (s), 136.8 (s), 135.0 (d), 127.8 (d), 124.9 (d), 120.7 (t), 113.8 (d), 55.1 (q), 42.1 (s), 40.1 (t), 34.4 (t), 25.2 (q) ppm; IR (film) 1659, 1245 cm^{-1}; MS, *m*/*z* 242 (M^+), 184 (base).

2-[3′-Methoxyphenyl]-3-vinylcyclohex-2-enone (12). To a solution of 1-bromo-3-methoxybenzene (1.59 g, 8.50 mmol) dissolved in 10 mL of dry THF was added 11.3 mL of *tert*-butyllithium (1.5 M solution in pentane), and the mixture was stirred for 1 h at −78 °C.

The above solution of organolithium reagent was treated with epoxide **1** (940 mg, 5.10 mmol) using procedure A to give 320 mg of 2-[3′-methoxyphenyl]cyclohex-2-enone (31%) which was homogeneous by TLC analysis [H:E, 1:1, R_f(enone) = 0.47]: ^{1}H NMR (250 MHz) δ 2.08 (pentet, 2 H, *J* = 6.9 Hz), 2.48−2.61 (m, 4 H), 3.79 (s, 3 H), 6.82−6.90 (m, 3 H), 7.03 (t, 1 H, *J* = 4.3 Hz), 7.25 (t, 1 H, *J* = 1.5 Hz); ^{13}C NMR (62.7 MHz) 197.8 (s), 159.1 (s), 148.2 (d), 140.1 (s), 137.9 (s), 128.9 (d), 121.0 (d), 114.1 (d), 113.1 (d), 55.1 (q), 39.0 (t), 26.5 (t), 22.8 (t) ppm; IR (film) 1673, 1574, 1234 cm^{-1}.

The above enone (300 mg, 1.49 mmol) was treated with 3.0 equiv of vinylmagnesium bromide using procedure B to provide 321 mg of a bis-allylic tertiary alcohol (94%) which was homogeneous by TLC analysis [H:E, 1:1, R_f(enone) = 0.47, R_f(alcohol) = 0.60]: ^{1}H NMR (250 MHz) δ 1.71−1.87 (m, 4 H), 2.08 (br s, 1 H), 2.20−2.27 (m, 2 H), 3.78 (s, 3 H), 5.15 (d, 1 H, *J* = 10.4 Hz), 5.26 (d, 1 H, *J* = 17.4 Hz), 5.98−6.02 (m, 2 H), 6.75−6.81 (m, 1 H), 6.98−7.00 (m, 2 H), 7.19 (t, 1 H, *J* = 8.0 Hz); ^{13}C NMR (62.5 MHz) 159.0 (s), 144.3 (d), 141.5 (s), 141.0 (s), 129.6 (d), 128.8 (d), 120.7 (t), 113.9 (d), 113.8 (d), 112.2 (d), 73.6 (s), 55.0 (q), 73.6 (s), 37.9 (t), 25.7 (t), 18.6 (t) ppm.

The above tertiary alcohol (300 mg, 1.30 mmol) was oxidized using procedure D and 1.22 mg of PDC (2.00 mmol) to furnish 202 mg of dienone **12** (68%) which was homogeneous by TLC analysis [H:E, 1:1, R_f(alcohol) = 0.60, R_f(**12**) = 0.46]: ^{1}H NMR (250 MHz) δ 2.13 (pentet, 2 H, *J* = 6.5 Hz), 2.58 (t, 2 H, *J* = 6.5 Hz), 2.65 (t, 2 H, *J* = 6.0 Hz), 3.78 (s, 3 H), 5.33 (d, 1 H, *J* = 11.0 Hz), 5.66 (d, 1 H, *J* = 17.6 Hz), 6.47 (dd, 1 H, *J* = 17.6 Hz, 11.0 Hz), 6.60−6.66 (m, 2 H), 6.84−6.87 (m, 1 H), 7.19 (t, 1 H, *J* = 7.9 Hz); ^{13}C NMR (62.5 MHz) 198.7 (s), 159.0 (s), 151.2 (s), 136.4 (s), 136.1 (d), 128.8 (d), 123.3 (s), 122.8 (d), 120.5 (t), 115.8 (d), 113.0 (d), 55.1 (q), 38.2 (t), 25.1 (t), 21.7 (t) ppm. Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.91; H, 7.06. Found: C, 79.15; H, 7.12.

4-[3′-Methoxyphenyl]-4-methyl-3-vinylcyclohex-2-enone (14). (3′-Methoxyphenyl)acetone (1.00 g, 6.10 mmol) was treated with NaH (60% suspension in mineral oil, 256 mg, 6.40 mmol) and iodomethane (1.29 g, 9.15 mmol) using procedure G to give 1.02 g of 3-(3′-methoxyphenyl)butan-2-one (92%) which was homogeneous by TLC analysis [H:E, 1:1, R_f(butanone) = 0.80]: ^{1}H (250 MHz) δ 1.37 (d, 3 H, *J* = 6.6 Hz), 2.05 (s, 3 H), 3.71 (q, 1 H, *J* = 6.6 Hz), 3.79 (s, 3 H), 6.73−6.83 (m, 3 H), 7.25 (t, 1 H, *J* = 7.8 Hz); ^{13}C NMR (62.5 MHz) 208.7 (s), 159.9 (s), 142.1 (s), 129.9 (d), 120.2 (d), 113.5 (d), 112.4 (d), 55.1 (q), 53.7 (d), 28.3 (q), 17.0 (q) ppm; IR (film) 1711, 1262 cm^{-1}; MS, *m*/*z* 178 (M^+).

The above butanone (1.00 g, 5.62 mmol) was treated with KO-*t*-Bu (660 mg, 5.90 mmol) and methyl acrylate (505 mg, 5.90 mmol) using procedure I to give 245 mg (23%) of unreacted butanone and 489 mg of the crude cyclohexane-1,3-dione which was converted, using procedure J, to 501 mg of 3-methoxy-6-(3′-methoxyphenyl)-6-methylcyclohex-2-enone (36% for two steps, 59% based on recovered butanone) which was homogeneous by TLC analysis [H:E, 1:1, R_f(enone) = 0.35]: ^{1}H NMR (300 MHz) δ 1.41 (s, 3 H), 2.02−2.11 (m, 1 H), 2.22−2.46 (m, 3 H), 3.65 (s, 3 H), 3.78 (s, 3 H), 5.44 (s, 1 H), 6.75−6.86 (m, 3 H), 7.23 (t, 1 H, *J* = 8.0 Hz); ^{13}C NMR (75.5 MHz) 201.9 (s), 177.3 (s), 159.6 (s), 144.3 (s), 129.3 (d), 118.5 (d), 112.7 (d), 111.3 (d), 102.0 (d), 55.6 (q), 55.1 (q), 48.9 (s), 34.5 (t), 26.5 (t), 26.5 (q) ppm; IR (film) 1650, 1249 cm^{-1}; MS, *m*/*z* 246 (M^+).

The above enone (210 mg, 0.91 mmol) was treated with 10.0 equiv of vinylmagnesium bromide and cerium chloride (20 mg, 0.08 mmol) using procedure K to give 195 mg of conjugated dienone **14** (89%) which was homogeneous by TLC analysis [H:E, 1:1, R_f(**14**) = 0.63]: ^{1}H NMR (300 MHz) δ 1.62 (s, 3 H), 2.03−2.48 (m, 4 H), 3.78 (s, 3 H), 5.28 (d, 1 H, *J* = 10.8 Hz), 5.62 (d, 1 H, *J* = 17.5 Hz), 6.10 (dd, 1 H, *J* = 17.6 Hz, 10.8 Hz), 6.34 (s, 1 H), 6.77−6.87 (m, 3 H), 7.25 (t, 1 H, *J* = 7.9 Hz); ^{13}C NMR (75.5 MHz) 199.6 (s), 163.3 (s), 159.7 (s), 146.7 (s), 135.0 (d), 129.5 (d), 125.0 (d), 120.9 (t), 119.2 (d), 113.4 (d), 111.2 (d), 55.2 (q), 42.9 (s), 40.1 (t), 34.4 (t), 25.1 (q) ppm; IR (film) 1663, 1258 cm^{-1}; MS, *m*/*z* 242 (M^+). Anal. Calcd for $C_{16}H_{18}O_2$: C, 79.30; H, 7.49. Found: C, 79.58; H, 7.58.

Cyclization of 12 To Give 13. A solution of 35 mg of **12** (0.15 mmol) and 100 μL of BF_3·Et_2O (0.82 mmol) in 5 mL of CCl_4 was refluxed for 24 h. The reaction mixture was diluted with 30 mL of ether and quenched with 10 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 3:1), gave 21 mg of **13** (60%) as an oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(**12**) = 0.46, R_f(**13**) = 0.53]: ^{1}H NMR (300 MHz) δ 2.05 (pentet, 2 H, *J* = 6.5 Hz), 2.41 (t, 2 H, *J* = 7.6 Hz), 2.56−2.62 (m, 4 H), 2.68 (t, 2 H, *J* = 7.6 Hz), 3.82 (s, 3 H), 6.73 (dd, 1 H, *J* = 8.2 Hz, 2.7 Hz), 7.04 (d, 1 H, *J* = 8.2 Hz), 7.74 (d, 1 H, *J* = 2.7 Hz); ^{13}C NMR (75.5 MHz) 197.3 (s), 160.9 (s), 158.0 (s), 131.7 (s), 130.3 (s), 127.8 (s), 127.6 (d), 112.8 (d), 112.5 (d), 55.4 (q), 39.4 (t), 32.3 (t), 31.2 (t), 26.5 (t), 21.8 (t) ppm.

Cyclization of 14 To Give 15. A solution of 70 mg of **14** (0.29 mmol) and 210 μL of BF_3·Et_2O (1.74 mmol) in 3 mL of CH_2Cl_2 was refluxed for 2 h. The reaction mixture was diluted with 30 mL of ether and neutralized with 10 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 1:1), gave 39 mg of **15** (56%) as a light solid which was homogeneous by TLC analysis [H:E, 1:1, R_f(**14**) = 0.69, R_f(**15**) = 0.50]: mp 60−61 °C; ^{1}H NMR (250 MHz) δ 1.57 (s, 3 H), 1.99−2.15 (m, 1 H), 2.30−2.40 (m, 1 H), 2.45−3.03 (m, 6 H), 3.81 (s, 3 H), 5.91 (s, 1 H), 6.73 (dd, 1 H, *J* = 8.4 Hz, 2.6 Hz), 6.82 (d, 1 H, *J* = 2.6 Hz), 7.03 (d, 1 H, *J* = 8.4 Hz); ^{13}C NMR (62.5 MHz) 198.8 (s), 169.8 (s), 158.4 (s), 144.8 (s), 129.4 (d), 126.8 (s), 124.1 (d), 111.8 (d), 111.5 (d), 55.2 (q), 39.3 (s), 36.8 (t), 34.6 (t), 31.3 (t), 30.2 (t), 27.5 (q) ppm; IR (film) 1666, 1280 cm^{-1}; MS, *m*/*z* 242 (M^+). Anal. Calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.35; H, 7.54.

2-[2′,3′-Dimethoxyphenyl]-3-vinylcyclohex-2-enone (16). To a solution of veratrole (2.83 g, 19.50 mmol) dissolved in 30 mL of dry THF was added 8.2 mL of *n*-butyllithium (2.5 M solution in hexanes), and the mixture was stirred for 2 h at 0 °C. The resulting organolithium reagent (a yellow slurry) was used directly without purification or characterization.

The above solution of organolithium reagent was treated with epoxide **1** (1.79 mg, 9.75 mmol) using procedure A to give 900 mg of 2-[3′,4′-dimethoxyphenyl]cyclohex-2-enone (40%) which was homogeneous by TLC analysis [H:E, 1:1, R_f(enone) = 0.30]: mp 85−86 °C; ^{1}H NMR (300 MHz) δ 2.15 (t, 2 H, *J* = 6.7 Hz), 2.45−2.67 (m, 4 H), 3.73 (s, 3 H), 3.88 (s, 3 H), 6.67 (d, 1 H, *J* = 7.0 Hz), 6.81−6.95 (m, 2 H), 7.05 (t, 1 H, *J* = 8.0 Hz); ^{13}C NMR (75.5 MHz) 197.9 (s), 152.5 (s), 148.4 (d), 146.7 (s), 138.5 (s), 131.6 (s), 123.6 (d), 122.5 (d), 112.4 (d), 60.4 (q), 55.8 (q), 38.7 (t), 26.3 (t), 23.1 (t) ppm; IR (film) 1671, 1261 cm^{-1}; MS, *m*/*z* 228 (M^+). Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.04; H, 7.00.

The above enone (122 mg, 0.53 mmol) was treated with 3.0 equiv of vinylmagnesium bromide using procedure B to provide

130 mg of the crude bis-allylic tertiary alcohol which was used without purification or characterization.

The crude tertiary alcohol was oxidized using procedure D and 402 mg of PDC (1.07 mmol) to furnish 70 mg of conjugated dienone **16** (51% for two steps) which was homogeneous by TLC analysis [H:E, 1:1, R_f(enone) = 0.30, R_f(**16**) = 0.20]: ^{1}H NMR (250 MHz) δ 2.10−2.25 (m, 2 H), 2.59−2.72 (m, 4 H), 3.66 (s, 3 H), 3.87 (s, 3 H), 5.33 (d, 1 H, J = 11.0 Hz), 5.65 (d, 1 H, J = 18.0 Hz), 6.48 (dd, 1 H, J = 18.0 Hz, 11.0 Hz), 6.57 (d, 1 H, J = 6.0 Hz), 6.93 (d, 1 H, J = 8.0 Hz), 7.06 (t, 1 H, J = 8.0 Hz); ^{13}C NMR (62.5 MHz) 198.8 (s), 152.6 (s), 151.5 (s), 146.9 (s), 136.2 (d), 135.5 (s), 129.8 (s), 123.6 (d), 123.5 (d), 120.4 (t), 112.2 (d), 60.4 (q), 55.7 (q), 38.2 (t), 25.1 (t) ppm; IR (film) 1664, 1576, 1471, 1260 cm^{-1}; MS, m/z 254 (M$^+$), 225 (base).

2-[3′,4′-Dimethoxyphenyl]-3-vinylcyclohex-2-enone (17). To a solution of 1-bromo-3,4-dimethoxybenzene (434 mg, 20.00 mmol) dissolved in 10 mL of dry THF was added 30.8 mL of *tert*-butyllithium (1.3 M solution in pentane), and the mixture was stirred for 1.5 h at −78 °C. The resulting solution of the organolithium reagent was used directly without purification or characterization.

The solution of organolithium reagent was treated with epoxide **1** (1.00 g, 5.43 mmol) using procedure A to give 520 mg of 2-[3′,4′-dimethoxyphenyl]cyclohex-2-enone (43%) which was homogeneous by TLC analysis [H:E, 1:1, R_f(enone) = 0.34]: ^{1}H NMR (250 MHz) δ 2.07 (t, 2 H, J = 6.8 Hz), 2.47−2.59 (m, 4 H), 3.85 (s, 3 H), 3.86 (s, 3 H), 6.83−6.86 (m, 3 H), 6.97 (t, 1 H, J = 4.2 Hz); ^{13}C NMR (62.5 MHz) 196.2 (s), 148.4 (s), 148.2 (s), 147.3 (d), 139.7 (s), 129.2 (s), 120.8 (d), 111.9 (d), 110.6 (d), 55.7 (q), 55.7 (q) (the preceding signals overlap), 39.0 (t), 26.6 (t), 22.9 (t) ppm; IR (film) 1677, 1513, 1249 cm^{-1}; MS, m/z 232 (M$^+$). Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.15; H, 6.74.

The enone (375 mg, 1.62 mmol) was treated with 3.0 equiv of vinyllithium using procedure B to provide 395 mg of the crude bis-allylic tertiary alcohol which was used directly in the next step without purification or characterization.

The crude tertiary alcohol was oxidized using procedure D and 1.00 g of PDC (2.66 mmol) to furnish 210 mg of dienone **17** (50% for two steps) which was homogeneous by TLC analysis [H:E, 2:1, R_f(**17**) = 0.37]: ^{1}H NMR (300 MHz) δ 2.11 (pentet, 2 H, J = 6.3 Hz), 2.56 (t, 2 H, J = 7.0 Hz), 2.64 (t, 2 H, J = 6.0 Hz), 3.82 (s, 3 H), 3.85 (s, 3 H), 5.32 (d, 1 H, J = 11.0 Hz), 5.64 (d, 1 H, J = 17.5 Hz), 6.49 (dd, 1 H, J = 17.5 Hz, 11.0 Hz), 6.58−6.66 (m, 2 H), 6.85 (d, 1 H, J = 7.9 Hz); ^{13}C NMR (75.5 MHz) 199.0 (s), 151.2 (s), 148.2 (s), 138.1 (s), 136.3 (d), 127.5 (s), 124.0 (s), 122.9 (d), 120.3 (t), 113.6 (d), 110.6 (d), 55.7 (q), 55.7 (q) (the preceding signals overlap), 38.3 (t), 25.3 (t), 21.7 (t) ppm.

2-[3′,5′-Dimethoxyphenyl]-3-vinylcyclohex-2-enone (19).[12] To a stirred slurry of NaH (60% dispersion in mineral oil, 353 mg, 8.81 mmol) in 80 mL of THF at 0 °C was added (3,5-dimethoxyphenyl)acetonitrile (**45**) (1.20 g, 6.78 mmol) in 20 mL of THF. The reaction mixture was stirred for 30 min at rt, and then 1.60 g of dimethyl glutarate (10.00 mmol) was added. The resulting mixture was refluxed for 5 h. The sodium salt was diluted with water and then acidified with 10% aqueous HCl. Standard ethereal workup provided 1.02 g of methyl 6-cyano-5-oxo-6-[3′,5′-dimethoxyphenyl]hexanoate (53%) as an oil which was homogeneous by TLC analysis [ether, R_f(nitrile) = 0.89, R_f(ketoester) = 0.62]: ^{1}H NMR (250 MHz) δ 1.83−1.92 (m, 2 H), 2.26 (t, 2 H, J = 7.1 Hz), 2.62−2.69 (m, 2 H), 3.61 (s, 3 H), 3.79 (s, 6 H), 4.62 (s, 1 H), 6.45 (t, 1 H, J = 2.0 Hz), 6.48 (d, 2 H, J = 2.0 Hz); ^{13}C NMR (62.7 MHz) 198.0 (s), 173.0 (s), 161.5 (s), 131.4 (s), 115.9 (s), 105.9 (d), 100.9 (d), 55.4 (q), 51.6 (q), 51.0 (d), 38.2 (t), 32.3 (t), 18.5 (t) ppm; IR (film) 2207, 1734, 1598, 1201 cm^{-1}; MS, m/z 304 (M$^+$), 129 (68), 101 (75), 59 (base).

A mixture of the above ketonitrile (1.13 g, 3.61 mmol), concentrated HCl (17 mL), and water (13 mL) was refluxed for 17 h under an atmosphere of nitrogen. The resulting solution was taken up in ethyl acetate (200 mL) and washed with water (2 × 30 mL) and then with a 5% aqueous $KHCO_3$ solution until the aqueous phase was slightly acidic. The organic phase was dried over anhydrous $MgSO_4$, filtered, and then concentrated *in vacuo* to provided a crude oil which consisted of several phenolic components. This oil was dissolved in methanol (25 mL), and *p*-TsOH (30 mg) was added. The mixture was refluxed for 12 h. The resulting solution was taken up in ether (100 mL) and washed with water and brine. The organic phase was dried over anhydrous $MgSO_4$, filtered, and then concentrated *in vacuo* to provide a crude residue which consisted of several esters. The residue was dissolved in acetone (30 mL), treated with anhydrous $KHCO_3$ (1.38 g, 10.00 mmol) and dimethyl sulfate (1.26 g, 10.00 mmol), and refluxed for 12 h. Standard ethereal workup, followed by chromatography (elution with H:E, 1:4), gave 434 mg of methyl 6-[3′5′-dimethoxyphenyl]-5-oxohexanoate (43% from the ketonitrile) which was homogeneous by TLC analysis [H:E, 1:3, R_f(ester) = 0.89]: ^{1}H NMR (300 MHz) δ 1.86 (pentet, 2 H, J = 7.1 Hz), 2.29 (t, 2 H, J = 7.2 Hz), 2.52 (t, 2 H, J = 7.3 Hz), 3.60 (s, 2 H), 3.64 (s, 3 H), 3.78 (s, 6 H), 6.30−6.38 (m, 3 H); ^{13}C NMR (75.5 MHz) 207.3 (s), 173.5 (s), 160.9 (s), 139.2 (s), 107.3 (d), 99.0 (d), 55.3 (q), 51.5 (q), 50.5 (t), 40.4 (t), 32.8 (t), 18.7 (t) ppm; IR (film) 1730, 1600, 1155 cm^{-1}; MS, m/z 280 (M$^+$).

The above ketoester (8 mg, 0.29 mmol) was added to a suspension of degreased NaH (60% suspension in mineral oil, 23 mg, 0.58 mmol) in 25 mL of THF. The resulting mixture was refluxed for 5 h and cooled to 0 °C. The mixture was dissolved in water (40 mL), extracted with ether (3 × 40 mL), and acidified (pH 1). Ethereal extraction and workup provided a crude 1,3-dione which was used directly in the next step without purification or characterization.

The crude dione was dissolved in 5 mL of methanol, and *p*-TsOH (10 mg, 0.10 mmol) was added. The resulting mixture was refluxed for 3 h. Standard ethereal workup, followed by chromatography (elution with H:E, 1:3), gave 35 mg of 2-[3′,5′-dimethoxyphenyl]-3-methoxycyclohex-2-enone (46% for two steps) as a light oil which was homogeneous by TLC analysis [ether; R_f(enone) = 0.28]: ^{1}H NMR (250 MHz) δ 2.10 (pentet, 2 H, J = 6.6 Hz), 2.49 (t, 2 H, J = 6.3 Hz), 2.70 (t, 2 H, J = 6.2 Hz), 3.72 (s, 3 H), 3.77 (s, 6 H), 6.31 (d, 2 H, J = 2.2 Hz), 6.38 (t, 1 H, J = 2.3 Hz); ^{13}C NMR (62.7 MHz) 197.1 (s), 172.5 (s), 160.9 (s), 133.6 (s), 117.9 (s), 108.3 (d), 99.4 (d), 56.1 (q), 55.2 (q), 36.8 (t), 25.9 (t), 20.6 (t) ppm; IR (film) 1665 cm^{-1}; MS, m/z 262 (M$^+$).

The above enone (32 mg, 0.12 mmol) was treated with 10.0 equiv of vinyllithium using procedure K to provide 20 mg of conjugated dienone **19** (64%) which was homogeneous by TLC analysis [ether, R_f(**19**) = 0.95]: ^{1}H NMR (300 MHz) δ 2.13 (t, 2 H, J = 6.5 Hz), 2.58 (t, 2 H, J = 6.3 Hz), 2.65 (t, 2 H, J = 6.1 Hz), 3.77 (s, 6 H), 5.34 (d, 1 H, J = 10.8 Hz), 5.66 (d, 1 H, J = 17.6 Hz), 6.21 (d, 2 H, J = 2.4 Hz), 6.43 (t, 1 H, J = 2.4 Hz), 6.49 (dd, 1 H, J = 17.7 Hz, 10.8 Hz); ^{13}C NMR (75.5 MHz) 198.6 (s), 160.3 (s), 151.2 (s), 138.5 (s), 137.1 (s), 136.2 (d), 120.5 (t), 108.4 (d), 99.8 (d), 55.2 (q), 38.3 (t), 25.1 (t), 21.8 (t) ppm; IR (film) 1663, 1248 cm^{-1}; MS, m/z 258 (M$^+$). Anal. Calcd for $C_{16}H_{18}O_3$: C, 74.38; H, 7.03. Found: C, 74.12; H, 6.95.

2-[2′,5′-Dimethoxyphenyl]-3-vinylcyclohex-2-enone (21). To 4.00 g of 1,4-dimethoxybenzene (29.00 mmol) dissolved in 30 mL of THF at 0 °C were added 15 mL of *n*-butyllithium (32.10 mmol, 2.14 M solution in hexanes) and 2 mL of TMEDA. The mixture was stirred for 6 h at rt. The resulting organolithium reagent (a yellow slurry) was used directly without purification or characterization.

The organolithium reagent was treated with epoxide **1** (2.20 g, 11.96 mmol) using procedure A to give 1.03 g of 2-(2′,5′-methoxyphenyl)cyclohex-2-enone (37%) which was homogeneous by TLC analysis [H:E, 1:1, R_f(enone) = 0.36]: ^{1}H NMR (300 MHz) δ 2.11 (pentet, 2 H, J = 6.0 Hz), 2.47−2.53 (m, 2 H), 2.59 (t, 2 H, J = 6.0 Hz), 3.70 (s, 3 H), 3.74 (s, 3 H), 6.64 (s, 1 H), 6.81 (s, 2 H), 6.89 (t, 1 H, J = 4.2 Hz); ^{13}C NMR (75.5 MHz) 197.4 (s), 153.4 (s), 151.2 (s), 148.1 (d), 138.8 (s), 127.6 (s), 116.5 (d), 113.6 (d), 112.1 (d), 56.3 (q), 55.6 (q), 38.6 (t), 26.3 (t), 23.0 (t) ppm; IR (film) 1668, 1497, 1222 cm^{-1}; MS, m/z 232 (M$^+$). Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.70%; H. 6.84.

The above enone (220 mg, 0.96 mmol) was treated with 4.5 equiv of vinyllithium using procedure B to provide 230 mg of the crude bis-allylic tertiary alcohol which was used directly in the next step without purification or characterization.

The crude tertiary alcohol was oxidized using procedure D and 840 mg of PDC (2.23 mmol) to furnish 125 mg of conjugated dienone **21** (50% for two steps) which was homogeneous by TLC analysis [H:E, 1:1, R_f(**21**) = 0.29]: ^{1}H NMR (300 MHz) δ 2.06−2.24 (m, 2 H), 2.49 (t, 2 H, J = 6.0 Hz), 2.67 (t, 2 H, J = 6.0 Hz), 3.69 (s, 3 H), 3.78 (s, 3 H), 5.33 (d, 1 H, J = 11.0 Hz), 5.65 (d, 1 H, J = 17.5 Hz), 6.41 (dd, 1 H, J = 17.5 Hz, 11.0 Hz), 6.53 (s, 1 H), 6.83 (s, 2 H); ^{13}C NMR (75.5 MHz) 198.4 (s), 151.6 (s), 153.2 (s), 151.3 (s), 136.2 (d), 135.7 (s), 125.5 (s), 120.2 (t), 117.4 (d), 113.7 (d), 112.3 (d), 56.5 (q), 55.6 (q), 38.2 (t), 25.1 (t), 21.9 (t) ppm.

4-[2′,3′-Dimethoxyphenyl]-4-methyl-3-vinylcyclohex-2-enone (22). The procedures used for the preparation of 2-(2′,3′-dimethoxyphenyl)butan-2-one from veratrole were presented earlier as general procedures E, F, and G.

This ketone (2.22 g, 10.70 mmol) was treated with KO-*t*-Bu (1.26 g, 11.20 mmol) and methyl acrylate (920 mg, 10.70 mmol) using procedure I to give 1.08 g (49%) of unreacted butanone and 1.25 g of the crude cyclohexane-1,3-dione which was converted, using procedure J, to 1.43 g of 6-(2′,3′-dimethoxyphenyl)-3-methoxy-6-methylcyclohex-2-enone (47% for two steps, 96% based recovered butanone) which was homogeneous by TLC analysis [H:E, 1:3, R_f(enone) = 0.29]: mp 114−115 °C; ^{1}H NMR (250 MHz) δ 1.52 (s, 3 H), 1.63−1.76 (m, 1 H), 2.27−2.38 (m, 1 H), 2.49−2.74 (m, 2 H), 3.71 (s, 3 H), 3.72 (s, 3 H), 3.84 (s, 3 H), 5.44 (s, 1 H), 6.83−6.94 (m, 2 H), 7.00 (t, 1 H, J = 8.0 Hz); ^{13}C NMR (62.5 MHz) 202.7 (s), 175.5 (s), 152.7 (s), 146.2 (s), 139.2 (s), 123.2 (d), 119.1 (d), 111.7 (d), 100.5 (d), 59.3 (q), 55.6 (q), 55.4 (q), 47.3 (s), 34.2 (t), 26.3 (t), 21.7 (q) ppm; IR (film) 1708, 1583, 1474, 1272, 1054 cm^{-1}; MS, m/z 276 (M$^+$), 178 (76), 163 (base). Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.47; H, 7.42.

The above enone (250 mg, 0.91 mmol) was treated with 7.0 equiv of vinylmagnesium bromide and cerium chloride (20 mg, 0.08 mmol) using procedure K to give 200 mg of dienone **22** (81%) which was homogeneous by TLC analysis [H:E, 1:2, R_f(**22**) = 0.78]: ^{1}H NMR (250 MHz) δ 1.67 (s, 3 H), 1.78−1.90 (m, 1 H), 2.33−2.81 (m, 3 H), 3.75 (s, 3 H), 3.85 (s, 3 H), 5.23 (d, 1 H, J = 11.0 Hz), 5.56 (d, 1 H, J = 18.0 Hz), 6.07 (dd, 1 H, J = 18.0 Hz, 11.0 Hz), 6.23 (s, 1 H), 6.85−6.94 (m, 2 H), 7.01 (t, 1 H, J = 8.0 Hz); ^{13}C NMR (62.5 MHz) 199.7 (s), 165.7 (s), 152.9 (s), 147.3 (s), 139.1 (s), 135.5 (d), 123.0 (d), 122.7 (d), 120.6 (t), 119.2 (d), 111.8 (d), 59.9 (q), 55.6 (q), 41.9 (s), 36.6 (t), 34.6 (t), 24.5 (q) ppm; IR (film) 1662, 1267, 1230 cm^{-1}; MS, m/z 272 (M$^+$).

4-[3′,4′-Dimethoxyphenyl]-4-methyl-3-vinylcyclohex-2-enone (24). 1-(3′,4′-Dimethoxyphenyl)propan-2-one (1.00 g, 5.15 mmol) was treated with NaH (60% suspension in mineral oil, 206 mg, 5.15 mmol) and iodomethane (1.45 g, 10.30 mmol) using procedure G to give 967 mg of 3-(3′,4′-dimethoxyphenyl)butan-2-one (92%) which was homogeneous by TLC analysis [H:E, 2:1, R_f(butanone) = 0.24]: ^{1}H NMR (250 MHz) δ 1.37 (d, 3 H, J = 7.1 Hz), 2.05 (s, 3 H), 3.68 (q, 1 H, J = 7.1 Hz), 3.85 (s, 6 H), 6.68 (d, 1 H, J = 1.5 Hz), 6.78−6.87 (m, 2 H).

The above butanone (416 mg, 2.00 mmol) was treated with KO-*t*-Bu (225 mg, 2.00 mmol) and methyl acrylate (189 mg, 2.20 mmol) using procedure I to give 190 mg (46%) of unreacted butanone and 202 mg of the crude cyclohexane-1,3-dione which was converted, using procedure J, to 220 mg of 6-(3′,4′-dimethoxyphenyl)-3-methoxy-6-methylcyclohex-2-enone (40% for two steps, 86% based on recovered butanone) which was homogeneous by TLC analysis [ether, R_f(enone) = 0.53]: ^{1}H NMR (250 MHz) δ 1.41 (s, 3 H), 1.99−2.12 (m, 1 H), 2.25−2.47 (m, 3 H), 3.63 (s, 3 H), 3.83 (s, 6 H), 5.42 (s, 1 H), 6.80 (s, 3 H); ^{13}C NMR (62.5 MHz) 201.1 (s), 177.2 (s), 148.8 (s), 147.0 (s), 135.0 (s), 118.1 (d), 110.8 (d), 109.8 (d), 101.9 (d), 55.8 (q), 55.6 (q), 48.4 (s), 34.5 (t), 26.8 (q), 26.5 (t) ppm.

The conversion of the above enone to conjugated dienone **24** is described as procedure K.

4-[3′,5′-Dimethoxyphenyl]-4-methyl-3-vinylcyclohex-2-enone (26). (3,5-Dimethoxyphenyl)acetic acid (500 mg, 2.55 mmol) was treated with oxalyl chloride (0.67 mL, 7.65 mmol) in 10 mL of benzene using procedure H to give 500 mg of the acid chloride in 93% yield which was used without further purification: ^{1}H NMR (250 MHz) δ 3.80 (s, 6 H), 4.08 (s, 2 H), 6.49−6.57 (m, 3 H).

To 17 mL of a solution of methyl cuprate (0.26 M solution) in ether at −78 °C was added dropwise the above acid chloride in 3 mL of ether. The mixture was stirred at −78 °C for 1 h before 1 mL of ethanol was added, and the resulting mixture was warmed to rt. Standard ethereal workup, followed by chromatography (elution with H:E, 1:1), gave 291 mg of 1-(3′,5′-dimethoxyphenyl)propan-2-one (64%) which was homogeneous by TLC analysis (H:E, 1:1, R_f(propanone) = 0.40): ^{1}H NMR (250 MHz) δ 2.16 (s, 3 H), 3.62 (s, 2 H), 3.78 (s, 6 H), 6.33−6.40 (m, 3 H).

The above propanone (404 mg, 2.08 mmol) was treated with NaH (60% suspension in mineral oil, 88 mg, 2.20 mmol) and iodomethane (323 mg, 2.29 mmol) using procedure G to give 421 mg of 3-(3′,5′-dimethoxyphenyl)butan-2-one (97%) which was homogeneous by TLC analysis (H:E, 3:1, R_f(butanone) = 0.50): ^{1}H NMR (250 MHz) δ 1.36 (d, 3 H, J = 7.0 Hz), 2.06 (s, 3 H), 3.66 (q, 1 H, J = 7.0 Hz), 3.78 (s, 6 H), 6.36 (s, 3 H).

The above butanone (421 mg, 2.02 mmol) was treated with KO-*t*-Bu (227 mg, 2.02 mmol) and methyl acrylate (174 mg, 2.02 mmol) using procedure I to give 1.83 mg of recovered butanone (43%) and 151 mg of the crude cyclohexane-1,3-dione which was converted, using procedure J, to 165 mg of 6-(3′,5′-dimethoxyphenyl)-3-methoxy-6-methylcyclohex-2-enone (30% for two steps, 83% based recovered butanone) which was homogeneous by TLC analysis [ether, R_f(enone) = 0.85]: ^{1}H NMR (250 MHz) δ 1.23 (s, 3 H), 1.97−2.12 (m, 1 H), 2.19−2.48 (m, 3 H), 3.65 (s, 3 H), 3.76 (s, 6 H), 5.43 (s, 1 H), 6.34 (t, 1 H, J = 2.0 Hz), 6.40 (d, 2 H, J = 2.0 Hz); ^{13}C NMR (62.5 MHz) 201.7 (s), 177.3 (s), 160.6 (s), 145.6 (s), 104.7 (d), 102.0 (d), 98.0 (d), 55.6 (q), 55.2 (q), 49.0 (s), 34.4 (t), 26.5 (t), 26.5 (q) ppm; IR (film) 1667 cm^{-1}; MS, m/z 276 (M$^+$), 178 (base).

The above enone (165 mg, 0.60 mmol) was treated with 5.0 equiv of vinylmagnesium bromide and cerium chloride (10 mg, 0.04 mmol) using procedure K to give 151 mg of dienone **26** (63%) which was homogeneous by TLC analysis [H:E, 1:1, R_f(**26**) = 0.60]: ^{1}H NMR (250 MHz) δ 1.60 (s, 3 H), 2.08−2.43 (m, 4 H), 3.78 (s, 6 H), 5.30 (d, 1 H, J = 11.0 Hz), 5.63 (d, 1 H, J = 17.0 Hz), 6.12 (dd, 1 H, J = 17.0 Hz, 11.0 Hz), 6.27−6.39 (m, 2 H), 6.42 (d, 2 H, J = 2.0 Hz); ^{13}C NMR (62.5 MHz) 199.8 (s), 163.3 (s), 160.8 (s), 147.7 (s), 135.0 (d), 125.0 (d), 120.9 (t), 105.5 (d), 97.8 (d), 55.3 (q), 43.1 (s), 39.9 (t), 34.4 (t), 25.1 (q) ppm; IR (film) 1666, 1597, 1202 cm^{-1}; MS, m/z 272 (M$^+$). Anal. Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 75.12; H, 7.40.

4-[2′,5′-Dimethoxyphenyl]-4-methyl-3-vinylcyclohex-2-enone (28). To a solution of 1,4-dimethoxybenzene (6.00 g, 43.40 mmol) dissolved in 30 mL of diethyl ether at 0 °C were added 19 mL of *n*-butyllithium (2.4 M solution in hexanes) and 6.9 mL of TMEDA. The mixture was stirred at rt for 6 h to generate the corresponding organolithium intermediate. The resulting suspension was treated with propene oxide (2.80 g, 48.70 mmol) using procedure E to give 5.04 g of 1-[2′,5′-dimethoxyphenyl]propan-2-ol (58%) as a light oil which was homogeneous by TLC analysis [H:E, 2:1, R_f(propanol) = 0.05]: ^{1}H NMR (250 MHz) δ 1.22 (d, 3 H, J = 6.4 Hz), 1.97 (br s, 1 H), 2.64−2.86 (m, 2 H), 3.76 (s, 3 H), 3.79 (s, 3 H), 3.97−4.02 (m, 1 H), 6.71−6.82 (m, 3 H); ^{13}C NMR (62.5 MHz) 153.5 (s), 151.8 (s), 128.2 (s), 117.6 (d), 111.8 (d), 111.4 (d), 68.1 (d), 55.9 (q), 55.7 (q), 40.6 (t), 23.0 (q) ppm; IR (film) 3447, 1496, 1223 cm^{-1}.

The above alcohol (2.95 g, 15 mmol) was treated with Jones reagent using procedure F to give 1.84 g of 1-[2′,5′-dimethoxyphenyl]propan-2-one (63%) as a clear oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(propanone) = 0.24]: ^{1}H NMR (250 MHz) δ 2.14 (s, 3 H), 3.64 (s, 2 H), 3.76 (s, 3 H), 3.77 (s, 3 H), 6.71 (d, 1 H, J = 2.3 Hz), 6.77−6.80 (m, 2 H); ^{13}C NMR (62.5 MHz) 206.9 (s), 153.4 (s), 151.5 (s), 124.5 (s), 117.2 (d), 112.6 (d), 111.3 (d), 55.8 (q), 55.6 (q), 45.6 (t), 29.2 (q) ppm; IR (film) 1713, 1502, 1225, 1046 cm^{-1}.

The above propanone (1.63 g, 8.39 mmol) was treated with NaH (60% suspension in mineral oil, 350 mg, 8.75 mmol) and iodomethane (3.60 g, 25.90 mmol) using procedure G to give 1.47 g of 3-(2′,5′-dimethoxyphenyl)butan-2-one (84%) which was homogeneous by TLC analysis [H:E, 3:1, R_f(butanone) = 0.32]: ^{1}H NMR (300 MHz) δ 1.33 (d, 3 H, J = 7.0 Hz), 2.03 (s, 3 H), 3.76 (s, 3 H), 3.79 (s, 3 H), 4.03 (q, 1 H, J = 7.0 Hz), 6.69 (d, 1 H, J = 2.7 Hz), 6.76−6.83 (m, 2 H); ^{13}C NMR (75.5 MHz)

209.5 (s), 153.8 (s), 150.9 (s), 130.6 (s), 114.6 (d), 112.2 (d), 111.6 (d), 55.9 (q), 55.7 (q), 46.9 (d), 28.2 (q), 15.8 (q) ppm; IR (film) 1708, 1498, 1216 cm^{-1}.

The above butanone (1.40 g, 6.72 mmol) was treated with KO-*t*-Bu (790 mg, 7.06 mmol) and methyl acrylate (581 mg, 6.75 mmol) using procedure I to give 789 mg of unreacted butanone (56%) and 626 mg of the crude cyclohexane-1,3-dione which was converted, using procedure J, to 650 mg of 6-(2′,5′-dimethoxyphenyl)-3-methoxy-6-methylcyclohex-2-enone (35% for two steps, 91% based on recovered butanone) as a light solid which was homogeneous by TLC analysis [H:E, 1:4, R_f(enone) = 0.25]: mp 85−86 °C; ^{1}H NMR (250 MHz) δ 1.51 (s, 3 H), 1.61−1.72 (m, 1 H), 2.27−2.39 (m, 1 H), 2.51−2.79 (m, 2 H), 3.69 (s, 3 H), 3.73 (s, 3 H), 3.77 (s, 3 H), 5.43 (s, 1 H), 6.72−6.91 (m, 3 H); ^{13}C NMR (62.5 MHz) 204.0 (s), 175.4 (s), 153.6 (s), 150.9 (s), 135.4 (d), 114.8 (d), 112.9 (d), 111.2 (d), 100.7 (d), 55.9 (q), 55.5 (q), 55.4 (q), 47.2 (s), 33.2 (t), 26.3 (t), 21.0 (q) ppm; IR (film) 1664 cm^{-1}; MS, *m*/*z* 276 (M^+), 178 (base), 163 (41).

The above enone (104 mg, 0.38 mmol) was treated with 7.0 equiv of vinylmagnesium bromide and cerium chloride (10 mg, 0.04 mmol) using procedure K to give 65 mg of dienone **28** (63%) which was homogeneous by TLC analysis [H:E, 1:2, R_f(**28**) = 0.75]: ^{1}H NMR (300 MHz) δ 1.49 (s, 3 H), 1.75 (dt, 1 H, *J* = 17.0 Hz, 4.5 Hz), 2.41 (dt, 1 H, *J* = 17.0 Hz, 4.5 Hz), 2.58 (td, 1 H, *J* = 13.0 Hz, 5.0 Hz), 2.78 (td, 1 H, *J* = 13.0 Hz, 5.0 Hz), 3.65 (s, 3 H), 3.77 (s, 3 H), 5.14 (d, 1 H, *J* = 11.0 Hz), 5.52 (d, 1 H, *J* = 18.0 Hz), 6.01 (dd, 1 H, *J* = 18.0 Hz, 11.0 Hz), 6.16 (s, 1 H), 6.77 (s, 2 H), 6.91 (s, 1 H); ^{13}C NMR (75.5 MHz) 199.8 (s), 166.7 (s), 153.4 (s), 151.5 (s), 135.3 (s), 135.2 (d), 122.4 (d), 119.8 (t), 115.0 (d), 112.0 (d), 111.0 (d), 55.6 (q), 55.2 (q), 41.6 (s), 35.4 (t), 34.6 (t), 23.9 (q) ppm; IR (film) 1659, 1228 cm^{-1}; MS, *m*/*z* 272 (M^+). Anal. Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 75.05; H, 7.47.

Attempted Cyclization of 16. A solution of 24 mg of **16** (0.094 mmol) and 115 μL of $BF_3{\cdot}Et_2O$ (0.94 mmol) in 4 mL of CCl_4 was refluxed for 12 h; however, no reaction was observed.

Cyclization of 17 To Give 18. A solution of 45 mg of **17** (0.20 mmol) and 300 μL of $BF_3{\cdot}Et_2O$ (2.42 mmol) in 4 mL of CCl_4 was refluxed for 18 h. The reaction mixture was diluted with 30 mL of ether and neutralized with 10 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 2:1), gave 25 mg of **18** (55% yield) as an oil which was homogeneous by TLC analysis [H:E, 1:2, R_f(**17**) = 0.53, R_f(**18**) = 0.58]: ^{1}H NMR (300 MHz) δ 2.04 (pentet, 2 H, *J* = 6.7 Hz), 2.41 (t, 2 H, *J* = 7.9 Hz), 2.55−2.60 (m, 4 H), 2.68 (t, 2 H, *J* = 7.4 Hz), 3.88 (s, 3 H), 3.91 (s, 3 H), 6.67 (s, 1 H), 7.81 (s, 1 H); ^{13}C NMR (75.5 MHz) 197.6 (s), 158.6 (s), 147.4 (s), 147.1 (s), 146.7 (s), 128.1 (s), 123.5 (s), 110.9 (d), 110.4 (d), 55.8 (q), 55.8 (q) (the preceding signals overlap), 39.4 (t), 32.1 (t), 30.9 (t), 26.9 (t), 21.8 (t) ppm.

Cyclization of 19 To Give 20. A solution of 20 mg of **19** (0.078 mmol) and 95 μL of $BF_3{\cdot}Et_2O$ (0.78 mmol) in 2.0 mL of CCl_4 was refluxed for 3 h. The reaction mixture was diluted with 20 mL of ether and quenched with 5 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 2:1), gave 12 mg of **20** (60% yield) as an oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(**19**) = 0.45, R_f(**20**) = 0.58]: ^{1}H NMR (250 MHz) δ 2.04 (t, 2 H, *J* = 6.4 Hz), 2.36 (t, 2 H, *J* = 7.9 Hz), 2.57 (t, 4 H, *J* = 6.4 Hz), 2.67 (t, 2 H, *J* = 8.0 Hz), 3.80 (s, 3 H), 3.83 (s, 3 H), 6.41 (d, 1H, *J* = 2.3 Hz). 7.34 (d, 1H, *J* = 2.3 Hz); ^{13}C NMR (62.7 MHz) 198.0 (s), 171.1 (s), 158.2 (s), 156.4 (s), 133.5 (s), 131.6 (s), 117.8 (s), 103.6 (d), 97.9 (d), 55.4 (q), 55.4 (q) (the preceding signals overlap), 39.4 (t), 32.5 (t), 30.2 (t), 23.6 (t), 21.7 (t) ppm; IR (film) 1664 cm^{-1}; MS, *m*/*z* 258 (M^+). Anal. Calcd for $C_{16}H_{18}O_3$: C, 74.38; H, 7.03. Found: C, 74.18; H, 7.23.

Attempted Cyclization of 21. A solution of 24 mg of **21** (0.094 mmol) and 114 μL of $BF_3{\cdot}Et_2O$ (0.94 mmol) in 4 mL of CCl_4 was refluxed for 12 h; however, no reaction was observed.

Cyclization of 22 To Give 23. A mixture of 13 mg of **22** (0.048 mmol) and 25 mg of $AlCl_3$ (0.19 mmol) in 3.0 mL of CH_2Cl_2 was stirred at rt for 8 h. The reaction mixture was diluted with 30 mL of ether and quenched with 10 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 2:1), gave 7.2 mg of **23** (57% yield) as an oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(**22**) = 0.37, R_f(**23**) = 0.43]: ^{1}H NMR (250 MHz) δ 1.38 (s, 3 H), 1.97−2.35 (m, 4 H), 2.82 (s, 2 H), 3.88 (s, 3 H), 5.16 (d, 1 H, *J* = 12.0 Hz), 5.31 (d, 1 H, *J* = 18.0 Hz), 5.89 (dd, 1 H, *J* = 18.0 Hz, 12.0 Hz), 6.70−6.82 (m, 2 H), 6.90 (d, 1 H, *J* = 8.0 Hz); ^{13}C NMR (62.5 MHz) 209.0 (s), 144.5 (s), 136.8 (s), 136.7 (d), 134.7 (s), 122.1 (d), 115.0 (d), 114.5 (t), 111.7 (d), 92.5 (s), 55.9 (q), 47.7 (s), 45.2 (t), 35.7 (t), 35.7 (t) (the preceding signals overlap), 24.0 (q) ppm; IR (film) 1721, 1289 cm^{-1}; MS, *m*/*z* 258 (M^+). Anal. Calcd for $C_{16}H_{18}O_3$: C, 74.38; H, 7.03. Found: C, 74.56; H, 7.20.

Cyclization of 24 To Give 25. A solution of 300 mg of **24** (1.10 mmol) and 1.3 mL of $BF_3{\cdot}Et_2O$ (10.64 mmol) in 6 mL of CH_2Cl_2 was refluxed for 24 h. The reaction mixture was diluted with 40 mL of ether and neutralized with 10 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 2:1), gave 155 mg of **25** (52% yield) as an light solid which was homogeneous by TLC analysis [H:E, 2:3, R_f(**24**) = 0.43, R_f(**25**) = 0.27]: mp 97−99 °C; ^{1}H NMR (300 MHz) δ 1.58 (s, 3 H), 2.00−2.13 (m, 1 H), 2.31−2.41 (m, 1 H), 2.47−2.60 (m, 2 H), 2.62-2.81 (m, 2 H), 2.82−3.01 (m, 2 H), 3.87 (s, 3 H), 3.89 (s, 3 H), 5.91 (s, 1 H), 6.57 (s, 1 H), 6.76 (s, 1 H); ^{13}C NMR (75.5 MHz) 198.9 (s), 169.8 (s), 148.0 (s), 147.3 (s), 135.4 (s), 126.9 (s), 124.1 (d), 110.9 (d), 108.9 (d), 56.0 (q), 55.8 (q), 38.8 (s), 37.0 (t), 34.7 (t), 31.2 (t), 30.6 (t), 27.4 (q) ppm; IR (film) 1662, 1257 cm^{-1}; MS, *m*/*z* 272 (M^+). Anal. Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 74.88; H, 7.48.

Cyclization of 26 To Give 27. A solution of 39 mg of **26** (0.14 mmol) and 180 μL of $BF_3{\cdot}Et_2O$ (1.40 mmol) in 2 mL of CH_2Cl_2 was refluxed for 8 h. The reaction mixture was diluted with 30 mL of ether and neutralized with 10 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 2:1), gave 21 mg of **27** (54% yield) as an oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(**26**) = 0.53, R_f(**27**) = 0.40]: ^{1}H NMR (250 MHz) δ 1.58 (s, 3 H), 1.96−2.12 (m, 1 H), 2.29−2.77 (m, 6 H), 3.10−3.19 (m, 1 H), 3.81 (s, 3 H), 3.82 (s, 3 H), 5.91 (s, 1 H), 6.33 (d, 1 H, *J* = 2.0 Hz), 6.42 (d, 1 H, *J* = 2.0 Hz); ^{13}C NMR (62.5 MHz) 199.0 (s), 170.0 (s), 159.3 (s), 157.4 (s), 145.6 (s), 124.0 (d), 116.4 (s), 102.1 (d), 95.7 (d), 55.4 (q), 55.2 (q), 39.5 (s), 37.0 (t), 34.7 (t), 30.7 (t), 27.3 (q), 24.1 (t) ppm; IR (film) 1669, 1200 cm^{-1}; MS, *m*/*z* 272 (M^+).

Attempted Cyclization of 28. A solution of 15 mg of **28** (0.059 mmol) and 72 μL of $BF_3{\cdot}Et_2O$ (0.59 mmol) in 4 mL of CH_2Cl_2 was refluxed for 12 h; however, no reaction was observed.

2-[2′,3′-Dimethoxyphenyl]-4,4-dimethyl-3-vinylcyclohex-2-enone (29). 2-[2′,3′-Dimethoxyphenyl]cyclohex-2-enone (230 mg, 1.00 mmol), the preparation of which is described in the preparation of substrate **16**, was alkylated with iodomethane using procedure L to provide 240 mg of crude 2-[2′,3′-dimethoxyphenyl]-6-methylcyclohex-2-enone which was used directly in the next step without purification or characterization.

The crude enone was further methylated with iodomethane using procedure L to provide 180 mg of 2-[2′,3′-dimethoxyphenyl]-6,6-dimethylcyclohex-2-enone (69% for two steps) as a light solid which was homogeneous by TLC analysis [H:E, 1:1, R_f(bis-alkylated enone) = 0.77]: mp 84−85 °C; ^{1}H NMR (250 MHz) δ 1.23 (s, 6 H), 1.95 (t, 2 H, *J* = 6.0 Hz), 2.48−2.54 (m, 2 H), 3.70 (s, 3 H), 3.86 (s, 3 H), 6.74 (t, 1 H, *J* = 4.0 Hz), 6.67 (dd, 1 H, *J* = 7.9 Hz, 1.9 Hz), 6.87 (dd, 1 H, *J* = 7.8 Hz, 1.8 Hz), 7.01 (t, 1 H, *J* = 7.6 Hz); ^{13}C NMR (62.7 MHz) 202.7 (s), 152.3 (s), 146.5 (s), 145.4 (d), 136.8 (s), 132.3 (s), 123.4 (d), 122.3 (d), 112.2 (d), 60.1 (q), 55.7 (q), 41.6 (s), 36.3 (t), 24.0 (q), 23.4 (t) ppm; IR (film) 1666, 1259 cm^{-1}; MS, *m*/*z* 260 (MH^+). Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.29; H, 7.69.

The bis-methylated enone (45 mg, 0.17 mmol) was treated with 3.0 equiv of vinylmagnesium bromide using procedure B to provide a crude bis-allylic tertiary alcohol which was used directly in the next step without purification or characterization.

The crude tertiary alcohol was oxidized using procedure D and 102 mg of PCC (0.27 mmol) to furnish 28 mg of conjugated dienone **29** (54% for two steps) which was homogeneous by

TLC analysis [H:E, 1:1, R_f(**29**) = 0.48]: ^{1}H NMR (250 MHz) δ 1.28 (s, 3 H), 1.30 (s, 3 H), 1.98 (t, 2 H, J = 6.7 Hz), 2.50−2.62 (m, 2 H), 3.66 (s, 3 H), 3.83 (s, 3 H), 5.00 (dd, 1 H, J = 17.7 Hz, 1.4 Hz), 5.11 (dd, 1 H, J = 12.1 Hz, 1.5 Hz), 6.19 (dd, 1 H, J = 17.7 Hz, 12.0 Hz), 6.52 (dd, 1 H, J = 7.4 Hz, 1.2 Hz), 6.84 (dd, 1 H, J = 7.3 Hz, 1.2 Hz), 6.98 (t, 1 H, J = 7.9 Hz); ^{13}C NMR (62.7 MHz) 198.1 (s), 163.0 (s), 152.4 (s), 146.4 (s), 133.5 (d), 132.7 (s), 131.3 (s), 123.4 (d), 123.1 (d), 121.0 (t), 111.4 (d), 60.2 (q), 55.5 (q), 37.5 (t), 35.2 (s), 34.5 (t), 27.4 (q), 27.0 (q) ppm; IR (film) 1667, 1459, 1262 cm^{-1}; MS, m/z 286 (M$^+$).

2-[3′,4′-Dimethoxyphenyl]-4,4-dimethyl-3-vinylcyclohex-2-enone (31). 2-[3′,4′-Dimethoxyphenyl]cyclohex-2-enone (500 mg, 2.20 mmol), the preparation of which is described in the preparation of substrate **17**, was alkylated with iodomethane using procedure L to provide 550 mg of 2-[3′,4′-dimethoxyphenyl]-6-methylcyclohex-2-enone as a crude oil which was used directly in the next step without purification or characterization.

The above monoalkylated enone was further alkylated with iodomethane using procedure L to provide 285 mg of 2-[3′,4′-dimethoxyphenyl]-6,6-dimethylcyclohex-2-enone (50% for two steps) which was homogeneous by TLC analysis [H:E, 1:1, R_f(bis-alkylated enone) = 0.48]: ^{1}H NMR (250 MHz) δ 1.19 (s, 6 H), 1.92 (t, 2 H, J = 6.0 Hz), 2.51 (dt, 2 H, J = 6.0 Hz, 4.2 Hz), 3.86 (s, 3 H), 3.87 (s, 3 H), 6.83−6.89 (m, 4 H); ^{13}C NMR (62.7 MHz) 203.0 (s), 148.4 (s), 148.1 (s), 1435.1 (d), 139.9 (s), 128.8 (s), 120.9 (d), 112.1 (d), 110.6 (d), 55.8 (q), 55.8 (q) (the preceding signals overlap), 41.6 (s), 36.0 (t), 24.3 (q), 23.6 (t) ppm; IR (film) 1673, 1514, 1245 cm^{-1}; MS, m/z 260 (M$^+$). Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.72; H, 7.75.

The above bis-methylated enone (170 mg, 0.65 mmol) was treated with 3.0 equiv of vinyllithium using procedure B to provide 200 mg of a crude bis-allylic tertiary alcohol which was used directly in the next step without purification: ^{1}H NMR (250 MHz) δ 0.95 (s, 3 H), 1.05 (s, 3 H), 1.45−1.75 (m, 2 H), 2.18−2.30 (m, 2 H), 3.84 (s, 3 H), 3.86 (s, 3 H), 5.22−5.27 (m, 2 H), 5.83 (t, 1 H, J = 3.8 Hz), 6.80 (dd, 1 H, J = 17.5 Hz, 11.8 Hz), 6.75−6.93 (m, 3 H).

The above crude alcohol was oxidized using procedure D and 500 mg of PDC (1.30 mmol) to furnish 88 mg of dienone **31** (47% for two steps) which was homogeneous by TLC analysis [H:E, 1:1, R_f(**31**) = 0.32]: ^{1}H NMR (250 MHz) δ 1.37 (s, 6 H), 1.97 (t, 2 H, J = 7.0 Hz), 2.63 (t, 2 H, J = 7.0 Hz), 3.84 (s, 3 H), 3.87 (s, 3 H), 5.03 (dd, 1 H, J = 18.0 Hz, 1.4 Hz), 5.18 (dd, 1 H, J = 12.0 Hz, 1.4 Hz), 6.20 (dd, 1 H, J = 18.0 Hz, 12.0 Hz), 6.52−6.57 (m, 2 H), 6.82 (d, 1 H, J = 8.0 Hz); ^{13}C NMR (62.7 MHz) 199.4 (s), 162.1 (s), 148.2 (s), 147.8 (s), 136.3 (s), 133.7 (d), 128.9 (s), 122.7 (d), 121.2 (t), 113.6 (d), 110.4 (d), 55.7 (q), 55.6 (q), 37.6 (t), 35.4 (s), 34.5 (t), 27.4 (q) ppm; IR (film) 1668, 1254 cm^{-1}; MS, m/z 286 (M$^+$). Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.48; H, 7.74. Found: C, 75.43; H, 7.70.

2-[3′,5′-Dimethoxyphenyl]-4,4-dimethyl-3-vinylcyclohex-2-enone (33).[12] To a stirred slurry of NaH (60% suspension in mineral oil, 1.04 g, 26.00 mmol) in 80 mL of THF at 0 °C was added (3,5-dimethoxyphenyl)acetonitrile (**45**) (3.54 g, 20.00 mmol) in 20 mL of THF. The mixture was stirred for 30 min at rt, and then dimethyl 2,2-dimethylglutarate (5.64 g, 30.00 mmol) was added. The resulting mixture was refluxed for 22 h. The sodium salt was diluted with water (20 mL) and then acidified with 10% aqueous HCl. Standard ethereal workup provided 5.71 g of methyl 6-cyano-5-oxo-6-[3′,5′-dimethoxyphenyl]-2,2-dimethylhexanoate (**46**) (86%) as an oil which was homogeneous by TLC analysis [ether, R_f(**45**) = 0.89, R_f(**46**) = 0.33]: ^{1}H NMR (300 MHz) δ 1.11 (s, 3 H), 1.12 (s, 3 H), 1.72−1.80 (m, 2 H), 2.50−2.61 (m, 2 H), 3.60 (s, 3 H), 3.79 (s, 6 H), 4.63 (s, 1 H), 6.40−6.40 (m, 3 H); ^{13}C NMR (75.5 MHz) 198.3 (s),177.5 (s), 161.5 (s), 131.6 (s), 116.0 (s), 106.1 (d), 100.9 (d), 55.5 (q), 55.4 (d), 51.9 (q), 41.4 (s), 35.4 (t), 33.7 (t), 25.2 (q), 24.9 (q) ppm; IR (film) 2204, 1729, 1597, 1206 cm^{-1}.

A mixture of nitrile **46** (2.00 g, 6.01 mmol), acetic acid (5.0 mL), concentrated HCl (30 mL), and water (10 mL) was refluxed for 30 h. The resulting solution was taken up in 200 mL of ethyl acetate and washed twice with water and then with 5% aqueous $KHCO_3$ solution until the aqueous phase was slightly acidic. The organic layer was dried over anhydrous $MgSO_4$ and then concentrated *in vacuo* to provide a crude oil which consisted of several acidic components. This oil was dissolved in 40 mL of methanol, *p*-TsOH (30 mg) was added, and the mixture was refluxed for 12 h. Standard ethereal workup provided a crude oil which consisted of several esters. The residue was dissolved in 30 mL of acetone and then treated with anhydrous $KHCO_3$ (2.49 g, 18.00 mmol) and dimethyl sulfate (1.50 g, 12.00 mmol). The mixture was refluxed for 12 h. Standard ethereal workup, followed by chromatography (elution with H:E, 1:4), gave 1.01 g of methyl 6-[3′5′-dimethoxyphenyl]-2,2-dimethyl-5-oxohexanoate (55% from **46**) which was homogeneous by TLC analysis [H:E, 1:2, R_f(ketoester) = 0.76]: ^{1}H NMR (250 MHz) δ 1.14 (s, 6 H), 1.79 (t, 2 H, J = 8.0 Hz), 2.42 (t, 2 H, J = 8.0 Hz), 3.62 (s, 5 H), 3.78 (s, 6 H), 6.33−6.37 (m, 3 H); ^{13}C NMR (62.7 MHz) 207.6 (s), 177.8 (s), 160.9 (s), 136.2 (s), 107.3 (d), 99.1 (d), 55.3 (q), 51.8 (q), 50.3 (t), 41.6 (s), 37.5 (t), 33.9 (t), 25.1 (q) ppm.

The above ketoester (308 mg, 1.00 mmol) was added to NaH (60% suspension in mineral oil, 104 mg, 2.60 mmol) in THF (25 mL) with stirring. The resulting mixture was refluxed for 21 h, cooled to 0 °C, and diluted with 40 mL of water. The aqueous layer was washed with ether (3 × 40 mL) and then acidified (pH = 1). Standard ethereal workup gave a crude cyclohexane-1,3-dione which was dissolved in 20 mL of methanol. *p*-TsOH (10 mg, 0.1 mmol) was added, and the solution was refluxed for 3 h. Standard ethereal workup, followed by chromatography (elution with H:E, 2:1), gave 160 mg of 2-[3′,5′-dimethoxyphenyl]-6,6-dimethyl-3-methoxycyclohex-2-enone (55% for two steps) as a white solid which was homogeneous by TLC analysis [H:E, 1:1; R_f(enone) = 0.27]: mp 124−125 °C; ^{1}H NMR (250 MHz) δ 1.18 (s, 6 H), 1.94 (t, 2 H, J = 8.0 Hz), 2.70 (t, 2 H, J = 8.0 Hz), 3.73 (s, 3 H), 3.77 (s, 6 H), 6.29 (d, 2 H, J = 2.0 Hz), 6.38 (t, 1 H, J = 2.0 Hz); ^{13}C NMR (62.7 MHz) 201.6 (s), 170.0 (s), 160.0 (s), 135.9 (s), 118.5 (s), 108.8 (d), 99.3 (d), 55.6 (q), 55.2 (q), 39.7 (s), 34.0 (t), 24.5 (q), 22.8 (t) ppm; IR (film) 1661, 1594, 1149 cm^{-1}; MS, m/z 290 (M$^+$). Anal. Calcd for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.13; H, 7.72.

The above enone (145 mg, 0.50 mmol) was treated with 5.0 equiv of vinyllithium using procedure K to provide 101 mg of dienone **33** (71%) which was homogeneous by TLC analysis [H:E, 1:1, R_f(enone) = 0.27, R_f(**33**) = 0.48]: mp 66−67 °C; ^{1}H NMR (300 MHz) δ 1.32 (s, 6 H), 1.98 (t, 2 H, J = 6.5 Hz), 2.63 (t, 2 H, J = 6.5 Hz), 3.76 (s, 6 H), 5.09 (d, 1 H, J = 18.0 Hz), 5.20 (d, 1 H, J = 12.0 Hz), 6.17 (d, 1 H, J = 2.0 Hz), 6.20 (dd, 1 H, J = 18.0 Hz, 12.0 Hz), 6.37 (t, 1 H, J = 2.0 Hz); ^{13}C NMR (75.5 MHz) 197.9 (s), 162.1 (s), 160.2 (s), 138.6 (s), 136.7 (s), 133.5 (d), 121.6 (t), 108.4 (d), 92.2 (d), 55.2 (q), 37.7 (t), 35.3 (s), 34.6 (t), 27.4 (q) ppm; IR (film) 1666, 1589, 1201 cm^{-1}; MS, m/z 286 (M$^+$). Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.50; H, 7.74. Found: C, 74.75; H, 7.75.

2-[2′,5′-Dimethoxyphenyl]-4,4-dimethyl-3-vinylcyclohex-2-enone (35). 2-[2′,5′-Dimethoxyphenyl]cyclohex-2-enone (820 mg, 4.30 mmol), the preparation of which is described in the preparation of substrate **21**, was alkylated with iodomethane using procedure L to provide a crude oil consisting primarily of 2-[2′,5′-dimethoxyphenyl]-6-methylcyclohex-2-enone which was used directly in the next step without purification or characterization.

The enone was further alkylated with iodomethane using procedure L to provide 470 mg of 2-[2′,5′-dimethoxyphenyl]-6,6-dimethylcyclohex-2-enone (42% for two steps) which was homogeneous by TLC analysis [H:E, 1:1, R_f(bis-methylated enone) = 0.54]: ^{1}H NMR (300 MHz) δ 1.21 (s, 6 H), 1.93 (t, 2 H, J = 6.0 Hz), 2.50 (dt, 2 H, J = 6.0 Hz, 4.0 Hz), 3.67 (s, 3 H), 3.75 (s, 3 H), 6.64 (t, 1 H, J = 1.5 Hz), 6.73 (t, 1 H, J = 4.0 Hz), 6.79 (d, 2 H, J = 4.2 Hz); ^{13}C NMR (75.5 MHz) 202.3 (s), 153.4 (s), 151.3 (s), 145.1 (d), 137.4 (s), 128.5 (s), 116.4 (d), 113.4 (d), 112.2 (d), 56.4 (q), 55.6 (q), 41.7 (s), 36.3 (t), 24.1 (q), 23.5 (t) ppm; IR (film) 1679, 1496, 1227 cm^{-1}; MS, m/z 260 (M$^+$). Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.72; H, 7.71.

The above bis-alkylated enone (330 mg, 1.26 mmol) was treated with 5.0 equiv of vinyllithium using procedure B to provide 240 mg of a bis-allylic tertiary alcohol (66%) which was homogeneous by TLC analysis [H:E, 1:1, R_f(enone) = 0.54, R_f(alcohol) = 0.79]: ^{1}H NMR (250 MHz) δ 0.93 (s, 3 H), 1.02 (s, 3 H), 1.40−1.50 (m, 1 H), 1.90−1.98 (m, 1 H), 2.19−2.27 (m, 2 H), 3.76 (s, 3 H), 3.77 (s, 3 H), 4.20 (br s, 1 H), 4.97 (d,

1 H, J = 10.5 Hz), 5.21 (d, 1 H, J = 16.6 Hz), 5.66−5.75 (m, 2 H), 6.58 (s, 1 H), 6.72 (s, 1 H), 6.73 (s, 1 H); ^{13}C NMR (62.7 MHz) 153.7 (s), 150.3 (s), 140.3 (d), 140.2 (s), 132.9 (s), 130.2 (d), 118.4 (d), 113.5 (t), 111.9 (d), 111.3(d), 56.2 (q), 55.6 (q), 36.6 (s), 32.0 (t), 23.6 (t), 23.4 (q), 23.1 (q); IR (film) 3494, 1489, 1210 cm^{-1}.

This tertiary alcohol (160 mg, 0.55 mmol) was then oxidized using procedure D and 500 mg of PDC (1.33 mmol) to furnish 130 mg of dienone **35** (81%) which was homogeneous by TLC analysis [H:E, 1:1, R_f(alcohol) = 0.79, R_f(**35**) = 0.35]: ^{1}H NMR (250 MHz) δ 1.29 (s, 6 H), 1.97 (t, 2 H, J = 8.0 Hz), 2.59−2.66 (m, 2 H), 3.67 (s, 3 H), 3.72 (s, 3 H), 5.00 (d, 1 H, J = 17.5 Hz), 5.12 (d, 1 H, J = 11.7 Hz), 6.18 (dd, 1 H, J = 17.5 Hz, 11.7 Hz), 6.47 (s, 1 H), 6.77 (s, 2 H); ^{13}C NMR (62.7 MHz) 197.7 (s), 162.7 (s), 153.1 (s), 151.4 (s), 133.6 (d), 133.1 (s), 127.4 (s), 120.7 (t), 117.2 (d), 112.9 (d), 111.9 (d), 56.3 (q), 55.6 (q), 37.5 (t), 35.3 (s), 34.5 (t), 27.7 (q), 26.9 (q) ppm; IR (film) 1668, 1495, 1221 cm^{-1}; MS, m/z 286 (M$^+$). Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.50; H, 7.74. Found: C, 75.37; H, 7.73.

4-[2′,3′-Dimethoxyphenyl]-2,4-dimethyl-3-vinylcyclohex-2-enone (38). Veratrole (8.30 g, 60.00 mmol) was treated with 26.4 mL of *n*-butyllithium (2.5 M solution in hexanes) and 1,2-butene oxide (5.19 g, 72.00 mmol) in 60 mL of THF using procedure E to give 9.58 g of 1-[2′,3′-dimethoxyphenyl]butan-2-ol (86%) as a light oil which was homogeneous by TLC analysis [H:E, 2:1, R_f(butanol) = 0.21]: ^{1}H NMR (300 MHz) δ 1.00 (t, 3 H, J = 7.2 Hz), 1.49−1.50 (m, 2 H), 2.26 (d, 1H, J = 5.8 Hz), 2.69−2.76 (m, 1 H), 2.84−2.90 (m, 1 H), 3.70−3.83 (br s, 1 H), 3.85 (s, 3 H), 3.88 (s, 3 H), 6.79−6.84 (m, 2 H), 7.02 (t, 1 H, J = 7.8 Hz); ^{13}C NMR (75.5 MHz) 152.7 (s), 147.2 (s), 132.6 (s), 124.0 (d), 122.9 (d), 110.8 (d), 73.8 (d), 60.4 (q), 55.6 (q), 37.9 (t), 29.9 (t), 10.0 (q) ppm; IR (film) 3433, 1583, 1474, 1267, 1082 cm^{-1}.

The above alcohol (4.95 g, 23.30 mmol) was treated with 13 mL of Jones reagent (2.7 M) in 30 mL of acetone using procedure F to give 1-[2′,3′-dimethoxyphenyl]butan-2-one (87%) as a light oil which was homogeneous by TLC analysis [H:E, 2:1, R_f(butanone) = 0.37]: ^{1}H NMR (300 MHz) δ 1.04 (t, 3 H, J = 7.8 Hz), 2.48 (q, 2 H, J = 7.9 Hz), 3.70 (s, 2 H), 3.79 (s, 3 H), 3.86 (s, 3 H), 6.74 (d, 1 H, J = 7.8 Hz), 6.85 (d, 1 H, J = 8.6 Hz), 7.01 (t, 1 H, J = 7.8 Hz); ^{13}C NMR (75.5 MHz) 209.2 (s), 152.7 (s), 147.1 (s), 128.9 (s), 123.9 (d), 122.7 (d), 111.4 (d), 60.3 (q), 55.6 (q), 44.1 (t), 35.2 (t), 7.8 (q) ppm; IR (film) 1714, 1474, 1273, 1082 cm^{-1}.

The above ethyl ketone (3.12 g, 15.00 mmol) was treated with NaH (60% suspension in mineral oil, 630 mg, 15.75 mmol) and iodomethane (4.24 g, 30.00 mmol) in 30 mL of THF using procedure G to yield 2.85 g of 2-[2′,3′-dimethoxyphenyl]pentan-3-one (86%) as a light oil which was homogeneous by TLC analysis [H:E, 2:1, R_f(pentanone) = 0.44]: ^{1}H NMR (250 MHz) δ 0.98 (t, 3 H, J = 7.4 Hz), 1.36 (d, 3 H, J = 6.5 Hz), 2.36 (q, 2 H, J = 7.5 Hz), 3.85 (s, 3 H), 3.89 (s, 3 H), 4.16 (q, 1 H, J = 6.8 Hz), 6.71 (d, 1 H, J = 7.6 Hz), 6.83 (d, 1 H, J = 8.1 Hz), 7.03 (t, 1 H, J = 7.6 Hz); ^{13}C NMR (62.7 MHz) 210.7 (s), 151.8 (s), 145.5 (s), 134.1 (s), 123.3 (d), 118.9 (d), 109.9 (d), 59.8 (q), 54.7 (q), 44.5 (d), 33.1 (t), 15.9 (q), 7.1 (q) ppm; IR (film) 1714, 1474, 1273 cm^{-1}.

6-[2′,3′-Dimethoxyphenyl]-3-methoxy-2,6-dimethylcyclohex-2-enone (320 mg, 1.10 mmol), the preparation of which was decribed as general procedures I and J, was treated with 7.0 equiv of vinyllithium using procedure K to provide 213 mg of dienone **38** (68%) as a yellow solid which was homogeneous by TLC analysis [H:E, 1:1, R_f(enone) = 0.38, R_f(**38**) = 0.58]: mp 97−99 °C; ^{1}H NMR (300 MHz) δ 1.68 (s, 3 H), 1.78−1.86 (m, 1 H), 2.00 (s, 3 H), 2.33−2.42 (m, 1 H), 2.50−2.69 (m, 2 H), 3.74 (s, 3 H), 3.85 (s, 3 H), 5.17 (d, 1 H, J = 17.0 Hz), 5.33 (d, 1 H, J = 11.0 Hz), 6.29 (dd, 1 H, J = 17.0 Hz, 11.0 Hz), 6.85−6.87 (m, 2 H), 6.99 (d, 1 H, J = 7.5 Hz); ^{13}C NMR (75.5 MHz) 199.4 (s), 159.3 (s), 153.1 (s), 147.4 (s), 140.1 (s), 134.4 (d), 130.5 (s), 123.0 (d), 122.2 (t), 119.5 (d), 111.4 (d), 60.0 (q), 55.6 (q), 42.7 (s), 36.6 (t), 34.6 (t), 25.5 (q), 12.8 (q) ppm; IR (film) 1652, 1258 cm^{-1}; MS, m/z 286 (M$^+$). Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.50; H, 7.74. Found: C, 75.21; H, 7.82.

4-[3′,4′-Dimethoxyphenyl]-2,4-dimethyl-3-vinylcyclohex-2-enone (40). (3,4-Dimethoxyphenyl)acetic acid (5.00 g, 25.50 mmol) was treated with 53.55 mmol of LDA[38] and 51.0 mmol of iodomethane using procedure L to give 5.12 g of 2-[3′,4′-dimethoxyphenyl]propionic acid [50463-74-6] as a white solid (98%): mp 67−68 °C; ^{1}H NMR (75.5 MHz) δ 1.50 (d, 3 H, J = 7.50), 3.70 (q, 1 H, J = 7.5 Hz), 3.90 (s, 6 H), 6.78−6.89 (m, 3 H).

The above propionic acid (2.14 g, 10.20 mmol) was treated with oxalyl chloride (1.10 mL, 12.24 mmol) and (MeO)-MeNH·HCl (1.09 g, 11.22 mmol) using procedure H to afford 2.03 g of *N*-methyl-*N*-methoxy-2-[3′,4′dimethoxyphenyl]propanamide (78%) as an oil which was homogeneous by TLC analysis [H:E, 4:1, R_f(amide) = 0.23]: ^{1}H NMR (300 MHz) δ 1.40 (d, 3 H, J = 6.0 Hz), 3.15 (s, 3 H), 3.45 (br s, 3 H), 3.85 (s, 6 H), 4.00−4.14 (m, 1 H), 6.75−6.85 (m, 3 H); ^{13}C NMR (75.5 MHz) 175.0 (s), 148.8 (s), 147.7 (s), 134.4 (s), 119.8 (d), 111.0 (d), 110.2(d), 61.1 (q), 55.8 (q), 55.7 (q), 41.3 (d), 32.3 (q), 19.7 (q) ppm; IR (film) 1659, 1590, 1261 cm^{-1}; MS, m/z 252 (M$^+$), 165 (base).

Ethylmagnesium bromide (7 mL of 3 M solution in Et$_2$O) was treated with the above amide (1.78 g, 7.04 mmol) using procedure H to afford 1.46 g (93%) of 2-[3′,4′-dimethoxyphenyl]pentan-3-one as an oil which was homogeneous by TLC analysis [H:E, 7:3, R_f(pentanone) = 0.30]: ^{1}H NMR (300 MHz) δ 0.90 (t, 3 H, J = 5.8 Hz), 1.35 (d, 3 H, J = 5.8 Hz), 2.30−2.48 (m, 2 H), 3.65 (q, 1 H, J = 5.8 Hz), 3.80 (s, 6 H), 6.70 (d, 1 H, J = 1.8 Hz), 6.75 (dd, 1 H, J = 6.8 Hz, 1.8 Hz), 6.8 (d, 1 H, J = 6.8 Hz); ^{13}C NMR (75.5 MHz) 211.7 (s), 149.1 (s), 148.0 (s), 133.3 (s), 119.9 (d), 111.3 (d), 110.5 (d), 55.8 (q), 55.8 (q), (the preceding signals overlap), 52.1 (d), 33.9 (t), 17.5 (q), 7.9 (q) ppm; IR (film) 1710, 1589, 1260, 1143, 1026 cm^{-1}; MS, m/z 222 (M$^+$), 165 (base).

The above pentanone (444 mg, 2.00 mmol) was treated with KO-*t*-Bu (2.00 mmol) and ethyl acrylate (250 μL, 2.00 mmol) using protocol I to afford 560 mg of crude 4-[3′,4′dimethoxyphenyl]-2,4-dimethylcyclohexane-1,3-dione which was homogeneous by TLC analysis [H:E, 1:4, R_f(dione) = 0.28]. This material was then converted, using protocol J, to give 452 mg of 6-[3′,4′-dimethoxyphenyl]-2,6-methyl-3-methoxycyclohex-2-enone as a light yellow solid (78% for two steps) which was homogeneous by TLC analysis [H:E, 3:7, R_f(enone) = 0.31]: mp 99−101 °C; ^{1}H NMR (300 MHz) δ 1.35 (s, 3 H), 1.70 (s, 3 H), 1.90−2.55 (m, 4 H), 3.65 (s, 3 H), 3.80 (s, 6 H), 6.64−6.75 (m, 3 H); ^{13}C NMR (75.5 MHz) 201.1 (s), 170.1 (s), 148.6 (s), 147.4 (s), 135.3 (s), 117.9 (d), 113.9 (s), 110.7 (d), 109.7 (d), 55.7 (q), 55.6 (q), 54.7 (q), 47.4 (s), 33.8 (t), 27.1 (q), 22.4 (t), 7.8 (q) ppm; IR (film) 1730, 1618, 1261, 1147, 1026 cm^{-1}; MS, m/z 290 (M$^+$), 178 (base). Anal. Calcd for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.06; H, 7.64.

The above cyclohexenone (840 mg, 2.89 mmol) was treated with excess vinyllithium (14.5 mmol) using procedure K to provide 740 mg of dienone **40** (89%) as a viscous oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(enone) = 0.31, R_f(**40**) = 0.35]: ^{1}H NMR (250 MHz) δ 1.60 (s, 3 H), 2.00 (s, 3 H), 2.05 (t, 2 H, J = 6.3 Hz), 2.30−2.42 (m, 2 H), 3.80 (s, 6 H), 5.10 (dd, 1 H, J = 18.2 Hz, 1.4 Hz), 5.35 (dd, 1 H, J = 12.1 Hz, 1.4 Hz), 6.20 (dd, 1 H, J = 18.2 Hz, 12.1 Hz), 6.73−6.82 (m, 3 H); ^{13}C NMR (62.7 MHz) 199.4 (s), 157.5 (s), 148.7 (s), 147.5 (s), 138.0 (s), 133.9 (d), 132.6 (s), 122.3 (t), 118.9 (d), 110.6 (d), 110.1 (d), 55.8 (q), 55.7 (q), 43.1 (s), 39.9 (t), 34.2 (t), 26.8 (q), 12.9 (q); MS, m/z 286 (M$^+$), 151 (base).

4-[3′,5′-Dimethoxyphenyl]-2,4-dimethyl-3-vinylcyclohex-2-enone (42). 1-[3′,5′-Dimethoxyphenyl]butan-2-one was prepared from (3,5-dimethoxyphenyl)acetic acid as decribed in procedure H.

The above butanone (0.69 g, 3.31 mmol) was alkylated with NaH (60% suspension in mineral oil, 146 mg, 3.64 mmol) and iodomethane (0.62 mL, 9.94 mmol) in 15 mL of THF using procedure G to afford 630 mg (86%) of 2-[3′,5′-dimethoxyphenyl]pentan-3-one as a oil which was homogeneous by TLC analysis [H:E, 4:1, R_f(pentanone) = 0.38]: ^{1}H NMR (250 MHz) δ 0.95 (t, 3 H, J = 7.3 Hz), 1.35 (d, 3 H, J = 7.0 Hz), 2.50−2.25 (m, 2 H), 3.66 (q, 1 H, J = 6.9 Hz), 3.76 (s, 6 H), 6.34 (s, 3 H); ^{13}C NMR (62.7 MHz) 211.2 (s), 161.0 (s), 143.2 (s), 105.8 (d), 98.7 (d), 55.2 (q), 52.8 (d), 34.0 (t), 17.2 (q), 7.9 (q) ppm; IR (film) 1712, 1607, 1203 cm^{-1}.

(38) Riggs, R. M.; McKenzie, A. T.; Byrn, S. R.; Nichols, D. E.; Foreman, M. M.; Truex, L. L. *J. Med. Chem.* **1987**, *30*, 1914.

The above pentanone derivative (575 mg, 2.59 mmol) was treated with KO-*t*-Bu (320 mg, 2.85 mmol) and ethyl acrylate (0.26 mL, 2.85 mmol) using procedure I to afford 700 mg of crude 4-[3′,5′-dimethoxyphenyl]-2,4-dimethylcyclohexane-1,3-dione [ether, R_f(dione) = 0.54] which was converted, using procedure J, to 125 mg of 6-[3′,5′-dimethoxyphenyl]-2,6-methyl-3-methoxycyclohex-2-enone as a light yellow oil (19% for two steps) which was homogeneous by TLC analysis [H:E, 7:3, R_f(enone) = 0.31]: ^{1}H NMR (250 MHz) δ 1.35 (s, 3 H), 1.71 (s, 3 H), 1.90−2.05 (m, 1 H), 2.25−2.55 (m, 3 H), 3.67 (s, 3 H), 3.72 (s, 6 H), 6.25−6.35 (m, 3 H); ^{13}C NMR (62.7 MHz) 200.7 (s), 170.2 (s), 160.6 (s), 145.3 (s), 113.9 (s), 104.6 (d), 97.8 (d), 55.1 (q), 54.7 (q), 48.0 (s), 33.7 (t), 27.0 (q), 22.4 (t), 7.9 (q) ppm; IR (film) 1650, 1238 cm^{-1}.

The above cyclohexenone (110 mg, 0.38 mmol) was treated with excess vinyllithium (3.16 mmol) using procedure K to provide 58 mg of dienone **42** (53%) as a viscous oil which was homogeneous by TLC analysis [H:E, 2:1, R_f(enone) = 0.31, R_f(**42**) = 0.46]: ^{1}H NMR (250 MHz) δ 1.58 (s, 3 H), 1.99 (s, 3 H), 2.03−2.12 (m, 2 H), 2.35−2.44 (m, 2 H), 3.77 (s, 6 H), 5.15 (dd, 1 H, J = 17.6 Hz, 1.4 Hz), 5.40 (dd, 1 H, J = 11.7 Hz, 1.4 Hz), 6.25 (dd, 1 H, J = 17.6 Hz, 11.7 Hz), 6.34 (t, 1 H, J = 2.2 Hz), 6.43 (d, 2 H, J = 2.2 Hz); ^{13}C NMR (62.7 MHz) 199.5 (s), 160.7 (s), 157.2 (s), 148.4 (s), 134.0 (d), 132.9 (s), 122.5 (t), 105.6 (d), 97.4 (d), 55.3 (q), 43.7 (s), 39.8 (t), 34.2 (t), 26.9 (q), 12.9 (q) ppm; IR (film) 1665, 1592, 1202 cm^{-1}. Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.50; H, 7.74. Found: C, 75.36; H, 7.57.

4-[2′,5′-Dimethoxyphenyl]-2,4-dimethyl-3-vinylcyclohex-2-enone (44). To a solution of 1,4-dimethoxybenzene (4.00 g, 28.90 mmol) dissolved in 15 mL of THF was added 12.6 mL of *n*-butyllithium (31.5 mmol, 2.5 M solution in hexanes) to generate the corresponding organolithium species *in situ*. To this solution was added 1,2-epoxybutane (2.50 g, 34.88 mmol) to provide 3.43 g of 1-[2′,5′-dimethoxyphenyl]butan-3-ol (55%) as a whitish solid which was homogenous by TLC analysis [H:E, 2:1, R_f(butanol) = 0.14]: mp 47−48 °C; ^{1}H NMR (300 MHz) δ 0.99 (t, 3 H, J = 7.7 Hz), 1.48−1.60 (m, 2 H), 2.21 (br s, 1 H), 2.66 (dd, 1 H, J = 13.4 Hz, 6.8 Hz), 2.85 (dd, 1 H, J = 13.4 Hz, 3.7 Hz), 3.70−3.81 (br s, 1 H), 3.75 (s, 3 H), 3.78 (s, 3 H), 6.70-6.75 (m, 2 H), 6.79 (d, 1 H, J = 8.1 Hz); ^{13}C NMR (75.5 MHz) 153.5 (s), 151.7 (s), 128.4 (s), 117.5 (d), 111.6 (d), 111.3 (d), 73.3 (d), 55.8 (q), 55.6 (q), 38.4 (t), 29.9 (t), 10.0 (q) ppm; IR (film) 3415, 1220 cm^{-1}. Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.45; H, 8.57.

The above butanol (3.26 g, 15.50 mmol) was oxidized using procedure F. Chromatography (elution with H:E, 4:1) of the residue gave 2.35 g of 1-[2′,5′-dimethoxyphenyl]butan-2-one (73%) which was homogeneous by TLC analysis [H:E, 3:2, R_f(butanone) = 0.52]: ^{1}H NMR (250 MHz) δ 1.02 (t, 3 H, J = 7.3 Hz), 2.45 (q, 2 H, J = 7.3 Hz), 3.62 (s, 2 H), 3.74 (s, 6 H), 6.71 (br s, 1 H), 6.76 (br s, 2 H); ^{13}C NMR (62.7 MHz) 209.3 (s), 153.3 (s), 151.5 (s), 124.7 (s), 117.2 (d), 112.4 (d), 111.2 (d), 55.8 (q), 55.5 (q), 44.3 (t), 35.0 (t), 7.7 (q) ppm; IR (film) 1714, 1227 cm^{-1}.

The above butanone (2.19 g, 10.53 mmol) was treated with NaH (60% suspension in mineral oil, 463 mg, 11.58 mmol) and iodomethane (1.96 mL, 31.50 mmol) in 23 mL of THF using procedure G. Standard ethereal workup, followed by chromatography (elution with H:E, 5:1), gave 2.07 g of 2-[2′,5′-dimethoxyphenyl]pentan-3-one (87%) which was homogeneous by TLC analysis [H:E, 3:1, R_f(pentanone) = 0.43]: ^{1}H NMR (250 MHz) δ 0.96 (t, 3 H, J = 7.3 Hz), 1.32 (d, 3 H, J = 6.9 Hz), 2.28−2.41 (m, 2 H), 3.73 (s, 3 H), 3.77 (s, 3 H), 4.06 (q, 1 H, J = 6.9 Hz), 6.60−6.85 (m, 3 H); ^{13}C NMR (62.7 MHz) 212.0 (s), 153.6 (s), 150.8 (s), 130.7 (s), 114.5 (d), 111.9 (d), 111.4 (d), 55.8 (q), 55.5 (q), 45.6 (d), 33.8 (t), 15.9 (q), 7.9 (q) ppm; IR (film) 1713, 1219 cm^{-1}.

The above pentanone derivative (1.98 g, 8.91 mmol) was treated with KO-*t*-Bu (1.10 g, 9.80 mmol) and methyl acrylate (0.25 mL, 2.00 mmol) using procedure I to afford 1.37 g of crude 4-[2′,5′-dimethoxyphenyl]-2,4-dimethylcyclohexane-1,3-dione which was converted, using procedure J, to give 1.41 g (54% for two steps) of 6-[2′,5′-dimethoxyphenyl]-2,6-methyl-3-methoxycyclohex-2-enone as a light yellow oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(enone) = 0.31]: ^{1}H NMR (300 MHz) δ 1.46 (s, 3 H), 1,64−1.70 (m, 1 H), 1.76 (s, 3 H), 2.40−2.70 (m, 2 H), 2.70−2.80 (m, 1 H), 3.66 (s, 3 H), 3.74 (s, 3 H), 3.76 (s, 3 H), 6.69−6.75 (m, 2 H), 6.79 (d, 1 H, J = 8.6 Hz); ^{13}C NMR (75.5 MHz) 201.5 (s), 168.2 (s), 153.5 (s), 151.3 (s), 135.6 (s), 125.5 (s), 114.9 (d), 113.1 (d), 111.1 (d), 56.1 (q), 55.5 (q), 54.7 (q), 47.0 (s), 32.7 (t), 22.3 (t), 21.4 (q), 7.9 (q) ppm; IR (film) 1660, 1227 cm^{-1}.

The above cyclohexenone (135 mg, 0.47 mmol) was treated with excess vinyllithium (2.32 mmol) using procedure K to provide 75 mg of dienone **44** (56%) as a viscous oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(enone) = 0.31, R_f(**44**) = 0.57]: ^{1}H NMR (250 MHz) δ 1.65 (s, 3 H), 1.66−1.75 (m, 1 H), 1.94 (s, 3 H), 2.35−2.50 (m, 1 H), 2.50−2.80 (m, 2 H), 3.65 (s, 3 H), 3.76 (s, 3 H), 5.11 (dd, 1 H, J = 17.7 Hz, 1.4 Hz), 5.22 (dd, 1 H, J = 11.8 Hz, 1.4 Hz), 6.14 (dd, 1H, J = 17.7 Hz, 11.8 Hz), 6.74 (br s, 2 H), 6.84 (d, 1 H, J = 1.3 Hz); ^{13}C NMR (62.7 MHz) 199.4 (s), 160.5 (s), 153.2 (s), 151.5 (s), 136.4 (s), 134.3 (d), 129.9 (s), 121.1 (t), 115.0 (d), 111.8 (d), 110.5 (d), 55.5 (q), 55.4 (q), 42.4 (s), 35.2 (t), 34.6 (t), 24.6 (q), 12.8 (q) ppm; IR (film) 1660, 1227 cm^{-1}. Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.50; H, 7.74. Found: C, 75.22; H, 7.49.

Cyclization of 29 To Give 30. A solution of 20 mg of **29** (0.07 mmol) and 43 μL of BF_3·Et_2O (0.35 mmol) in 2 mL of CH_2Cl_2 was refluxed for 8 h. The reaction mixture was diluted with 10 mL of ether and neutralized with 10 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 1:1), gave 11 mg of **30** (55% yield) as an oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(**29**) = 0.48, R_f(**30**) = 0.42]: ^{1}H NMR (300 MHz) δ 1.19 (s, 6 H), 1.93 (t, 2 H, J = 6.9 Hz), 2.29 (t, 2 H, J = 6.8 Hz), 2.53 (t, 2 H, J = 7.0 Hz), 2.64 (t, 2 H, J = 7.0 Hz), 3.83 (s, 3 H), 3.84 (s, 3 H), 6.79 (ABq, 2 H, $\Delta\nu_{AB}$ = 25.5 Hz, J_{AB} = 8.5 Hz); ^{13}C NMR (75.5 MHz) 195.1 (s), 166.2 (s), 151.8 (s), 151.3 (s), 130.5 (s), 125.5 (s), 123.6 (s), 121.1 (d), 108.5 (d), 56.0 (q), 55.6 (q), 36.0 (s), 35.7 (t), 34.2 (t), 28.7 (t), 25.7 (q), 25.5 (t) ppm; IR (film) 1665, 1250 cm^{-1}.

Cyclization of 31 To Give 32. A solution of 24 mg of **31** (0.84 mmol) and 12 μL of BF_3·Et_2O (0.10 mmol) in 2 mL of CCl_4 was refluxed for 30 min. The reaction mixture was diluted with 20 mL of ether and neutralized with 5 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 1:1), gave 21 mg of **32** (88% yield) as an oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(**31**) = 0.32, R_f(**32**) = 0.42]: ^{1}H NMR (300 MHz) δ 1.24 (s, 6 H), 1.92 (t, 2 H, J = 7.0 Hz), 2.39 (t, 2 H, J = 7.9 Hz), 2.58−2.64 (m, 4 H), 3.88 (s, 3 H), 3.90 (s, 3 H), 6.66 (s, 1 H), 7.68 (s, 1 H); ^{13}C NMR (75.5 MHz) 197.1 (s), 165.2 (s), 147.5 (s), 146.7 (s), 128.9 (s), 128.4 (s), 123.6 (s), 111.4 (d), 110.0 (d), 56.0 (q), 55.9 (q), 36.2 (t), 35.9 (s), 35.4 (t), 27.7 (t), 26.4 (q), 25.9 (t) ppm; IR (film) 1663, 1266 cm^{-1}; MS, m/z 286 (M^+). Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.50; H, 7.74. Found: C, 75.40; H, 7.70.

Cyclization of 33 To Give 34. A solution of 40 mg of **33** (0.14 mmol) and 21 μL of BF_3·Et_2O (0.017 mmol) in 2 mL of CH_2Cl_2 was refluxed for 10 min. The reaction mixture was diluted with 30 mL of ether and neutralized with 10 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 2:1), gave 31 mg of **34** (78% yield) as a light yellow solid which was homogeneous by TLC analysis [H:E, 1:1, R_f(**33**) = 0.48, R_f(**34**) = 0.60]: mp 80−82 °C; ^{1}H NMR (300 MHz) δ 1.25 (s, 6 H), 1.92 (t, 2 H, J = 7.0 Hz), 2.34 (t, 2 H, J = 7.0 Hz), 2.58−2.65 (m, 4 H), 3.80 (s, 3 H), 3.83 (s, 3 H), 6.41 (d, 1 H, J = 2.5 Hz), 7.21 (d, 1 H, J = 2.5 Hz); ^{13}C NMR (75.5 MHz) 196.7 (s), 167.8 (s), 158.3 (s), 156.0 (s), 132.5 (s), 129.5 (s), 116.6 (s), 104.2 (d), 98.1 (d), 55.5 (q), 55.3 (q), 36.2 (s), 36.2 (t), 35.5 (t), 26.2 (q), 25.5 (t), 19.2 (t) ppm; IR (film) 1661, 1594, 1149 cm^{-1}; MS, m/z 286 (M^+). Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.50; H, 7.74. Found: C, 75.56; H, 7.72.

Cyclization of 35 To Give 36 and 37. A solution of 170 mg of **35** (0.59 mmol) and 220 μL of BF_3·Et_2O (1.78 mmol) in 7 mL of CH_2Cl_2 was refluxed for 3 h. The reaction mixture was diluted with 50 mL of ether and neutralized with 10 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 1:1), gave 85 mg of **37** (56% yield) as a light solid which was homogeneous by TLC analysis [H:E, 2:3, R_f(**35**) = 0.44, R_f(**37**) = 0.74]: mp 107.5−108 °C; ^{1}H NMR (250 MHz) δ 1.44 (s, 3 H), 2.06 (t, 2

H, J = 7.0 Hz), 2.84 (t, 2 H, J = 7.0 Hz), 3.97 (s, 3 H), 7.15 (d, 1 H, J = 8.8 Hz), 7.38 (d, 1 H, J = 8.8 Hz), 7.67 (d, 1 H, J = 8.8 Hz), 7.88 (d, 1 H, J = 8.6 Hz), 8.93 (s, 1 H); ^{13}C NMR (62.7 MHz) 200.9 (s), 160.3 (s), 154.4 (s), 134.3 (d), 132.6 (s), 129.4 (d), 127.8 (s), 124.9 (s), 121.3 (d), 116.5 (d), 105.3 (d), 55.2 (q), 37.3 (t), 36.7 (t), 35.1 (s), 29.9 (q) ppm; IR (film) 1647, 1209 cm^{-1}; ESI-MS, m/z 255 (MH^+). Anal. Calcd for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13. Found: C, 80.09; H, 7.24.

Continued elution afforded 70 mg of **36** (41%) which was homogeneous by TLC analysis [H:E, 2:3, R_f(**35**) = 0.44, R_f(**36**) = 0.37]: mp 131−132 °C; ^{1}H NMR (250 MHz) δ 1.19 (s, 6 H), 1.93 (t, 2 H, J = 6.8 Hz), 2.27 (t, 2 H, J = 7.3 Hz), 2.62 (t, 4 H, J = 6.8 Hz), 3.75 (s, 3 H), 3.76 (s, 3 H), 6.76 (s, 2 H); ^{13}C NMR (62.7 MHz) 194.3 (s), 166.1 (s), 150.4 (s), 149.8 (s), 131.0 (s), 126.9 (s), 122.4 (s), 110.7 (d), 110.3 (d), 56.1 (q), 56.1 (q) (the preceding signals overlap), 35.8 (s), 35.7 (t), 34.1 (t), 25.7 (q), 24.6 (t), 21.3 (t) ppm; IR (film) 1668, 1481, 1251 cm^{-1}; MS, m/z 286 (M^+). Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.50; H, 7.74. Found: C, 75.26; H, 7.82.

Cyclization of 38 To Give 39. A solution of 50 mg of **38** (0.17 mmol) and 214 μL of BF_3·Et_2O (1.75 mmol) in 3 mL of CCl_4 was refluxed for 10 h. The reaction mixture was diluted with 30 mL of ether and neutralized with 10 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 3:1), gave 29 mg of **39** (58% yield) as a light yellow solid which was homogeneous by TLC analysis [H:E, 2:1, R_f(**38**) = 0.58, R_f(**39**) = 0.38]: mp 87−89 °C; ^{1}H NMR (300 MHz) δ 1.69 (s, 3 H), 1.85 (s, 3 H), 1.87−1.94 (m, 1 H), 2.24−2.37 (m, 1 H), 2.44−2.51 (m, 1 H), 2.65−2.77 (m, 2 H), 2.87−3.00 (m, 3 H), 3.85 (s, 3 H), 3.89 (s, 3 H), 6.78 (s, 1 H), 6.79 (s, 1 H); ^{13}C NMR (75.5 MHz) 200 (s), 164.2 (s), 151.7 (s, 148.5 (s), 137.6 (s), 129.4 (s), 126.8 (s), 123.5 (d), 110.8 (d), 60.5 (q), 55.8 (q), 41.1 (s), 34.2 (t), 33.4 (t), 30.8 (t), 27.2 (t), 24.0 (q), 10.8 (q) ppm; IR (film) 1655, 1207 cm^{-1}; MS, m/z 286 (M^+). Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.50; H, 7.74. Found: C, 75.55; H, 7.75.

Cyclization of 40 To Give 41. A solution of 120 mg of **40** (0.41 mmol) and 400 μL of BF_3·Et_2O (3.28 mmol) in 3 mL of CH_2Cl_2 was refluxed for 12 h. The reaction mixture was diluted with 10 mL of ether and neutralized with 10 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 2:3), gave 100 mg of **41** (80% yield) as a viscous yellow oil which was homogeneous by TLC analysis [H:E, 2:3, R_f(**40**) = 0.35, R_f(**41**) = 0.30]: ^{1}H NMR (250 MHz) δ 1.50 (s, 3 H), 1.80 (s, 3 H), 1.95−2.12 (m, 1 H), 2.28−2.30 (m, 1 H), 2.42−2.60 (m, 2 H), 2.52−2.98 (m, 4 H), 3.85 (s, 6 H), 6.60 (s, 1 H), 6.75 (s, 1 H); ^{13}C NMR (62.7 MHz) 198.2 (s), 162.2 (s), 147.8 (s), 147.1 (s), 136.6 (s), 128.4 (s), 127.7 (s), 110.9 (d), 108.8 (d), 56.0 (q), 55.8 (q), 39.4 (s), 36.4 (t), 34.1 (t), 29.7 (t), 27.3 (t), 26.9 (q), 10.9 (q) ppm; IR (film) 1660, 1617, 1249, 1145, 1059 cm^{-1}; MS: m/z 286 (M^+), 271 (base).

Cyclization of 42 To Give 43. A solution of 14 mg of **42** (0.05 mmol) and 60 μL of BF_3·Et_2O (0.50 mmol) in 2 mL of CH_2Cl_2 was refluxed for 5 h. The reaction mixture was diluted with 20 mL of ether and quenched with 10 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 2:1), gave 10 mg of **43** (71% yield) as an oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(**42**) = 0.46, R_f(**43**) = 0.33]: ^{1}H NMR (250 MHz) δ 1.54 (s, 3 H), 1.85 (s, 3 H), 1.95−2.10 (m, 1 H), 2.25−2.55 (m, 4 H), 2.60−2.70 (m, 1 H), 2.85−2.95 (m, 1 H), 3.00−3.12 (m, 1 H), 3.81 (s, 6 H), 6.32 (d, 1 H, J = 2.3 Hz), 6.43 (d, 1 H, J = 2.3 Hz); ^{13}C NMR (62.7 MHz) 198.3 (s), 162.5 (s), 159.2 (s), 157.3 (s), 146.8 (s), 128.3 (s), 117.1 (s), 102.0 (d), 95.5 (d), 55.4 (q), 55.3 (q), 40.1 (s), 36.4 (t), 34.2 (t), 26.8 (q), 26.6 (t), 23.1 (t), 10.9 (q) ppm; IR (film) 1667 cm^{-1}.

Attempted Cyclization of 44. A solution of 34 mg of **44** (0.12 mmol) and 150 μL of BF_3·Et_2O (1.22 mmol) in 4 mL of CH_2Cl_2 was refluxed for 12 h; however, no reaction was observed.

2-[2′,3′-Dimethoxyphenyl]-3-[1′-(trimethylsilyl)vinyl-]cyclohex-2-one (46). To 15 mL of ether at −78 °C was added 5.06 mL of *tert*-butyllithium (1.5 M solution in pentane). To this solution was added a solution of (1-bromovinyl)trimethylsilane [13683-41-5][39] (679 mg, 3.79 mmol) in 5 mL of ether. The mixture was allowed to warm to −15 °C over a period of 2.5 h.

To a solution of 2-[2′,3′-dimethoxyphenyl]cyclohexen-2-one [cf. the preparation of **16**, 60 mg, 0.26 mmol] dissolved in 2 mL of ether and 2 mL of THF at 0 °C was added 5 mg of cerium chloride (0.02 mmol) and 2.0 equiv (3.5 mL) of the above cold solution of [1-(trimethylsilyl)vinyl]lithium (**45**) over a 20-min period. The resulting mixture was stirred at 0 °C for 2 h. Standard ethereal workup afford 94 mg of crude 2-[2′,3′-dimethoxyphenyl]-1-[1′-(trimethylsilyl)vinyl]cyclohex-2-enol which was used without purification: ^{1}H NMR (300 MHz) δ −0.06 (s, 9 H), 1.60−1.74 (m, 2 H), 1.82−2.33 (m, 2 H), 2.08−2.36 (m, 2 H), 3.76 (s, 3 H), 3.84 (s, 3 H), 5.08 (s, 1 H), 5.36 (d, 1 H, J = 2.0 Hz), 5.55 (d, 1 H, J = 2.0 Hz), 5.81−5.85 (m, 1 H), 6.55 (d, 1 H, J = 8.4 Hz), 6.79 (d, 1 H, J = 7.9 Hz), 6.95 (t, 1 H, J = 8.1 Hz).

The above alcohol was oxidized with PDC (194 mg, 0.52 mmol) using procedure F to afford 42 mg of dienone **46** (49% for two steps) as an oil which was homogeneous by TLC analysis [H:E, 2:1, R_f(**46**) = 0.28]: ^{1}H NMR (250 MHz) δ −0.24 (s, 9 H), 2.05−2.17 (m, 2 H), 2.47 (t, 2 H, J = 5.9 Hz), 2.50−2.61 (m, 2 H), 3.71 (s, 3 H), 3.83 (s, 3 H), 5.24 (d, 1 H, J = 2.7 Hz), 5.52 (d, 1 H, J = 2.8 Hz), 6.49 (d, 1 H, J = 7.7 Hz), 6.80 (d, 1 H, J = J = 7.8 Hz), 6.93 (t, 1 H, J = 7.8 Hz); ^{13}C NMR (62.7 MHz) 198.1 (s), 164.5 (s), 153.2 (s), 152.3 (s), 147.0 (s), 131.4 (s), 130.7 (s), 125.9 (t), 123.7 (d), 122.9 (d), 111.6 (d), 60.1 (q), 55.5 (q), 37.9 (t), 32.7 (t), 22.5 (t), −0.96 (q) ppm. Anal. Calcd for $C_{19}H_{26}O_3Si$: C, 69.06; H, 7.94. Found: C, 69.30; H, 8.20.

Cyclization of 46 To Give 47. A solution of 28 mg of **46** (0.08 mmol) and 34 μL of BF_3·Et_2O (0.28 mmol) in 4 mL of CCl_4 was refluxed for 17 h. The reaction mixture was diluted with 30 mL of ether and neutralized with 5 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 2:1), gave 12 mg of **47** (58% yield) as an oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(**46**) = 0.54, R_f(**47**) = 0.28]: ^{1}H NMR (250 MHz) δ 2.05 (pentet, 2 H, J = 6.4 Hz), 2.29 (t, 2 H, J = 6.6 Hz), 2.50 (t, 2 H, J = 5.9 Hz), 2.55−2.63 (m, 4 H), 3.83 (s, 3 H), 3.86 (s, 3 H), 6.75 (d, 2 H, J = 8.1 Hz), 6.83 (d, 2 H, J = 8.1 Hz); ^{13}C NMR (62.7 MHz) 195.3 (s), 159.6 (s), 151.8 (s), 145.6 (s), 132.5 (s), 130.5 (s), 124.9 (s), 121.3 (d), 111.4 (d), 60.0 (q), 38.0 (t), 31.4 (t), 30.6 (t), 27.9 (t), 21.6 (t) ppm.

4-[2′,3′-Dimethoxyphenyl]-4-methyl-3-[1′-(trimethylsilyl)vinyl]cyclohex-2-enone (48). To 7 mL of ether at −78 °C was added 5.06 mL of *tert*-butyllithium (1.5 M solution in pentane). To this solution was added a solution of (1-bromovinyl)trimethylsilane [13683-41-5][39] (340 μL, 2.18 mmol) in 3 mL of ether. The mixture was allowed to warm up to −15 °C over a period of 2.5 h.

A solution of 6-(2′,3′-dimethoxyphenyl)-3-methoxy-6-methylcyclohex-2-enone (cf. preparation of **22**, 150 mg, 0.54 mmol) in 1 mL of THF and 2 mL of ether was added slowly to the above solution of [1-(trimethylsilyl)vinyl]lithium (**45**) at −78 °C. The mixture was allowed to warm to rt and stirred at rt for 13 h. After following the workup procedure in procedure K, 110 mg of dienone **48** (60%) were obtained as a light oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(**48**) = 0.40]: ^{1}H NMR (250 MHz) δ 0.16 (s, 9 H), 1.64 (s, 3 H), 1.90−2.05 (m, 1 H), 2.08−2.23 (m, 1 H), 2.25−2.40 (m, 1 H), 2.49−2.59 (m, 1 H), 3.82 (s, 3 H), 3.84 (s, 3 H), 5.55 (d, 1 H, J = 1.9 Hz), 5.62 (d, 1 H, J = 1.9 Hz), 6.00 (s, 1 H), 6.80−6.95 (m, 3 H); ^{13}C NMR (62.7 MHz) 200.0 (s), 169.7 (s), 153.3 (s), 150.1 (s), 148.0 (s), 137.1 (s), 130.3 (t), 126.8 (d), 122.7 (d), 121.7 (d), 111.6 (d), 60.2 (q), 55.7 (q), 44.2 (s), 38.1 (t), 34.6 (t), 27.4 (q), −0.26 (q) ppm.

Cyclization of 48 To Give 49. A solution of 45 mg of **48** (0.13 mmol) and 54 μL of BF_3·Et_2O (0.44 mmol) in 3 mL of CCl_4 was refluxed for 24 h. The reaction mixture was diluted with 30 mL of ether and neutralized with 5 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 3:1), gave 32 mg of **49** (90%

(39) (a) Ottolenghi, A.; Fridkin, M.; Zikha, A. *Can. J. Chem.* **1963**, *41*, 2977. (b) Chan, T. H.; Mychajlowskij, W.; Ong, B. S.; Harpp, D. N. *J. Org. Chem.* **1978**, *43*, 1526.

yield) as an oil which was homogeneous by TLC analysis [H:E, 2:1, R_f(**49**) = 0.25]: ^{1}H NMR (250 MHz) δ 1.69 (s, 3 H), 1.85−2.03 (m, 1 H), 2.38−2.45 (m, 1 H), 2.46−2.51 (m, 1 H), 2.52-2.74 (m, 2 H), 2.75−2.85 (m, 1 H), 2.87−3.05 (m, 2 H), 3.85 (s, 3 H), 3.89 (s, 3 H), 5.82 (s, 1 H), 6.79 (s, 2 H); ^{13}C NMR (62.7 MHz) 199.6 (s), 171.8 (s), 151.8 (s), 148.4 (s), 136.3 (s), 128.7 (s), 123.6 (d), 123.0 (d), 111.0 (d), 60.5 (q), 55.8 (q), 40.3 (s), 34.7 (t), 33.9 (t), 31.9 (t), 31.5 (t), 24.2 (q) ppm.

4-[2′,5′-Dimethoxyphenyl]-4-methyl-3-[1′-(trimethylsilyl)vinyl]cyclohex-2-enone (50). To 6 mL of ether at −78 °C was added 1.5 mL of *tert*-butyllithium (1.5 M solution in pentane). To this solution was added a solution of (1-bromovinyl)trimethylsilane [13683-41-5][39] (418 μL, 2.70 mmol) in 2 mL of ether. The mixture was allowed to warm to −15 °C over a period of 2.5 h.

To a mixture of 6-[2′,5′-dimethoxyphenyl]-3-methylcyclohex-2-enone [cf. the preparation of **28**] (150 mg, 0.54 mmol) in 2 mL of ether and 1 mL of THF at 0 °C was added cerium chloride (67 mg, 0.27 mmol). The above cold solution of [1-(trimethylsilyl)vinyl]lithium (**45**) was added dropwise over a period of 20 min. The resulting mixture was stirred at rt for 14 h. After following the workup in procedure K, 119 mg of dienone **50** (64%) were obtained as a tan amorphous solid which was homogeneous by TLC analysis [H:E, 1:2, R_f(**50**) = 0.78]: mp 74−75 °C; ^{1}H NMR (250 MHz) δ 0.14 (s, 9 H), 1.69 (s, 3 H), 1.70−1.88 (m, 1 H), 2.20−2.36 (m, 1 H), 2.38−2.55 (m, 1 H), 2.66−2.85 (m, 1 H), 3.70 (s, 3 H), 3.74 (s, 3 H), 5.46 (d, 1 H, J = 1.8 Hz), 5.63 (d, 1 H, J = 1.8 Hz), 5.94 (s, 1 H), 6.70−6.80 (m, 2 H), 6.89 (d, 1 H, J = 1.9 Hz); ^{13}C NMR (62.7 MHz) 199.8 (s), 170.3 (s), 153.1 (s), 151.7 (s), 149.6 (s), 134.4 (s), 130.2 (t), 126.3 (d), 116.2 (d), 111.8 (d), 110.8 (d), 55.6 (q), 55.3 (q), 43.5 (s), 36.7 (t), 34.6 (t), 26.1 (q), −0.1 (q) ppm.

Cyclization of 50 To Give 51. A solution of 16 mg of **50** (0.05 mmol) and 60 μL of BF_3·Et_2O (0.50 mmol) in 2 mL of CCl_4 was refluxed for 15 h. The reaction mixture was diluted with 20 mL of ether and neutralized with 5 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 3:1), gave 9.2 mg of **51** (71% yield) as an oil which was homogeneous by TLC analysis [H:E, 2:1, R_f(**51**) = 0.22]: ^{1}H NMR (250 MHz) δ 1.69 (s, 3 H), 1.75−2.00 (m, 1 H), 2.30−2.80 (m, 5 H), 3.05−3.17 (m, 1 H), 3.20-3.35 (m, 1 H), 3.78 (s, 3 H), 3.80 (s, 3 H), 5.83 (s, 1 H), 6.69 (d, 1 H, J = 8.9 Hz), 6.76 (d, 1 H, J = 8.9 Hz); ^{13}C NMR (62.7 MHz) 199.9 (s), 171.9 (s), 152.4 (s), 150.8 (s), 126.4 (s), 122.9 (d), 111.1 (s), 109.9 (d), 108.0 (d), 55.7 (q), 55.4 (q), 40.2 (s), 34.7 (t), 32.9 (t), 30.9 (t), 25.4 (t), 22.8 (q) ppm.

2-[2′-Methoxyphenyl]-3-[1′-(trimethylsilyl)vinyl]cyclohex-2-enone (52). To 8.0 mL of ether at −78 °C was added 2.1 mL of *tert*-butyllithium (1.35 M solution in pentane). To this solution was added a solution of (1-bromovinyl)trimethylsilane [13683-41-5][39] (252 mg, 1.41 mmol) in 2 mL of ether. The mixture was allowed to warm to −15 °C over a period of 2.5 h.

To a solution of 2-[2′-methoxyphenyl]cyclohexen-2-one [cf. the preparation of **7**, 95 mg, 0.47 mmol] in 2 mL of ether and 2 mL of THF containing 23 mg of cerium chloride (0.0.94 mmol) at −60 °C was added the above cold solution of [1-(trimethylsilyl)vinyl]lithium (**45**) over a 5-min period. The resulting mixture was stirred at 0 °C for 1 h. Standard ethereal workup afforded 120 mg of crude 2-[2′-dimethoxyphenyl]-1-[1′-(trimethylsilyl)vinyl]cyclohex-2-enol which was used without purification or characterization.

The above crude alcohol was oxidized with PDC (376 mg, 1.00 mmol) using procedure F to afford 43 mg of dienone **52** (28% for two steps) as an oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(**52**) = 0.38]: ^{1}H NMR (250 MHz) δ −0.06 (s, 9 H), 2.00−2.18 (m, 2 H), 2.40−2.51 (m, 4 H), 3.71 (s, 3 H), 5.27 (d, 1 H, J = 2.9 Hz), 5.51 (d, 1 H, J = 2.8 Hz), 6.78−6.93 (m, 3 H), 7.17−7.27 (m, 1 H); ^{13}C NMR (62.7 MHz) 197.4 (s), 163.6 (s), 157.3 (s), 153.6 (s), 147.8 (s), 132.3 (d), 128.5 (d), 125.5 (t), 120.2 (s), 119.7 (d), 110.3 (d), 55.1 (q), 37.9 (t), 32.8 (t), 22.5 (t), −1.1 (q) ppm.

2-[4′-Methoxyphenyl]-3-[1′-(trimethylsilyl)vinyl]cyclohex-2-enone (54). To 9 mL of ether at −78 °C was added 2.2 mL of *tert*-butyllithium (1.39 M solution in pentane). To this solution was added a solution of (1-bromovinyl)trimethylsilane [13683-41-5][39] (269 mg, 3.79 mmol) in 2 mL of ether. The mixture was allowed to warm to −15 °C over a period of 2.5 h.

To a solution of 2-[4′-methoxyphenyl]cyclohexen-2-one [cf. the preparation of **8**, 101 mg, 0.50 mmol] in 4 mL of ether and 4 mL of THF containing 25 mg of cerium chloride (0.10 mmol) at −60 °C was added the above cold solution of [1-(trimethylsilyl)vinyl]lithium (**45**) over a 5-min period. The resulting mixture was stirred at 0 °C for 1 h. Standard ethereal workup afforded 120 mg of crude 2-[4′-dimethoxyphenyl]-1-[1′-(trimethylsilyl)vinyl]cyclohex-2-enol which was uesd without purification or characterization.

The above crude alcohol was oxidized with PDC (376 mg, 1.00 mmol) using procedure F to afford 66 mg of dienone **54** (40% for two steps) as an oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(**54**) = 0.29]: ^{1}H NMR (250 MHz) δ −0.12 (s), 2.07 (pentet, J = 6.9 Hz), 2.45−2.58 (m, 4 H), 3.78 (s, 3 H), 5.41 (d, 1 H, J = 2.9 Hz), 5.58 (d, 1 H, J = 2.9 Hz), 6.79 (d, 2 H, J = 6.9 Hz), 6.98 (d, 2 H, J = 6.8 Hz); ^{13}C NMR (62.7 MHz) 198.1 (s), 163.2 (s), 158.3 (s), 154.2 (s), 133.8 (s), 132.4 (d), 127.6 (s), 126.4 (t), 112.7 (d), 55.1 (q), 38.1 (t), 33.6 (t), 22.4 (t), −1.12 (q) ppm.

4-[2′-Methoxyphenyl]-4-methyl-3-[1′-(trimethylsilyl)vinyl]cyclohex-2-enone (56). To 8 mL of ether at −78 °C was added 5.6 mL of *tert*-butyllithium (1.39 M solution in pentane). To this solution was added a solution of (1-bromovinyl)trimethylsilane [13683-41-5][39] (604 μL, 3.9 mmol) in 2 mL of ether. The mixture was allowed to warm to −15 °C over a period of 2.5 h.

To a mixture of 3-methoxy-6-[2′-methoxyphenyl]-6-methylcyclohex-2-enone [cf. the preparation of **10**] (192 mg, 0.78 mmol) in 2 mL of ether and 2 mL of THF at 0 °C was added cerium chloride (96 mg, 0.39 mmol). The cold solution of [1-(trimethylsilyl)vinyl]lithium was added dropwise to the above mixture over a period of 5 min. The resulting mixture was stirred at 0 °C for 3 h. After following the workup in procedure K, 65 mg of dienone **56** (53%) was obtained as a light oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(**56**) = 0.62]: ^{1}H NMR (250 MHz) δ 0.14 (s, 9 H), 1.25 (s, 3 H), 1.72−1.85 (m, 1 H), 2.17−2.51 (m, 1 H), 2.68−2.81 (m, 1 H), 2.66−2.85 (m, 1 H), 3.75 (s, 3 H), 5.44 (d, 1 H, J = 1.8 Hz), 5.58 (d, 1 H, J = 1.8 Hz), 5.95 (s, 1 H), 6.82−6.92 (m, 2 H), 7.20−7.30 (m, 2 H); ^{13}C NMR (62.7 MHz) 199.8 (s), 170.6 (s), 157.4 (s), 149.7 (s), 132.7 (s), 130.0 (t), 128.6 (d), 128.0 (d), 126.3 (d), 120.1 (d), 111.2 (d), 54.7 (q), 43.5 (s), 36.5 (t), 34.5 (t), 26.1 (q), −0.16 (q) ppm. Anal. Calcd for $C_{19}H_{26}O_2Si$: C, 72.57; H, 8.34. Found: C, 72.44; H, 8.22.

4-[4′-Methoxyphenyl]-4-methyl-3-[1′-(trimethylsilyl)vinyl]cyclohex-2-enone (58). To 8 mL of ether at −78 °C was added 5.8 mL of *tert*-butyllithium (1.39 M solution in pentane). To this solution was added a solution of (1-bromovinyl)trimethylsilane [13683-41-5][39] (619 μL, 3.9 mmol) in 2 mL of ether. The mixture was allowed to warm to −15 °C over a period of 2.5 h.

To a mixture of 3-methoxy-6-[4′-dimethoxyphenyl]-3-methylcyclohex-2-enone [cf. the preparation of **10**] (246 mg, 1.00 mmol) in 4 mL of ether and 4 mL of THF at 0 °C was added cerium chloride (49 mg, 0.20 mmol). The cold solution of [1-(trimethylsilyl)vinyl]lithium was added dropwise to the above mixture over a period of 5 min. The resulting mixture was stirred at 0 °C for 1 h. After following the workup in procedure K, 198 mg of dienone **58** (66%) was obtained as an oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(**58**) = 0.70]: ^{1}H NMR (250 MHz) δ 0.11 (s, 9 H), 1.52 (s, 3 H), 1.87−1.97 (m, 1 H), 2.11−2.32 (m, 3 H), 3.80 (s, 3 H), 5.40 (d, 1 H, J = 2.6 Hz), 5.47 (d, 1 H, J = 2.6 Hz), 6.02 (s, 1 H), 6.86 (d, 2 H, J = 7.7 Hz), 7.30 (d, 2 H, J = 7.7 Hz); ^{13}C NMR (62.7 MHz) 199.7 (s), 169.2 (s), 158.2 (s), 150.8 (s), 134.6 (s), 129.0 (t), 128. (d), 128.0 (d), 113.6 (d), 55.1 (q), 43.2 (s), 41.0 (t), 33.8 (t), 27.3 (q), −0.63 (q) ppm.

Attempted Cyclization of 52. A solution of 16 mg of **52** (0.48 mmol) and 58 μL of BF_3·Et_2O (0.48 mmol) in 2 mL of CCl_4 was refluxed for 36 h. However, only the decomposition of **52** was observed.

Attempted Cyclization of 54. A solution of 33 mg of **54** (0.10 mmol) and 122 μL of BF_3·Et_2O (1.00 mmol) in 2 mL of

CCl_4 was refluxed for 44 h. However, only decomposition and <2 mg of desilylated conjugated dienone **8** (<5%) was obtained.

Cyclization of 56 To Give 57. A solution of 17 mg of dienone **56** (0.056 mmol) and 69 μL of $BF_3{\cdot}Et_2O$ (0.56 mmol) in 2 mL of CCl_4 was refluxed for 44 h. The reaction mixture was diluted with 20 mL of ether and neutralized with 5 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 3:1), gave 5.5 mg of tricycle **57** (43% yield) as an oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(**57**) = 0.44]: ^{1}H NMR (250 MHz) δ 1.59 (s, 3 H), 1.94−2.14 (m, 1 H), 2.31−2.87 (m, 6 H), 3.20−3.31 (m, 1 H), 3.83 (s, 3 H), 5.91 (s, 1 H), 6.72 (d, 1 H, J = 8.0 Hz), 6.92 (d, 1 H, J = 8.0 Hz), 7.32 (t, 1 H, J = 8.1 Hz); ^{13}C NMR (62.7 MHz) 198.9 (s), 169.8 (s), 156.4 (s), 145.0 (s), 139.2 (s), 127.2 (d), 123.9 (d), 118.0 (d), 107.1 (d), 55.3 (q), 39.1 (s), 36.9 (t), 34.7 (t), 30.5 (t), 27.4 (q), 24.5 (t) ppm.

Cyclization of 58 To Give 59. A solution of 23 mg of **58** (0.076 mmol) and 93 μL of $BF_3{\cdot}Et_2O$ (0.76 mmol) in 2 mL of CCl_4 was refluxed for 30 h. The reaction mixture was diluted with 20 mL of ether and neutralized with 5 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 3:1), gave 7.6 mg of tricycle **59** (45% yield) as an oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(**59**) = 0.55]: ^{1}H NMR (250 MHz) δ 1.55 (s, 3 H), 1.95−2.15 (m, 1 H), 2.30−2.41 (m, 1 H), 2.44−2.59 (m, 2 H), 2.62-3.04 (m, 4 H), 3.79 (s, 3 H), 5.90 (s, 1 H), 6.61 (d, 1 H, J = 2.6 Hz), 6.81 (dd, 1 H, J = 8.7 Hz, 2.6 Hz), 7.21 (d, 1 H, J = 8.7 Hz); ^{13}C NMR (62.7 MHz) 199.1 (s), 170.1 (s), 157.6 (s), 136.0 (s), 129.5 (s), 127.2 (d), 124.2 (d), 113.3 (d), 112.9 (d), 55.2 (q), 38.7 (s), 37.4 (t), 34.8 (t), 31.3 (t), 31.1 (t), 27.8 (q) ppm.

Attempted Thermal Rearrangement of 60. Compound **60** (22 mg, 0.067 mmol) was placed in a sealed tube and heated at 250 °C for 10 h. However, only unreacted **60** was isolated (21 mg).

Electrocyclization of 60 To Give 61. Compound **60** (20 mg, 0.061 mmol) was dissolved in 1 mL of tetradecane, placed in a sealed tube, and heated at 250 °C for 22 h. The reaction vessel was cooled and opened, and the reaction mixture was directly placed on a silica gel column. Chromatography (elution with H:E, 4:1) gave 15 mg of **61** (83%) which was homogeneous by TLC analysis [H:E, 1:1, R_f(**60**) = 0.60, R_f(**61**) = 0.76]: mp 80−81 °C; ^{1}H NMR (300 MHz) δ 1.30 (d, 6 H, J = 6.9 Hz), 1.44 (s, 6 H), 2.08 (t, 2 H, J = 6.8 Hz), 2.84 (t, 2 H, J = 6.8 Hz), 3.56 (septet, 1 H, J = 6.9 Hz), 3.90 (s, 3 H), 7.53−7.57 (m, 2 H), 8.66 (ABq, 2 H, $\Delta\nu_{AB}$ = 216.0 Hz, J_{AB} = 9.0 Hz); ^{13}C NMR (75.5 MHz) 200.7 (s), 152.8 (s), 151.9 (s), 136.8 (s), 130.6 (s), 128.4 (d), 127.4 (d), 127.1 (s), 126.7 (s), 123.6 (d), 123.2 (d), 62.8 (q), 37.2 (t), 36.9 (t), 29.9 (q), 26.1 (d), 23.6 (q) ppm; IR (film) 1672, 1588, 1457, 1223 cm^{-1}; MS, m/z 296 (M^+). Anal. Calcd for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16. Found: C, 80.88; H, 8.14.

Continued elution furnished 3 mg (15%) of unreacted **60**.

12,13-Dimethyl-8,11,13-podocarpatrien-3-one (68). To a solution of Li (43 mg, 6.10 mmol) in 10 mL of liquid NH_3 (distilled from Na) at −78 °C was added a solution of enone **41** (175 mg, 0.61 mmol) and *tert*-butyl alcohol (60 μL, 0.61 mmol) in 8 mL of THF. After a 45-min period, 800 μL of iodomethane (12.20 mmol) was added. After 1 h, the NH_3 was allowed to evaporate. Standard ethereal workup, followed by chromatography (elution with H:E, 1:1), gave 140 mg (75% yield) of an off-white solid which was homogeneous by TLC analysis [H:E, 2:3, R_f(**41**) = 0.23, R_f(**68**) = 0.37]: mp 121−122 °C; ^{1}H NMR (300 MHz) δ 1.12 (s, 3 H), 1.16 (s, 3 H), 1.28 (s, 3 H), 1.68−2.02 (m, 4 H), 2.36−2.50 (m, 1 H), 2.59−2.70 (m, 2 H), 2.80−2.90 (m, 2 H), 3.79 (s, 3 H), 3.81 (s, 3 H), 6.50 (s, 1 H), 6.70 (s, 1 H); ^{13}C NMR (75.5 MHz) 214.7 (s), 147.2 (s), 147.0 (s), 139.1 (s), 126.9 (s), 111.1 (d), 108.4 (d), 55.9 (q), 55.6 (q), 50.5 (d), 47.1 (s), 37.5 (t), 36.9 (s), 34.5 (t), 30.4 (t), 26.9 (q), 24.4 (q), 20.9 (q), 20.2 (t) ppm; IR (KBr) 1698, 1608, 1253, 1150, 1063 cm^{-1}; MS, m/z 302 (M^+), 287 (base). Anal. Calcd for $C_{19}H_{26}O_3$: C, 75.45; H, 8.67. Found: C, 75.57; H, 8.66.

12,13-Dimethoxy-8,11,13-podocarpatriene (69). 1,3-Propanedithiol (40 μL, 0.45 mmol) and $BF_3{\cdot}Et_2O$ (10 μL, 0.09 mmol) were added to a solution of **68** (90 mg, 0.30 mmol) in 2 mL of CH_2Cl_2. After 12 h of stirring, the reaction mixture was diluted with Et_2O (10 mL) and washed with 5% aqueous NaOH (5 mL). Standard ethereal workup, followed by chromatography (elution with H:E, 4:1), afforded 110 mg of a thioketal as a white amorphous solid which was homogeneous by TLC analysis [H:E, 4:1, R_f(thioketal) = 0.22]: ^{1}H NMR (300 MHz) δ 1.10 (s, 3 H), 1.25 (s, 3 H), 1.30 (s, 3 H), 1.66−1.90 (m, 3 H), 1.97−2.04 (m, 5 H), 2.22−2.37 (m, 1 H), 2.53−2.73 (m, 4 H), 2.76−2.90 (m, 3 H), 3.07−3.22 (m, 1 H), 3.80 (s, 6 H), 6.50 (s, 1 H), 6.70 (s, 1 H); IR (KBr) 1609, 1256, 1151, 1021 cm^{-1}.

Freshly prepared Raney nickel (from 1.5 g of Ni/Al alloy) was added to the above thioketal (39 mg, 0.10 mmol) in absolute ethanol (4 mL), and the mixture was refluxed. After 2 h, the reaction mixture was filtered and concentrated. The residue was diluted with Et_2O (10 mL) and washed with 10 mL of 10% aqueous HCl. Standard ethereal workup, followed by chromatography (elution with H:E, 5:1), gave 22 mg (71% for two steps) of tricycle **69** as a viscous oil which was homogeneous by TLC analysis [H:E, 4:1, R_f(thioketal) = 0.22, R_f(**69**) = 0.31]: ^{1}H NMR (300 MHz) δ 0.95 (s, 6 H), 1.20 (s, 3 H), 1.18−1.95 (m, 7 H), 2.18−2.45 (m, 2 H), 2.78−2.88 (m, 2 H), 3.85 (s, 6 H), 6.50 (s, 1 H), 6.80 (s, 1 H); ^{13}C NMR (75.5 MHz) 146.9 (s), 146.6 (s), 142.1 (s), 127.3 (s), 111.3 (d), 107.8 (d), 55.9 (q), 55.6 (q), 50.6 (d), 41.6 (t), 39.0 (t), 37.5 (s), 33.3 (q), 30.1 (t), 29.6 (s), 24.8 (q), 21.5 (q), 19.3 (t), 19.1 (t) ppm; IR (film) 1606, 1254, 1152, 1073 cm^{-1}.

12,13-Dimethoxy-8,11,13-podocarpatrien-7-one (70). PCC (104 mg, 0.48 mmol) was added to tricycle **69** (34 mg, 0.12 mmol) dissolved in 2 mL of CH_2Cl_2. After 5 h, the reaction was diluted with Et_2O (10 mL) and the resulting mixture was filtered through a short pad of silica gel. Concentration of the combined ethereal phases provided 27 mg of ketone **70** (77%) as a viscous yellow oil which was homogeneous by TLC analysis [H:E, 3:2, R_f(**70**) = 0.30]: ^{1}H NMR (300 MHz) δ 0.90 (s, 3H), 1.00 (s, 3 H), 1.24 (s, 3 H), 1.08−1.35 (m, 1 H), 1.47−1.92 (m, 5 H), 2.22−2.33 (m, 1 H), 2.57−2.70 (m, 2 H), 3.90 (s, 6 H), 6.80 (s, 1 H), 7.5 (s, 1 H); ^{13}C NMR (75.5 MHz) 198.3 (s), 153.8 (s), 151.3 (s), 147.3 (s), 124.2 (s), 108.6 (d), 105.6 (d), 55.9 (q), 55.9 (q), (the preceding signals overlap), 49.9 (d), 41.3 (t), 38.1 (t), 38.1 (s), (the preceding signals overlap), 35.9 (t), 33.2 (s), 32.6 (q), 23.2 (q), 21.3 (q), 18.9 (t) ppm.

Nimbidiol Acetate (71). Boron tribromide (0.60 mL of 1.0 M solution in CH_2Cl_2) was added to a solution of bis-ether **70** (27 mg, 0.90 mmol) in CH_2Cl_2 (1 mL) cooled to 0 °C. After 2 h, the reaction was neutralized with saturated aqueous $NaHCO_3$. Standard ethereal workup gave 17.4 mg of (±)-nimbidiol (**62**) as a viscous oil which was homogeneous by TLC analysis [H:E, 3:2, R_f(**70**) = 0.30, R_f(**62**) = 0.05]: ^{1}H NMR (300 MHz) δ 0.98 (s, 3 H), 0.92 (s, 3 H), 1.23 (s, 3 H), 1.45−1.68 (m, 2 H), 1.69−1.90 (m, 4 H), 2.15−2.31 (m, 2 H), 2.57−2.70 (m, 2 H), 6.37 (br s, 1 H), 6.87 (s, 1 H), 7.73 (s, 1 H).

Nimbidiol was further characterized as its diacetate. The above crude nimbidiol was dissolved in pyridine (2 mL), and Ac_2O (0.5 mL) was added. After 4 h, the reaction was diluted with ether (10 mL). Standard ethereal workup, followed by chromatography (elution with H:E, 3:2), provided 22 mg (71% for two steps) of nimbidiol acetate (**71**) as an off-white solid which was homogeneous by TLC analysis [H:E, 3:2, R_f(**71**) = 0.25]: mp 158−160 °C (lit.[22] mp 160 °C); ^{1}H NMR (250 MHz) δ 0.93 (s, 3 H), 0.99 (s, 3 H), 1.26 (s, 3 H), 1.48−1.85 (m, 6 H), 1.91 (dd, 1 H, J = 13.0 Hz, 5.0 Hz), 2.29 (s, 3 H), 2.30 (s, 3 H), 2.61−2.75 (m, 2 H), 7.19 (s, 1 H), 7.80 (s, 1 H); ^{13}C NMR (62.5 MHz) 197.6 (s), 168.2 (s), 167.8 (s), 155.0 (s), 146.4 (s), 140.4 (s), 129.6 (s), 122.4 (d), 119.2 (d), 49.1 (d), 41.1 (t), 38.2 (s), 37.8 (t), 35.9 (t), 33.3 (s), 32.5 (q), 23.4 (q), 21.3 (q), 20.7 (q), 20.6 (q), 18.7 (t) ppm.

5-Allyl-2-isopropyl-1-methoxybenzene (73). To a cold (−40 °C) solution of cuprous iodide (1.35 g, 7.06 mmol) suspended in ether (30 mL) was added 70.6 mL of vinylmagnesium bromide (71.0 mmol, 1 M solution in THF). After the solution was stirred for 15 min, 11.45 g of benzyl bromide **72** (4.71 mmol) in 40 mL of ether was added. The reaction mixture was maintained at −40 °C for 1 h, then warmed up to −25 °C, and stirred for a period of 10 h. Standard ethereal workup, followed by chromatography (elution with hexanes), gave 8.44 g of adduct **73** (95%) as a slightly yellow liquid which was homogeneous by TLC analysis [hexanes, R_f(**73**) = 0.40]: ^{1}H NMR (300 MHz) δ 1.20 (d, 6 H, J = 6.9 Hz), 3.28 (septet, 1 H, J = 6.9 Hz), 3.37 (d, 2 H, J = 6.6 Hz), 3.82 (s, 3 H), 5.05−

5.15 (m, 2 H), 5.90−6.05 (m, 1 H), 6.68 (br s, 1 H), 6.77 (d, 1 H, J = 7.9 Hz), 7.13 (d, 1 H, J = 7.8 Hz); ^{13}C NMR (75.5 MHz) 156.7 (s), 138.5 (s), 137.5 (d), 134.7 (s), 125.9 (d), 120.5 (d), 115.7 (t), 110.7 (d), 55.3 (q), 40.2 (t), 26.4 (d), 22.7 (q) ppm; IR (film) 3076, 1637, 1608, 1578, 1502, 1464, 1418, 914, 817 cm^{-1}; MS, m/z 158 (M^+ − MeOH). Anal. Calcd for $C_{13}H_{18}O$: C, 82.05; H, 9.54. Found: C, 82.16; H, 9.47.

5-[2′,3′-Epoxypropyl]-2-isopropyl-1-methoxybenzene (74). Arene **73** (8.44 g, 4.44 mmol) was dissolved in CH_2Cl_2 (150 mL) followed by the addition of 18.63 g (0.22 mol) of $NaHCO_3$. The mixture was cooled to −5 °C, and 18.00 g of MCPBA (85%, 8.87 mmol) was added in small portions. The reaction mixture was stirred and allowed to warm to rt over a 4-h period. The solids were then filtered, and the filtrate was washed with saturated aqueous $NaHCO_3$ (15 mL). Standard ethereal workup, followed by chromagotraphy (elution with H:E, 4:1), gave 5.95 g of epoxide **74** (65%) which was homogeneous by TLC analysis [H:E, 4:1, R_f(**74**) = 0.30]: ^{1}H NMR (250 MHz) δ 1.20 (d, 6 H, J = 6.9 Hz), 2.58 (dd, 1 H, J = 2.7 Hz, 4.7 Hz), 2.80−2.88 (m, 3 H), 3.16−3.20 (m, 1 H), 3.29 (septet, 1 H, J = 6.9 Hz), 3.83 (s, 3 H), 6.74 (br s, 1 H), 6.81 (d, 1 H, J = 7.8 Hz), 7.15 (d, 1 H, J = 7.6 Hz); ^{13}C NMR (62.5 MHz) 156.7 (s), 135.6 (s), 135.2 (s), 125.9 (d), 120.8 (d), 111.0 (d), 55.2 (q), 52.5 (d), 46.9 (t), 38.7 (t), 26.4 (d), 22.6 (q) ppm; IR (film) 1613, 1576, 1505, 1463, 1040 cm^{-1}; MS, m/z 206 (M^+).

5-[2′-Hydroxybutyl]-2-isopropyl-1-methoxybenzene (75). To a cold (−30 °C) solution of cuprous iodide (1.08 g, 5.70 mmol) suspended in ether (40 mL) was added 19.0 mL of methylmagnesium bromide (5.70 mmmol, 1 M solution in ether) followed by the addition of 5.87 g of epoxide **74** (2.85 mmol). The reaction mixture was stirred at −30 °C for 4 h, warmed to −10 °C, and carefully quenched with saturated NH_4Cl. Standard ethereal workup, followed by chromatography (elution with H:E, 2:1), gave 5.88 g of alcohol **75** (93%) which was homogeneous by TLC analysis [H:E, 2:1, R_f(**75**) = 0.27]: ^{1}H NMR (250 MHz) δ 1.02 (t, 3 H, J = 7.3 Hz), 1.22 (d, 6 H, J = 7.0 Hz), 1.50−1.65 (m, 2 H), 2.60 (dd, 1 H, J = 13.8 Hz, 8.5 Hz), 2.83 (dd, 1 H, J = 13.8 Hz, 5.5 Hz), 3.27 (septet, 1 H, J = 7.0 Hz), 3.70−3.80 (m, 1 H), 3.84 (s, 3 H), 6.72 (d, 1 H, J = 1.0 Hz), 6.80 (dd, 1 H, J = 7.7 Hz, 1.0 Hz), 7.16 (d, 1 H, J = 7.7 Hz); ^{13}C NMR (62.5 MHz) 156.8 (s), 136.9 (s), 135.0 (s), 126.1 (d), 121.3 (d), 111.4 (d), 74.0 (d), 55.3 (q), 43.5 (t), 29.6 (t), 26.4 (d), 22.7 (q), 10.1 (q) ppm; IR (film) 3389, 1608, 1576, 1505, 1096, 1040 cm^{-1}; MS, m/z 222 (M^+).

2-[4′-Isopropyl-3′-methoxyphenyl]butan-3-one (76). Alcohol **75** (620 mg, 2.81 mmol) was oxidized using procedure F. Chromatography (elution with H:E, 4:1) of the residue gave 560 mg of butanone **76** (90%) which was homogeneous by TLC analysis [H:E, 3:1, R_f(**76**) = 0.38]: ^{1}H NMR (250 MHz) δ 1.03 (t, 3 H, J = 7.3 Hz), 1.20 (d, 6 H, J = 7.1 Hz), 2.49 (q, 2 H, J = 7.3 Hz), 3.29 (septet, 1 H, J = 7.1 Hz), 3.65 (s, 2 H), 3.82 (s, 3 H), 6.68 (d, 1 H, J = 1.2 Hz), 6.77 (dd, 1 H, J = 7.7 Hz, 1.2 Hz), 7.15 (d, 1 H, J = 7.7 Hz); ^{13}C NMR (62.5 MHz) 209.3 (s), 156.8 (s), 135.6 (s), 132.7 (s), 126.1 (d), 121.4 (d), 111.2 (d), 55.3 (q), 49.8 (t), 35.0 (t), 26.4 (d), 22.6 (q), 7.7 (q) ppm; IR (film) 1689, 1604, 1580, 1500, 1256 cm^{-1}; MS, m/z 220 (M^+). Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 76.21; H, 9.30.

2-[4′-Isopropyl-3′-methoxyphenyl]pentan-3-one (77). Butanone **76** (500 mg, 2.36 mmol) was treated with NaH (60% suspension in mineral oil, 104 mg, 2.60 mmol) and iodomethane (0.44 mL, 7.08 mmol) using procedure G. Standard ethereal workup, followed by chromatography (elution with H:E, 5:1), gave 400 mg of pentanone **77** (75%) which was homogeneous by TLC analysis [H:E, 4:1, R_f(**77**) = 0.49]: ^{1}H NMR (250 MHz) δ 0.97 (t, 3 H, J = 7.3 Hz), 1.19 (d, 6 H, J = 6.9 Hz), 1.38 (d, 3 H, J = 7.2 Hz), 2.31−2.47 (m, 2 H), 3.26 (septet, 1 H, J = 6.9 Hz), 3.72 (q, 1 H, J = 7.1 Hz), 3.81 (s, 3 H), 6.64 (d, 1 H, J = 1.5 Hz), 6.77 (dd, 1 H, J = 7.8 Hz, 1.5 Hz), 7.13 (d, 1 H, J = 7.8 Hz); ^{13}C NMR (62.5 MHz) 211.7 (s), 157.0 (s), 139.1 (s), 135.6 (s), 126.2 (d), 119.9 (d), 109.3 (d), 55.2 (q), 52.5 (d), 34.0 (t), 26.4 (d), 22.5 (q), 17.4 (q), 7.9 (q) ppm; IR (film) 2966, 2872, 1717, 1609, 1576 cm^{-1}; MS, m/z 234 (M^+).

2,4-Dimethyl-6-[4′-isopropyl-3′-methoxyphenyl]-3-methoxycyclohex-2-enone (78). The above pentanone derivative (2.30 g, 9.81 mmol) was treated with KO-*t*-Bu (1.21 g, 11.0 mmol) and methyl acrylate (1.0 mL, 11.0 mmol) using protocol I to afford 1.78 g of crude 4-[4′-isopropyl-3′-methoxyphenyl]-2,4-dimethylcyclohexane-1,3-dione which was converted, using procedure J, to 820 mg (30% from **77**) of enone **78** as a light yellow oil which was homogeneous by TLC analysis [H:E, 3:1, R_f(**78**) = 0.19]: ^{1}H NMR (250 MHz) δ 1.17 (d, 6 H, J = 6.9 Hz), 1.39 (s, 3 H), 1.75 (s, 3 H), 1.95−2.10 (m, 1 H), 2.25−2.55 (m, 3 H), 3.24 (septet, 1 H, J = 6.9 Hz), 3.70 (s, 3 H), 3.76 (s, 3 H), 6.63 (d, 1 H, J = 1.8 Hz), 6.75 (dd, 1 H, J = 1.8 Hz, 7.9 Hz), 7.09 (d, 1 H, J = 7.9 Hz); ^{13}C NMR (62.7 MHz) 201.3 (s), 170.2 (s), 156.6 (s), 141.1 (s), 135.0 (s), 125.6 (d), 117.8 (d), 114.0 (s), 108.6 (d), 55.2 (q), 54.8 (q), 47.8 (s), 33.8 (t), 27.2 (q), 26.4 (d), 22.6 (q), 22.6 (t), 7.9 (q) ppm; IR (film) 1650, 1625 cm^{-1}; MS, m/z 302 (M^+).

4-[4′-Isopropyl-3′-methoxyphenyl]-2,4-dimethyl-3-vinylcyclohex-2-enone (79). Enone **78** (800 mg, 2.65 mmol) was treated with excess vinyllithium (13.20 mmol) using procedure K to provide 710 mg of dienone **79** (90%) as a bright yellow solid which was homogeneous by TLC analysis [H:E, 4:1, R_f(**79**) = 0.31]: mp 43−44 °C; ^{1}H NMR (250 MHz) δ 1.19 (d, 6 H, J = 6.8 Hz), 1.60 (s, 3 H), 2.00 (s, 3 H), 2.04−2.15 (m, 2 H), 2.30−2.42 (m, 2 H), 3.26 (septet, 1 H, J = 6.8 Hz), 3.78 (s, 3 H), 5.15 (dd, 1 H, J = 1.5 Hz, 18.0 Hz), 5.40 (dd,1 H, J = 1.5 Hz, 11.7 Hz), 6.23 (dd, 1 H, J = 18.0 Hz, 11.7 Hz), 6.72 (d, 1 H, J = 1.6 Hz), 6.81 (dd, 1 H, J = 7.9 Hz, 1.6 Hz), 7.12 (d, 1 H, J = 7.9 Hz); ^{13}C NMR (62.5 MHz) 199.6 (s), 157.7 (s), 156.7 (s), 143.9 (s), 135.1 (s), 134.2 (d), 132.6 (s), 125.7 (d), 122.3 (t), 118.9 (d), 108.9 (d), 55.3 (q), 43.5 (s), 39.8 (t), 34.3 (t), 26.9 (q), 26.4 (d), 22.6 (q), 12.9 (q) ppm; IR (film) 1690, 1606, 1571 cm^{-1}; MS, m/z 298 (M^+). Anal. Calcd for $C_{20}H_{26}O_2$: C, 80.50; H, 8.78. Found: C, 80.65; H, 8.70.

Cyclization of 79 To Give 80. A solution of 100 mg of **79** (0.34 mmol) and 410 μL of $BF_3{\cdot}Et_2O$ (3.35 mmol) in 8 mL of CH_2Cl_2 was refluxed for 8 h. The reaction mixture was diluted with 10 mL of ether and quenched with 10 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 3:1), gave 87 mg of known enone **80** (87% yield) as a white solid which was homogeneous by TLC analysis [H:E, 3:1, R_f(**80**) = 0.23]: mp 91−92 °C (lit.[30] mp 91−92 °C); ^{1}H NMR (250 MHz) δ 1.18 (d, 3 H, J = 7.0 Hz), 1.21 (d, 3 H, J = 7.0 Hz), 1.53 (s, 3 H), 1.84 (s, 3 H), 2.00−2.20 (m, 1 H), 2.30−2.45 (m, 1 H), 2.47−2.53 (m, 1 H), 2.55−2.60 (m, 1 H), 2.65−3.00 (m, 4 H), 3.26 (septet, 1 H, J = 7.0 Hz), 3.82 (s, 3 H), 6.73 (s, 1 H), 6.92 (s, 1 H); ^{13}C NMR (62.5 MHz) 198.1 (s), 162.6 (s), 155.7 (s), 142.5 (s), 134.9 (s), 128.4 (s), 127.2 (s), 125.8 (d), 107.4 (d), 55.4 (q), 39.6 (s), 36.1 (t), 34.1 (t), 29.3 (t), 27.5 (t), 26.8 (q), 26.3 (d), 22.6 (q), 10.8 (q) ppm; IR (film) 1686, 1614 cm^{-1}; MS, m/z 298 (M^+).

2-[2′,3′-Dimethoxy-4′-isopropylphenyl]cyclohex-2-enone (81). To a solution of isopropylveratrole (5.0 g, 27.78 mmol) dissolved in 45 mL of dry ether at 0 °C was added 12.8 mL (32.00 mmol) of *n*-butyllithium (2.5 M solution in hexanes), and the mixture was stirred for 3 h at rt. The resulting solution of the organolithium reagent was used directly without purification or characterization.

The above solution of organolithium reagent was reacted with epoxide **1** (2.50 g, 13.89 mmol) using procedure A to give 3.52 g of recovered isopropylveratrole and 1.95 g of enone **81** (51%) which was homogeneous by TLC analysis [H:E, 1:1, R_f(**81**) = 0.31]: ^{1}H NMR (250 MHz) δ 1.22 (d, 6 H, J = 6.7 Hz), 2.14 (pentet, 2 H, J = 6.6 Hz), 2.49−2.64 (m, 4 H), 3.32 (septet, 1 H, J = 6.6 Hz), 3.77 (s, 3 H), 3.84 (s, 3 H), 6.86 (ABq, 2 H, $\Delta\nu_{AB}$ = 42.5 Hz, J_{AB} = 8.0 Hz), 6.91 (t, 1 H, J = 4.0 Hz); ^{13}C NMR (62.7 MHz) 197.9 (s), 150.3 (s), 149.9 (s), 146.1 (d), 142.8 (s), 136.6 (s), 129.2 (s), 125.1 (d), 120.9 (d), 60.4 (q), 60.1 (q), 36.6 (t), 26.7 (d), 26.3 (t), 23.5 (q), 23.1 (t) ppm; IR (film) 1679, 1453, 1405, 1268 cm^{-1}; MS, m/z 274 (M^+). Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.42; H, 8.09. Found: C, 74.31; H, 8.13.

2-[2′,3′-Dimethoxy-4′-isopropylphenyl]-6,6-dimethylcyclohex-2-enone (82). The procedure used for the preparation of 2-[2′,3′-dimethoxy-4′-isopropylphenyl]-6-methylcyclohex-2-enone were presented earlier as procedure L.

This enone (1.20 g, 4.17 mmol) was further alkylated with iodomethane using procedure K to provide 1.21 g of enone **82** (95%) which was homogeneous by TLC analysis [H:E, 2:1, R_f(**82**) = 0.75]: ^{1}H NMR (250 MHz) δ 1.21 (d, 6 H, J = 6.8 Hz), 1.22 (s, 6 H), 1.94 (t, 2 H, J = 6.2 Hz), 2.47−2.54 (m, 2

H), 3.31 (septet, 1 H, J = 6.8 Hz), 3.71 (s, 3 H), 3.81 (s, 3 H), 6.74 (t, 1 H, J = 3.9 Hz), 6.84 (ABq, 2 H, $\Delta\nu_{AB}$ = 41.0 Hz, J_{AB} = 7.8 Hz); ^{13}C NMR (62.7 MHz) 202.6 (s), 150.3 (s), 149.8 (s), 145.3 (d), 142.6 (s), 137.1 (s), 129.9 (s), 125.1 (d), 120.8 (d), 60.4 (q), 59.9 (q), 41.6 (s), 36.3 (t), 29.6 (t), 26.6 (d), 24.1 (q), 23.5 (q) ppm; IR (film) 1679, 1452, 1405, 1268 cm^{-1}; MS, m/z 302 (M$^+$). Anal. Calcd for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.58; H, 8.78.

2-[2′,3′-Dimethoxy-4′-isopropylphenyl]-6,6-dimethyl-1-vinylcyclohex-2-en-1-ol (83). Enone **82** (783 mg, 2.54 mmol) was treated with 4.0 equiv of vinyllithium using procedure B to provide 720 mg of bis-allylic tertiary alcohol **83** (86%) which was homogeneous by TLC analysis [H:E, 1:1, R_f(**82**) = 0.64, R_f(**83**) = 0.78]: mp 60−62 °C; ^{1}H NMR (300 MHz) δ 0.95 (s, 3 H), 1.08 (s, 3 H), 1.19−1.24 (m, 6 H), 1.55−1.66 (m, 1 H), 1.71−1.83 (m, 1 H), 2.16−2.30 (m, 2 H), 3.27 (septet, 1 H, J = 6.9 Hz), 3.80 (s, 3 H), 3.81 (s, 3 H), 4.33 (s, 1 H), 5.01 (d, 1 H, J = 10.9 Hz), 5.17 (d, 1 H, J = 17.0 Hz), 5.70−5.79 (m, 2 H), 6.78 (ABq, 2H, $\Delta\nu_{AB}$ = 60.0 Hz, J_{AB} = 7.9 Hz); ^{13}C NMR (75.5 MHz) 149.8 (s), 148.5 (s), 141.6 (s), 140.5 (d), 139.9 (s), 134.1 (s), 129.3 (d), 126.6 (d), 121.3 (d), 113.7 (t), 77.9 (s), 60.8 (q), 60.0 (q), 36.7 (s), 32.6 (t), 32.6 (t) (the preceding signals overlap), 26.8 (d), 23.8 (q), 23.6 (q), 23.3 (q), 22.6 (q) ppm; IR (film) 3475, 1452, 1403, 1268 cm^{-1}.

2-[2′,3′-Dimethoxy-4′-isopropylphenyl]-4,4-dimethyl-3-vinylcyclohex-2-enone (60). Tertiary alcohol **83** (695 mg, 2.11 mmol) was oxidized over a period of 2 days using procedure D and 1.58 g of PDC (4.21 mmol) to furnish 470 mg of dienone **60** (68%) as a yellow oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(**83**) = 0.90, R_f(**60**) = 0.60]: ^{1}H NMR (300 MHz) δ 1.21 (d, 6 H, J = 6.9 Hz), 1.30 (s, 3 H), 1.32 (s, 3 H), 1.99 (t, 2 H, J = 6.9 Hz), 2.63 (t, 2 H, J = 7.2 Hz), 3.29 (septet, 1 H, J = 6.9 Hz), 3.68 (s, 3 H), 3.79 (s, 3 H), 5.03 (dd, 1 H, J = 17.7 Hz, 1.5 Hz), 5.14 (dd, 1 H, J = 12.0 Hz, 1.5 Hz), 6.21 (dd, 1 H, J = 17.7 Hz, 1.23 Hz), 6.74 (ABq, 2 H, $\Delta\nu_{AB}$ = 89.5 Hz, J_{AB} = 7.9 Hz); ^{13}C NMR (75.5 MHz) 198.1 (s), 162.3 (s), 150.4 (s), 150.3 (s), 141.9 (s), 133.8 (d), 133.3 (s), 128.7 (s), 126.0 (d), 120.8 (t), 120.7 (d), 60.6 (q), 60.6 (q), 37.7 (t), 35.4 (s), 34.5 (t), 27.6 (q), 27.3 (q), 26.8 (d), 23.6 (q), 23.5 (q) ppm; IR (film) 1673, 1450, 1406, 1261 cm^{-1}; MS, m/z 328 (M$^+$). Anal. Calcd for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found: C, 76.78; H, 8.53.

Cyclization of 60 To Give 84 and 61. A solution of 130 mg of **60** (0.40 mmol) and 317 μL of BF_3·Et_2O (2.59 mmol) in 5 mL of CCl_4 was refluxed for 6 h. The reaction mixture was diluted with 100 mL of ether and neutralized with 15 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 1:1, R_f(**60**) = 0.60, R_f(**61**) = 0.76), gave 18 mg of **61** (15% yield) as a light yellow solid which was identical to that previosuly characterized in the thermal rearrangement of **60**.

Continued elution gave 83 mg of enone **84** (64%) as a light yellow solid which was homogeneous by TLC analysis [H:E, 1:1, R_f(**84**) = 0.53]: mp 100−101 °C (lit.[37] oil); ^{1}H NMR (250 MHz) δ 1.19 (s, 9 H), 1.21 (s, 3 H), 1.93 (t, 2 H, J = 7.0 Hz), 2.31 (t, 2 H, J = 7.0 Hz), 2.54 (t, 2 H, J = 7.0 Hz), 2.64 (t, 2 H, J = 7.0 Hz), 3.30 (septet, 1 H, J = 7.0 Hz), 3.79 (s, 3 H), 3.83 (s, 3 H), 6.76 (s, 1 H); ^{13}C NMR (75.5 MHz) 195.0 (s), 165.7 (s), 149.3 (s), 148.8 (s), 141.6 (s), 133.3 (s), 131.2 (s), 123.1 (s), 119.1 (d), 60.4 (q), 59.7 (q), 36.0 (s), 35.8 (t), 34.2 (t), 29.0 (t), 26.5 (d), 25.8 (q), 25.4 (t), 23.6 (q) ppm; IR (film) 1673, 1450, 1407, 1227 cm^{-1}; MS, m/z 328 (M$^+$). Anal. Calcd for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found: C, 76.73; H, 8.62.

Sageone (67). To a solution of bis-ether **84** (31 mg, 0.095 mmol) in 3 mL of CH_2Cl_2 at −78 °C was added 0.47 mL of BBr_3 (1 M solution in CH_2Cl_2). The mixture was allowed to warmed up to −10 °C over 2 h. The resulting solution was diluted with ether (30 mL) and neutralized with 10 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 2:3), gave 25 mg of sageone (**67**) (88% yield) as a milky white oil which was homogeneous by TLC analysis [H:E, 1:1, R_f(**67**) = 0.32]: ^{1}H NMR (250 MHz) δ 1.24 (d, 6 H, J = 6.8 Hz), 1.28 (s, 6 H), 1.94 (t, 2 H, J = 6.8 Hz), 2.43−2.37 (m, 2 H), 2.50−2.58 (m, 2 H), 2.69 (t, 2 H, J = 6.7 Hz), 3.30 (septet, 1 H, J = 6.8 Hz), 6.19 (s, 1 H), 6.59 (s, 1 H), 9.46 (s, 1 H); ^{13}C NMR (62.7 MHz) 202.0 (s), 175.7 (s), 143.2 (s), 139.8 (s), 133.0 (s), 130.2 (s), 127.4 (s), 116.5 (d), 116.5 (d) (the preceding signals overlap), 37.1 (s), 35.5 (t), 35.2 (t), 28.3 (t), 27.3 (t), 27.1 (d), 26.1 (q), 22.4 (q) ppm.

Aromatization of 84 Using DDQ. Compound **84** (15 mg, 0.046 mmol) and DDQ (20.8 mg, 0.091 mmol) were dissolved in 2 mL of benzene, and the resulting mixture was refluxed for 12 h. The reaction mixture was diluted with ether (25 mL) and filtered through a short pad of silica gel. Removal of the volatiles, followed by chromatography (elution with H:E, 2:1), gave 8 mg of naphthalene **85** (51%) as an off-white solid which was homogeneous by TLC analysis [H:E, 1:1, R_f(**84**) = 0.53, R_f(**85**) = 0.62]: mp 64−66 °C; ^{1}H NMR (250 MHz) δ 1.31 (d, 6 H, J = 6.9 Hz), 1.38 (s, 6 H), 2.12 (t, 2 H, J = 7.1 Hz), 2.95 (t, 2 H, J = 7.1 Hz), 3.42 (septet, 1 H, J = 6.9 Hz), 3.90 (s, 3 H), 3.93 (s, 3 H), 7.40 (s, 1 H), 7.57 (ABq, 2 H, $\Delta\nu_{AB}$ = 110 Hz, J_{AB} = 8.6 Hz); ^{13}C NMR (62.7 MHz) 199.8 (s), 151.2 (s), 150.1 (s), 147.8 (s), 143.0 (s), 131.8 (d), 130.7 (s), 129.7 (s), 124.1 (s), 121.3 (d), 119.8 (d), 60.5 (q), 59.5 (q), 36.6 (t), 36.6 (t) (the preceding signals overlap), 35.1 (s), 28.6 (q), 27.3 (d), 23.4 (q) ppm; IR (film) 1674, 1454, 1405, 1259 cm^{-1}; MS, m/z 326 (M$^+$). Anal. Calcd for $C_{21}H_{26}O_3$: C, 77.27; H, 8.03. Found: C, 77.11; H, 8.07.

Aromatization of 84 Using KOC(CH$_3$)$_3$ in *tert*-Butyl Alcohol. Compound **84** (300 mg, 0.91 mmol) and KO-*t*-Bu (205 mg, 1.83 mmol) in 15 mL of *t*-butanol was refluxed for 4.5 h. Standard ethereal workup, followed by chromatography (elution with H:E, 2:1), gave 224 mg of **85** (75%) as a yellow solid which was identical to that previously characterized.

Aromatization of 84 Using Dimyslsodium. Compound **84** (11 mg, 0.038 mmol) and NaH (60% suspended in oil, 2 mg, 0.05 mmol) were heated in 3 mL of DMSO for 30 min. Standard ethereal workup, followed by chromatography (elution with H:E, 2:1), gave 8 mg of naphthalene **85** (74%) which was identical to that previously characterized.

Aromatization of 84 Using KOH. Compound **84** (8 mg, 0.024 mmol) and KOH (2.7 mg, 0.05 mmol) was dissolved in 2 mL of ethanol and 200 μl of water, and the resulting mixture was refluxed for 16 h. Standard ethereal workup, followed by chromatography (elution with H:E, 2:1), gave 5 mg of naphthalene **85** (62%) which was identical to that previously characterized.

Aromatization of 84 Using KOC(CH$_3$)$_3$ in THF. Compound **84** (13 mg, 0.040 mmol) and KO-*t*-Bu (12 mg, 0.11 mmol) were dissolved in 2 mL of THF, and the resulting mixture was refluxed for 4 h. Standard ethereal workup, followed by chromatography (elution with H:E, 2:1), gave 8 mg of naphthalene **85** (61%) which was identical to that previously characterized.

Aromatization of 84 Using Catalytic KOC(CH$_3$)$_3$. Compound **84** (72 mg, 0.22 mmol) and KO-*t*-Bu (5 mg, 0.044 mmol) were dissolved in 3 mL of *t*-butanol, and the resulting mixture was refluxed for 4 days. Standard ethereal workup, followed by chromatography (elution with H:E, 2:1), gave 38 mg of naphthalene **85** (53%) which was identical to that previously characterized, along with 19 mg (26%) of recovered **84**.

Aromatization of 32 To Give 86. Compound **32** (90 mg, 0.31 mmol) and KO-*t*-Bu (67 mg, 0.61 mmol) were dissolved in 6 mL of *t*-butanol, and the resulting mixture was refluxed for 3 h. Standard ethereal workup, followed by chromatography (elution with H:E, 2:1), gave 81 mg of naphthalene **86** (90%) which was homogeneous by TLC analysis [H:E, 2:1, R_f(**86**) = 0.47]: ^{1}H NMR (250 MHz) δ 1.45 (s, 6 H), 2.09 (t, 2 H, J = 6.8 Hz), 2.85 (t, 2 H, J = 6.8 Hz), 4.01 (s, 3 H), 4.06 (s, 6 H), 7.09 (s, 1 H), 7.42 (d, 1 H, J = 8.6 Hz), 7.85 (d, 1 H, J = 8.6 Hz), 8.97 (s, 1 H); ^{13}C NMR (62.7 MHz) 201.3 (s), 152.0 (s), 151.6 (s), 148.9 (s), 132.9 (d), 128.5 (s), 127.1 (s), 124.8 (s), 122.0 (d), 106.3 (d), 106.1 (d), 55.9 (q), 55.7 (q), 37.3 (t), 36.9 (t), 35.0 (s), 30.3 (q) ppm; IR (film) 1667 cm^{-1}; MS, m/z 284 (M$^+$). Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.02; H, 7.09. Found: C, 75.83; H, 6.97.

Aromatization of 34 To Give 87. Compound **34** (18 mg, 0.063 mmol) and KO-*t*-Bu (13 mg, 0.12 mmol) were dissolved in 2 mL of *t*-butanol, and the resulting mixture was refluxed for 3 h. Standard ethereal workup, followed by chromatography (elution with H:E, 2:1), gave 13 mg of naphthalene **87** (73%) which was homogeneous by TLC analysis [H:E, 2:1, R_f(**87**) = 0.47]: mp 109−111 °C; ^{1}H NMR (250 MHz) δ 1.45 (s,

6 H), 2.07 (t, 2 H, J = 6.6 Hz), 2.84 (t, 2 H, J = 6.6 Hz), 3.96 (s, 6 H), 6.52 (d, 1 H, J = 2.0 Hz), 7.37 (d, 1 H, J = 8.9 Hz), 8.36 (d, 1 H, J = 8.9 Hz), 8.47 (d, 1 H, J = 2.0 Hz); ^{13}C NMR (62.7 MHz) 201.1 (s), 160.9 (s), 156.2 (s), 154.9 (s), 133.2 (s), 128.3 (d), 124.8 (s), 120.7 (s), 120.4 (d), 97.5 (d), 97.4 (d), 55.5 (q), 55.3 (q), 37.3 (t), 36.6 (t), 35.1 (s), 29.9 (q) ppm; IR (film) 1663, 1619, 1592, 1260 cm^{-1}; MS, m/z 284 (M^+).

Aromatization of 36 To Give 88. Compound **36** (28 mg, 0.097 mmol) and KO-*t*-Bu (32 mg, 0.29 mmol) were dissolved in 2 mL of *t*-butanol, and the resulting mixture was refluxed for 3 h. Standard ethereal workup, followed by chromatography (elution with H:E, 2:1), gave 20 mg of naphthalene **88** (72%) which was homogeneous by TLC analysis [H:E, 2:1, R_f(**88**) = 0.67]: mp 109−111 °C; ^{1}H NMR (250 MHz) δ 1.37 (s, 6 H), 2.11 (t, 2 H, J = 7.1 Hz), 2.92 (t, 2 H, J = 7.1 Hz), 3.88 (s, 3 H), 3.95 (s, 3 H), 6.76 (d, 1 H, J = 8.6 Hz), 6.89 (d, 1 H, J = 8.6 Hz), 7.44 (d, 1 H, J = 8.8 Hz), 8.29 (d, 1 H, J = 8.8 Hz); ^{13}C NMR (62.7 MHz) 199.8 (s), 151.7 (s), 149.6 (s), 130.4 (s), 125.8 (d), 125.7 (s), 122.7 (s), 125.4 (s), 122.1 (d), 108.1 (d), 104.3 (d), 58.1 (q), 55.8 (q), 36.5 (t), 36.5 (t) (the preceding signals overlap), 35.0 (s), 28.6 (q) ppm; IR (film) 1684, 1593, 1258 cm^{-1}; MS, m/z 284 (M^+).

Arucadiol (64). Boron tribromide (530 μL of 1.0 M solution in CH_2Cl_2) was added to a solution of bis-ether **85** (35 mg, 0.11 mmol) in CH_2Cl_2 (3 mL) cooled to −78 °C. The mixture was allowed to warm to 0 °C over a period of 2 h. The reaction was neutralized with 10 mL saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 4:1), gave 31 mg (95%) of synthetic arucadiol (**64**) as a red solid which was homogeneous by TLC analysis [H:E, 4:1, R_f(**64**) = 0.72]: mp 99−101 °C (lit.[29] mp 98−100 °C); ^{1}H NMR (300 MHz) δ 1.35 (d, 6 H, J = 6.8 Hz), 1.44 (s, 6 H), 2.07 (t, 2 H, J = 6.9 Hz), 2.92 (t, 2 H, J = 6.9 Hz), 3.44 (septet, 1 H, J = 6.8 Hz), 6.90 (s, 1 H), 7.28 (s, 1 H), 7.64 (ABq, 2 H, $\Delta\nu_{AB}$ = 186.0 Hz, J_{AB} = 8.5 Hz), 10.60 (s, 1 H); ^{13}C NMR (75.5 MHz) 204.3 (s), 158.2 (s), 144.9 (s), 138.1 (d), 137.6 (s), 136.5 (s), 127.7 (s), 125.3 (s), 120.3 (d), 120.1 (s), 118.7 (d), 36.3 (t), 36.0 (s), 35.4 (t), 29.6 (q), 27.7 (d), 22.2 (q) ppm; IR (film) 3472, 1637, 1413, 1313 cm^{-1}.

Miltirone (65). A mixture of ketone **85** (127 mg, 0.39 mmol) and tosylhydrazine (80 mg, 0.43 mmol) dissolved in 4 mL of absolute ethanol was stirred at rt for 15 h. After evaporation of the solvent, the resulting hydrazone was used directly without purification or charaterization.

To a solution of the above hydrazone (40 mg, 0.12 mmol) dissolved in 2mL of DMF and 2 mL of sulfolane were added 42 mg of sodium cyanoborohydride (0.68 mmol) and 1 mg of bromocresol green. The mixture was heated at 110 °C using an oil bath, and HCl was added until the color of the reaction mixture remained tan-yellow. The resulting mixture was heated at 110 °C for 5 h. Standard ethereal workup, followed by chromatography (elution with H:E, 6:1), gave 20 mg of **86** (52%) as a light oil which was homogeneous by TLC analysis [H:E, 4:1, R_f(**87**) = 0.79]: ^{1}H NMR (300 MHz) δ 1.29 (d, 6 H, J = 6.9 Hz), 1.35 (s, 6 H), 1.69−1.73 (m, 2 H), 1.80−1.89 (m, 2 H), 3.38 (septet, 1 H, J = 6.9 Hz), 3.43 (t, 2 H, J = 6.1 Hz), 3.86 (s, 3 H), 3.94 (s, 3 H), 7.34 (s, 1 H), 7.44 (ABq, 2 H, $\Delta\nu_{AB}$ = 49.5 Hz, J_{AB} = 8.7 Hz); ^{13}C NMR (75.5 MHz) 150.0 (s), 149.4 (s), 142.6 (s), 141.3 (s), 131.1 (s), 130.4 (s), 126.7 (s), 125.6 (d), 124.7 (d), 120.6 (d), 60.7 (q), 60.6 (q), 38.7 (t), 34.7 (s), 31.9 (q), 30.0 (t), 27.3 (d), 23.5 (q), 20.3 (t) ppm; IR (film) 1450, 1259 cm^{-1}.

BBr_3 (203 μL of 1.0 M in CH_2Cl_2) was added to a solution of bis-ether **86** (20 mg, 0.064 mmol) in CH_2Cl_2 (2 mL) cooled to −78 °C. The mixture was warmed to 0 °C over a period of 3 h. The reaction was neutralized with 5 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup provided a crude catechol (cf. **87**) which was used immediately without purification or characterization.

To a solution of the above catechol in 2 mL of a 3:1 mixture of acetonitrile and water was added cerium ammonium nitrate (126 mg, 0.23 mmol). A bright yellow solution was formed immediately. TLC analysis indicated that oxidation was complete; hence, the resulting solution was quenched with 1 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 6:1), gave 11 mg of **65** (61% for two steps) as a reddish solid which was homogeneous by TLC analysis [H:E, 2:1, R_f(**65**) = 0.52]: mp 97−99 °C (lit.[29] mp 99−101 °C); ^{1}H NMR (250 MHz) δ 1.16 (d, 6 H, J = 6.9 Hz), 1.29 (s, 6 H), 1.60−1.69 (m, 2 H), 1.74−1.86 (m, 2 H), 3.02 (septet, 1 H, J = 6.9 Hz), 3.17 (t, 2 H, J = 6.2 Hz), 7.07 (s, 1 H), 7.10, 7.35 (ABq, 2 H, $\Delta\nu_{AB}$ = 121.3 Hz, J_{AB} = 8.0 Hz); ^{13}C NMR (62.7 MHz) 182.3 (s), 181.4 (s), 149.5 (s), 144.9 (s), 144.4 (s), 139.8 (d), 134.3 (s), 133.7 (d), 128.1 (s), 127.8 (d), 37.7 (t), 34.4 (s), 31.6 (q), 29.8 (t), 26.7 (d), 21.4 (q), 18.9 (t) ppm.

1,2-Didehydromiltirone (66). To a solution of the hydrazone derived from **85** [cf. preparation of **65**] (127 mg, 0.39 mmol) dissolved in ether (6 mL) was added 0.75 mL of *n*-butyllithium (1.49 mmol, 1.98 M solution in hexanes). A brown solution was formed immediately. TLC analysis indicated that the reaction was complete. Standard ethereal workup, followed by chromatography (elution with H:E, 6:1), gave 100 mg of **88** (83%) which was homogeneous by TLC analysis [H:E, 2:1, R_f(**88**) = 0.83]: ^{1}H NMR (250 MHz) δ 1.31 (d, 6 H, J = 7.0 Hz), 1.32 (s, 6 H), 2.26−2.28 (m, 2 H), 3.29 (septet, 1 H, J = 7.0 Hz), 3.83 (s, 3 H), 3.93 (s, 3 H), 6.07 (dt, 1 H, J = 10.0 Hz, 5.0 Hz), 7.36 (s, 1 H), 7.52 (ABq, 2 H, $\Delta\nu_{AB}$ = 50.0 Hz, J_{AB} = 8.4 Hz), 7.93 (d, 1 H, J = 10.0 Hz); ^{13}C NMR (62.7 MHz) 150.0 (s), 149.4 (s), 142.1 (s), 141.4 (s), 131.0 (s), 127.5 (d), 127.0 (s), 126.5 (d), 125.6 (d), 123.6 (s), 121.8 (d), 120.8 (d), 61.1 (q), 60.4 (q), 37.6 (t), 34.1 (s), 28.0 (q), 27.3 (d), 23.3 (q) ppm; IR (film) 1652, 1460 cm^{-1}; MS, m/z 310 (M^+).

A solution of **88** (31mg, 0.10 mmol), NaH (60% suspension in mineral oil, 120 mg, 3.00 mmol), and 222 μL of ethanethiol in DMF (2 mL) was heated in 130 °C oil bath for 10 h. After standard ethereal workup, the crude catechol **89** was used immdiately without purification or characterization.

To a solution of the above catechol in 4 mL of a 3:1 mixture of acetonitrile was added cerium ammonium nitrate (164 mg, 0.30 mmol). A bright yellow solution was formed immediately. TLC analysis indicated that the oxidation was complete. The reaction mixture was quenched with1 mL of saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 6:1), gave 13 mg of **66** (43% for two steps) as a red solid which was homogeneous by TLC analysis [H:E, 2:1, R_f(**66**) = 0.83]: mp 69−73 °C (lit.[29] mp 71−75 °C); ^{1}H NMR (300 MHz) δ 1.16 (d, 6 H, J = 7.0 Hz), 1.28 (s, 6 H), 2.28 (dd, 2 H, J = 5.0 Hz, 2.0 Hz), 3.03 (septet, 1 H, J = 7.0 Hz), 6.33 (dt, 1 H, J = 10.0 Hz, 5.0 Hz), 7.09 (s, 1 H), 7.30 (ABq, 2 H, $\Delta\nu_{AB}$ = 117.0 Hz, J_{AB} = 7.8 Hz), 7.86 (d, 1H, J = 10.0 Hz); ^{13}C NMR (62.7 MHz) 183.1 (s), 181.4 (s), 147.9 (s), 147.9 (s) (the preceding signals overap), 144.9 (s), 139.9 (d), 137.2 (s), 134.4 (d), 134.1 (s), 130.5 (d), 129.1 (d), 124.6 (d), 37.9 (t), 33.9 (s), 28.3 (q), 26.9 (d), 21.6 (q) ppm.

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Supporting Information Available: ^{1}H and ^{13}C NMR for the intermediate prepared in the course of preparing substrates **6**, **7**, **8**, **9**, **10**, **11**, **12**, **13**, **14**, **15**, **16**, **17**, **18**, **19**, **20**, **21**, **22**, **23**, **24**, **25**, **26**, **27**, **28**, **29**, **30**, **31**, **32**, **33**, **34**, **35**, **36**, **37**, **38**, **39**, **40**, **41**, **42**, **43**, **44**, **45**, **46**, **47**, **48**, **49**, **50**, **51**, **52**, **53**, **54**, **55**, **56**, **57**, **58**, **58**, **59**, **60**, **61**, **62**, **63**, **64**, **65**, **66**, **67**, **68**, **69**, **70**, **71**, **72**, **73**, **74**, **75**, **76**, **77**, **78**, **79**, **80**, **81**, **82**, **83**, **84**, **85**, **86**, **87**, and **88** (146 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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