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Polyene Cascade Cyclizations Mediated by $BF_3 \cdot CH_3NO_2$. An Unusually Efficient Method for the Direct, Stereospecific Synthesis of Polycyclic Intermediates via Cationic Initiation at Non-functionalized 3° Alkenes. An Application to the Total Synthesis of (±)-Taxodione.†

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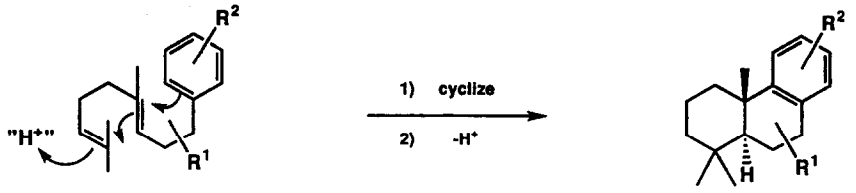
Abstract. Convenient stock solutions of BF_3 gas in nitromethane have been shown to promote "H^+ catalyzed" polyene cyclizations that proceed with excellent levels of regio- and stereocontrol. A *direct* comparison of this new method for effecting cationic polyannulations to several modern as well as classical procedures has conclusively defined the preparative advantages of the $BF_3 \cdot CH_3NO_2$ medium. The utilization of these new conditions for cationic polycyclization in a concise total synthesis of the antineoplastic agent (±)-taxodione is described.

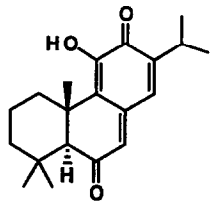
Introduction.

Cationic polyene cyclizations have enjoyed enduring popularity for the synthesis of multiply fused carbocyclic structures.[2] The power of this methodology derives in large part from the high levels of relative and absolute stereocontrol that typically accompany cyclization as well as the excellent regioselection that can be associated with the initiation and subsequent bond forming events.[3] Although numerous, elegant strategies have been developed for asymmetric initiation,[4] cyclization rate enhancement via internal cation stabilization[5] and initiation with the *net* incorporation of new functionality,[6] relatively little *recent* effort has been directed toward the improvement of polycyclization reactions that commence via *formal* protonation of non-functionalized 3° alkenes.[7] From a historical standpoint, Brönsted acids (e.g., H_2SO_4, FSO_3H),[8,9] and Lewis acids including $BF_3 \cdot OEt_2$[10-12] have been found useful to initiate just this kind of process. Regrettably, virtually *all* of these examples involve cyclizations that proceed with relatively low overall efficiency.[12] We have previously shown that solutions of gaseous BF_3 in CH_3NO_2 are vastly more effective than simple $BF_3 \cdot OEt_2$ (or other Lewis acids) for promoting sulfenylative and selenenylative cationic cyclizations.[6a] The unusual chemical reactivity of $BF_3 \cdot CH_3NO_2$ prompted us to examine the efficacy of this medium for inducing "H^+-initiated" cascade cyclizations (Scheme I). The successful development and utilization of an optimized experimental protocol for effecting "$BF_3 \cdot CH_3NO_2$" promoted polyene cycli-

zations as well as the application of this method in an unusually efficient total synthesis of the antineoplastic diterpene (±)-taxodione (1) are described below.



Scheme I



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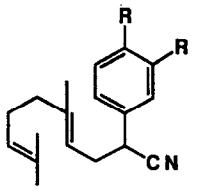
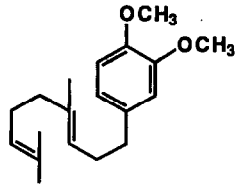
Cationic Cascade Annulations Mediated by $BF_3 \cdot CH_3NO_2$.

a) Synthesis of Precyclization Substrates.

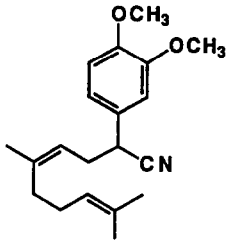
The precyclization substrates **2a** and **b** were readily prepared by sequential lithiation-alkylation of (3,4-dimethoxyphenyl)acetonitrile and phenylacetonitrile respectively with (*E*)-1-bromo-3,7-dimethyl-2,6-octadiene. Reductive decyanation of **2a** (Li/NH_3) provided precycle **2c** in good (66%) isolated yield. In a similar fashion, lithiation-alkylation of (3,4-dimethoxyphenyl)acetonitrile with (*Z*)-1-chloro-3,7-dimethyl-2,6-octadiene[13] or (*E,E*)-1-chloro-3,7,11-trimethyl-2,6,10-dodecatriene[13] gave the precycles **3** and **5**. The precyclization substrate **4** was efficiently prepared via the sequential lithiation-alkylation of (*E*)-4,8-dimethyl-3,7-nonadienonitrile with 1-(chloromethyl)-3,4-dimethoxybenzene. Alkylation of the dienolate derived from methyl 3-oxobutanoate with (*E*)-1-bromo-3,7-dimethyl-2,6-octadiene furnished dieneketoester **6** (85%) which upon silylation [a. NaH (4 equiv), b. TBDMSOTf] or (TBDMSCl-imidazole) provided the silyloxytrienoates **7a** and **7c** respectively. Alternatively, acetylation of **6** (isopropenyl acetate – TsOH, cat.)[14] gave the (*Z*)-acetoxytrienoate **7b**.



2a : R = OCH_3
2b : R = H



2c



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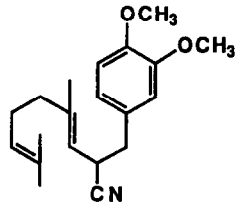

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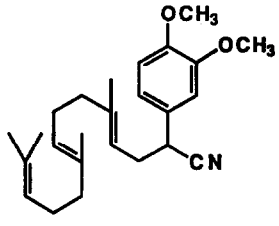

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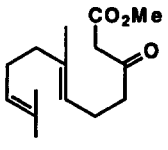

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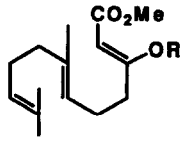
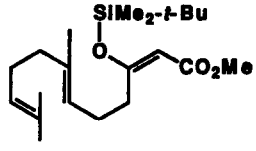


7a : (R = $SiMe_2$-*t*-Bu)
7b : (R = Ac)

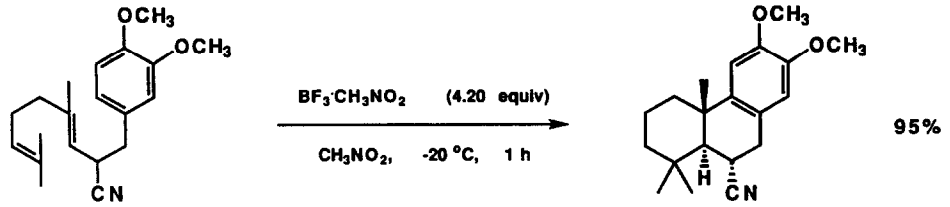


7c

On the Cationic Cyclization of 1-[(*E*)-2-cyano-4,8-dimethyl-3,7-nonadienyl]-3,4-dimethoxybenzene (4) in the Presence of Brönsted and Lewis Acids. A Comparative Study.

We have previously shown that appropriately situated cyano moieties can exert a pronounced regiochemical enhancement with respect to site-selective initiation in *sulfenylative* polyene cyclizations.[6a] We have suggested that this effect may arise as a consequence of "selective electronic deactivation" of alkene linkages in the proximity of cyano groups toward *intermolecular* attack by sulfenylating reagents. In order to take full advantage of this effect (if present *at all* in "H^+ catalyzed" polyene cyclizations), the precyclization substrate 4 was selected for initial study. The optimum cyclization conditions for 4 were determined empirically by exposure of this substrate to various concentrations of $BF_3 \cdot CH_3NO_2$ at reaction temperatures ranging from −20 °C to 25 °C. It was readily determined that the *stereoselective* cyclization of 4 to tricycle 8 could be achieved in 95% isolated yield in *less than 1 h in the presence of 3.15-4.20 equiv of* BF_3 *in* CH_3NO_2 *at −20 °C.* Increasing the amount of BF_3 relative to 4 had no beneficial impact on the efficiency of cyclization whereas lowering the amount to 2.10 equiv resulted in a marked inhibition of cyclization (30-35% conversion after 1 h). In the case of 8, the stereochemical outcome of cyclization was fully supported by a variety of spectroscopic techniques and ultimately confirmed by single crystal X-ray diffraction analysis. The nature of the actual cyclization catalyst was then briefly investigated. To this end, addition of the hindered proton scavengers 2,6-lutidine *or* 1,8-bis(dimethylamino)naphthalene to the reaction medium (containing 4.20 equiv of BF_3) at −20 °C *immediately prior* to the addition of 4 led to complete suppression of cyclization. In addition, ^1H and ^{13}C NMR revealed no appreciable proton transfer from CH_3NO_2 *or* amine coordination with BF_3 under these conditions. These results are consistent with an adventitious "H^+" source serving as the active catalyst. Evidence that *rapid* proton exchange involving the solvent was not a predominant factor during cyclization was provided by the following experiment. Cyclization of 4 with 4.20 equiv of BF_3 in CD_3NO_2 *(99 atom % D) at −20 °C followed by quenching with* D_2O provided 8 with less than 1% of deuterium incorporation as determined by mass spectroscopy and NMR.

A comparative study of a variety of alternative Lewis acids (e.g., $BF_3 \cdot OEt_2$, BCl_3, $SnCl_4$ and $TiCl_4$) *and* Brönsted acids (e.g., HF, $HBF_4 \cdot OMe_2$, FSO_3H and CF_3SO_3H) as cyclization catalysts for the substrate 4 was subsequently undertaken using CH_3NO_2 as the reaction medium. In no instance did cyclization of 4 to 8 (at −20 °C) proceed with any of the above catalysts with efficiencies remotely comparable to $BF_3 \cdot CH_3NO_2$. The results of this study are compiled in **Tables I and II.**



4 8

Table I. The Effect of Alternative Lewis Acids as Cyclization Initiators on the Yield of 8.

Entry	Lewis acid (equiv)	Solvent	Time	Temperature	Yield of 8
1	$BF_3 \cdot CH_3NO_2$ (4.20)	CH_3NO_2	1 h	−20 °C	95%[a]
2	$BF_3 \cdot OEt_2$ (4.20)	CH_3NO_2	1 h	−20 °C	0%[b]
3	$BF_3 \cdot OEt_2$ (4.20)	CH_3NO_2	4 h	25 °C	91%[a]
4	$BF_3 \cdot OEt_2$ (4.20)	CH_2Cl_2	4 h	25 °C	82%[a]
5	$BCl_3 \cdot CH_3NO_2$ (2.10)	CH_3NO_2	1 h	−20 °C	0%[b]
6	$BCl_3 \cdot CH_3NO_2$ (4.20)	CH_3NO_2	1 h	−20 °C	30-35%[c]
7	$BCl_3 \cdot CH_3NO_2$ (6.30)	CH_3NO_2	1 h	−20 °C	30-35%[c]
8	$SnCl_4$ (1.10)	CH_3NO_2	4 h	25 °C	0%[d]
9	$TiCl_4$ (1.10)	CH_3NO_2	4 h	25 °C	0%[d]

[a]Chromatographed yield.
[b]Afforded precyclization nitrile 4 quantitatively after chromatography.
[c]Uncorrected GLC yield, remainder of reaction mixture was 4.
[d]Gave a complex, tarry reaction mixture with no precyclization nitrile 4 and no product 8 detected by GLC.

Table II. Control Reactions on the Transformation of 4 → 8. The Effect of Protic Acids as Alternative Cyclization Initiators on the Yield of 8.

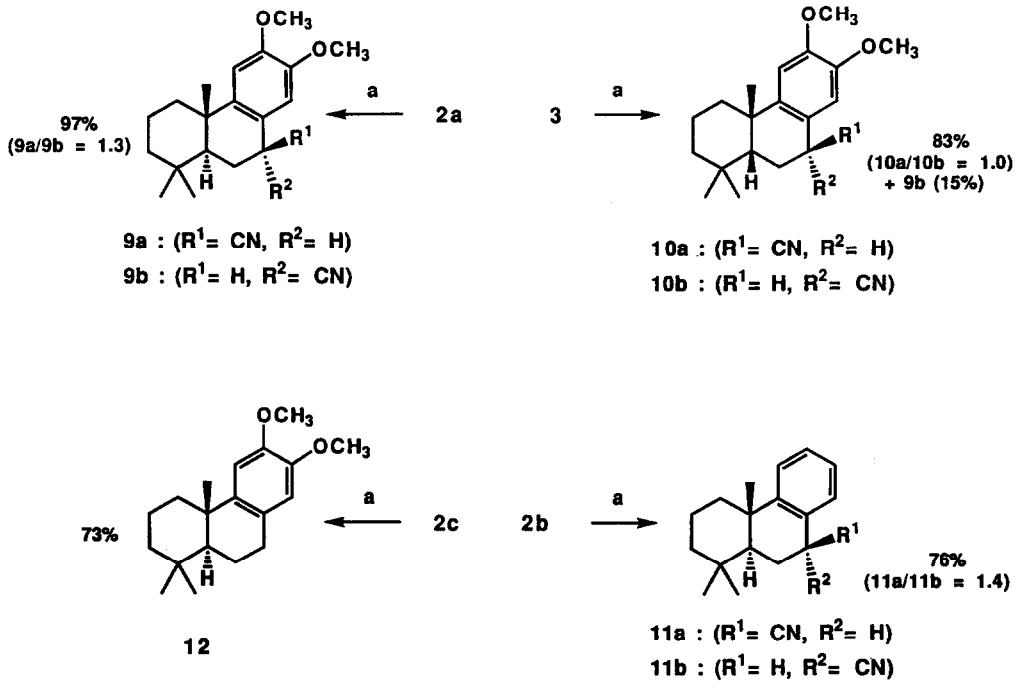
Entry	Protic Acid (equiv)	Solvent	Time	Temperature	Yield of 8
1	HF (anhydrous) (1.10)	CH_3NO_2	1 h	−20 °C	0%[a,c]
2	$HBF_4 \cdot OMe_2$ (1.10)	CH_3NO_2	1 h	−20 °C	0%[a,c]
3	FSO_3H (1.10)	*i*-$PrNO_2$	1 h	−78 °C	0%[a]
4	FSO_3H (1.10)	CH_3NO_2	1 h	−20 °C	35-40%[b]
5	TfOH (0.06)	CH_3NO_2	4 h	−20 °C	0%[a]
6	TfOH (1.10)	CH_3NO_2	4 h	−20 °C	55-60%[b]
7	TfOH (0.06)	CH_2Cl_2	4 h	−20 °C	0%[a]
8	TfOH (1.10)	CH_2Cl_2	4 h	−20 °C	45-50%[b]

[a]Starting nitrile 4 recovered quantitatively following chromatography.
[b]Uncorrected GLC yield, the remainder of the reaction mixture was predominantly starting nitrile 4.
[c]Although HF and $HBF_4 \cdot OMe_2$ were examined, no attempt was made to modify the activity of $BF_3 \cdot CH_3NO_2$ by the addition of anhydrous HF.

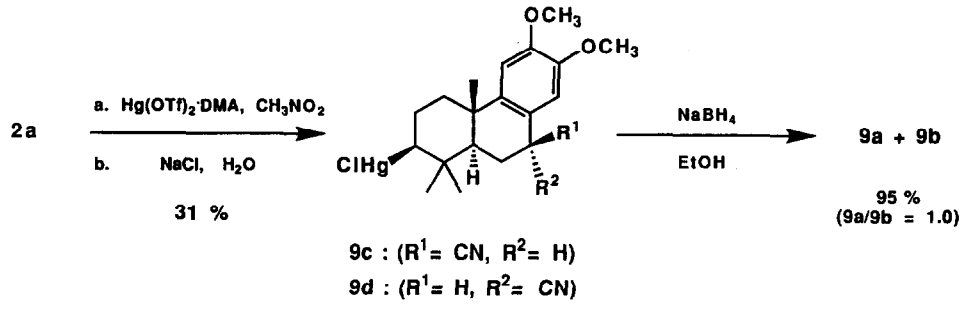
Representative Cationic Cascade Cyclizations Promoted by $BF_3 \cdot CH_3NO_2$.

Subsequent to the preceding studies, cyclizations of the substrates **2a-c**, **3**, **5**, **6**, and **7a-c** were performed under the reaction conditions that had been determined optimum for the conversion of **4** to **8**. Cyclization of the precycles **2a-c** which possess a single internal (*E*) alkene moiety proceeded without incident in high isolated yield. In each case stereoselective formation of products containing *trans* A,B ring junctions was observed. In the cases of **2a** and **b**, separable diastereomers at the nitrile bearing benzylic carbon were produced (**9a/9b** = 1.3 and **11a/11b** = 1.4). It is of considerable preparative interest that the cyclization of aryldiene **2c** (in which the internal alkene moiety is *not* "inductively deactivated") also proceeded stereoselectively and in high (73%) yield to deliver the *fully cyclized* product **12** upon exposure to 4.20 equiv of BF_3 in CH_3NO_2 at −20 °C.[15] By way of contrast, cyclization of the (*Z*)-alkene bearing substrate **3** proceeded with slightly diminished control of ring junction stereochemistry. In this case cyclization under the standard set of experimental conditions gave the diastereomeric *cis* **10a** and **10b** (**10a/10b** = 1.0) in 83% isolated yield along with 15% of **9b**.

The production of **9b** in the cyclization of **3** may have arisen as a result of a stepwise cationic cyclization or via competing alkene isomerization prior to cyclization. Although the former might appear more likely,[7] an effort was not made to distinguish between these two mechanistic possibilities. Stereochemical assignments of the tricyclic products synthesized in the foregoing studies were made spectroscopically *and* by chemical correlation to known compounds as described previously.[6a] Mercuric triflate·N,N-dimethylaniline complex has been reported to efficiently mediate a number of polyene cascade cyclizations.[6e] In an experiment intended to provide a *direct* comparison of this reagent to $BF_3 \cdot CH_3NO_2$ for inducing aryldiene cyclizations, **2a** was treated with $Hg(OTf)_2 \cdot DMA$ (CH_3NO_2, −20 °C, 2 h) and subsequently quenched (NaCl aq.). Interestingly, cyclization under these conditions provided the corresponding chloromercurio derivatives **9c** and **d** as a mixture of diastereomers in only 31% isolated yield. Subsequent reduction of **9c** and **d** ($NaBH_4$, EtOH) gave rise to **9a** and **b** (9a/9b = 1.0) in 95% yield.

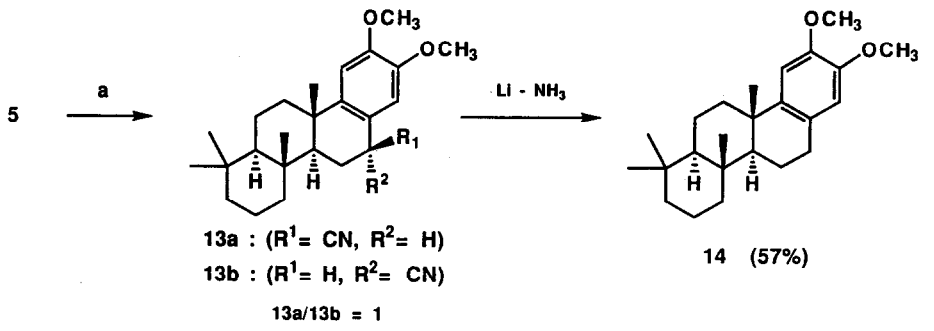


a. $BF_3 \cdot CH_3NO_2$ (4.20 equiv), CH_3NO_2, −20 °C, 1h.



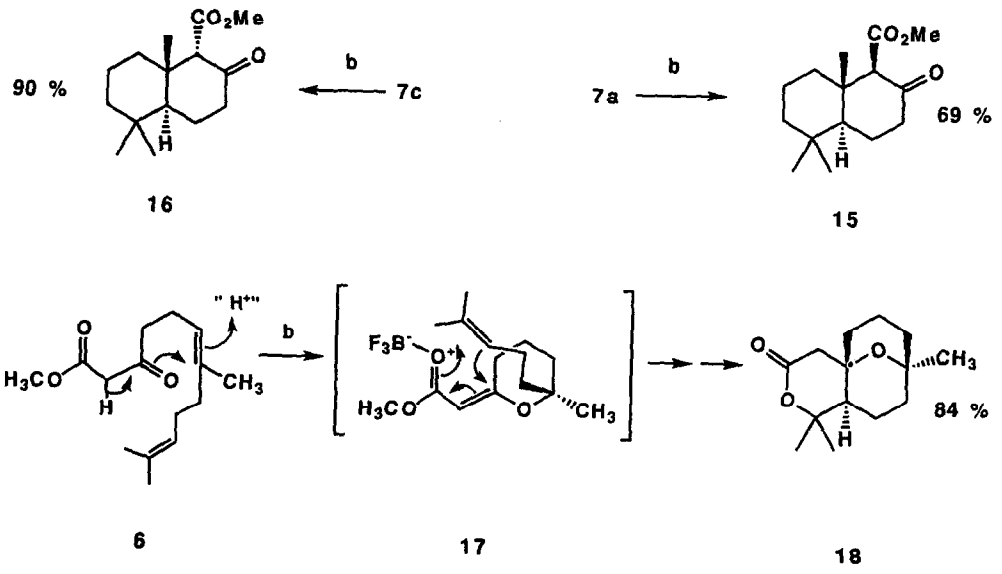
9c : (R^1= CN, R^2= H)
9d : (R^1= H, R^2= CN)

Cationic cyclization of the (*E,E*)-aryltriene **5** under the aforementioned set of reaction conditions apparently proceeded with somewhat diminished product selectivity when compared to the previous examples and accordingly may represent a limiting case. Nonetheless, an excellent yield of fully cyclized product was achieved even with this more structurally complicated substrate. Cyclization of **5** in the presence of 4.20 equiv of BF_3 in CH_3NO_2 at −20 °C for 1 h provided a mixture consisting of two major tetracyclic products (in a 1:1 ratio) admixed with two relatively minor products in 92% combined yield. Chromatography of this mixture afforded two fractions each consisting of one of the primary products along with a minor product. The major tetracyclic products were tentatively assigned the structures **13a** and **13b** based on the close resemblance of their respective benzylic C*H*CN ^{1}H NMR resonances [δ 3.95, dd, J = 6.8, 11.9 Hz (**13a**); δ 3.99, d, J = 5.8 Hz (**13b**)] to those of the stereoisomerically characterized octahydrophenanthrenes **9a,b** and **11a,b**. In accordance with these assignments, reductive deletion of the cyano moieties from both **13a** and **13b** [*as a mixture or in the form of the separated chromatographic fractions (vide infra)*], gave *a common dodecahydrochrysene **14** in 57% combined yield (from **5**) after recrystallization*. The *trans-anti-trans* ring junction stereochemistry assigned to **14**, although not conclusively established at this time, was supported by nOed spectroscopic analysis.



a. $BF_3 \cdot CH_3NO_2$ (4.20 equiv), CH_3NO_2, −20 °C, 1h.

That the geometry of *alkene* terminators could also translate to product stereochemistry under the strongly acidic conditions utilized in this study was demonstrated by the following experiments. Exposure of **7a** to 4.20 equiv of BF_3 in CH_3NO_2 at −20 °C for **3 h** provided the known [4·4·0] bicyclodecalone **15**[16] in 69% isolated yield after recrystallization. Analogous treatment of the corresponding (*E*)-isomer **7c** furnished the *axial*-carbomethoxydecalone **16** in 90% isolated yield. The stereochemical assignment of **16** was unambiguously established by single crystal X-ray diffraction analysis. Moreover, exposure of **16** to a catalytic quantity of DABCO in C_6D_6 (25 °C) resulted in its rapid conversion to the thermodynamic isomer **15** (^{1}H NMR). Not surprisingly, cyclization of the (*Z*)-acetoxytriene **7b** (which bears a poorer terminating moiety) proceeded with lower selectivity and efficiency. Accordingly, cyclization of **7b** under the usual reaction conditions provided a 5:1 ratio of **15** and **16** in 40% overall yield. Presumably in this case, partial scrambling of terminator geometry occurred prior to cyclization. White has shown that the direct cyclization of the parent ketoester **6** in the presence of $SnCl_4$ (CH_2Cl_2, 20 °C, 17 h) leads to the formation of **15** in 68% yield.[16] In sharp contrast, exposure of **6** to BF_3 (4.20 equiv) in CH_3NO_2 at −20 °C for 3 h produced the interesting bicyclic lactone **18** in 84% recrystallized yield! The structure of **18** was established by single crystal X-ray diffraction analysis (Figure 1). A plausible mechanism leading to the formation of **18** involved exclusive initiation of cyclization at the *internal* alkene of **6** with concomitant nucleophilic trapping by the β-carbonyl oxygen to generate **17**. Subsequent cyclization of **17**, either by an inverse electron demand [4+2] cycloaddition or a stepwise cationic process involving the peripheral alkene followed by O-demethylation, would then provide **18** (Scheme 2).[17]



Scheme 2

b. $BF_3 \cdot CH_3NO_2$ (4.20 equiv), CH_3NO_2, −20 °C, 3h.

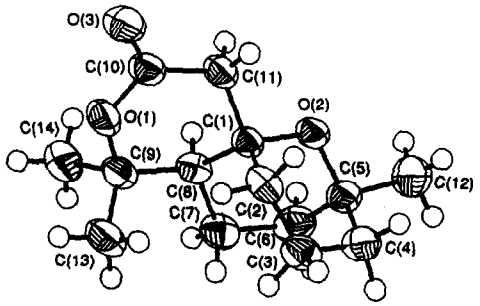


Figure 1

Synthetic Applications of $BF_3 \cdot CH_3NO_2$ Promoted Cationic Cascade Annulations. A Concise Biomimetic Total Synthesis of (±)-Taxodione.[18]

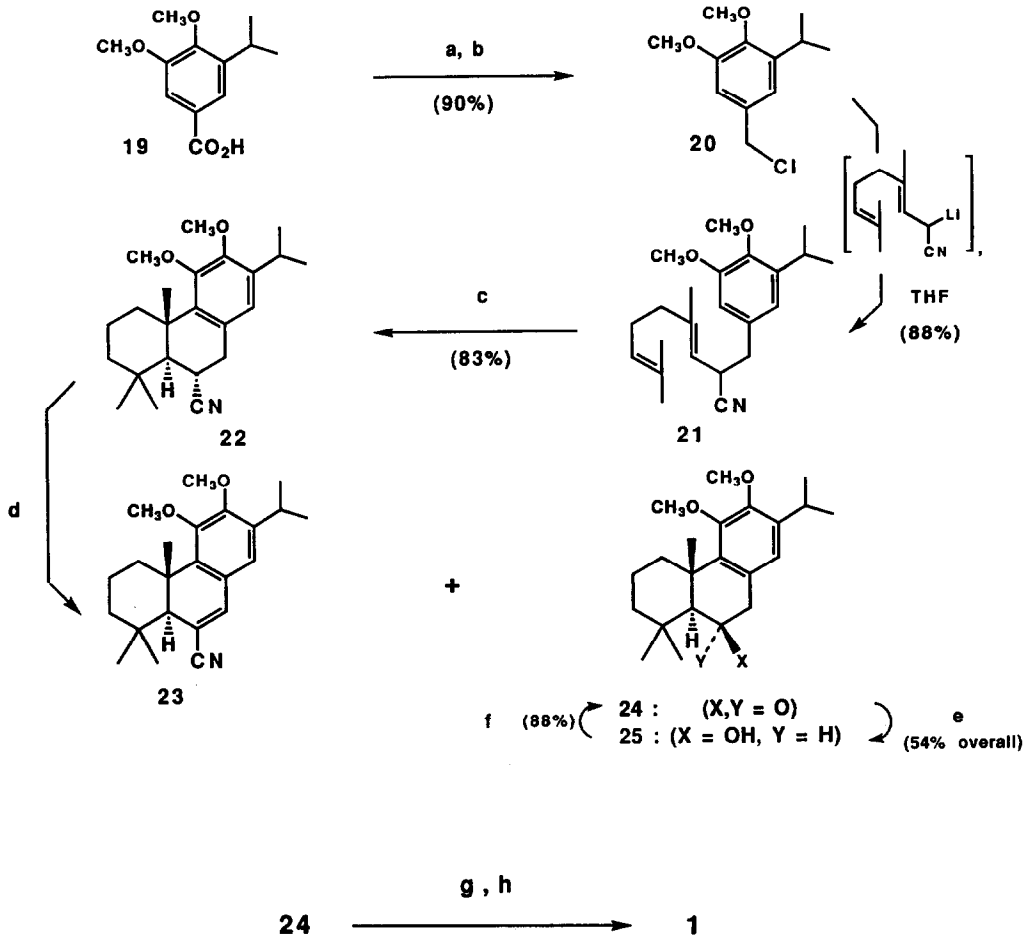
The interesting quinone methide diterpene taxodione (1), isolated in 1968[19] from extracts of *Taxodium distichum* Rich (*Taxodiaceae*), has been shown to exhibit significant activity *in vivo* against cells derived from human carcinoma of the nasopharynx (KB). To date seven total syntheses[20a-g] and a relay synthesis[21] for this deceptively simple molecule have been reported. All of these, although interesting from an academic perspective, suffer from undue length and modest overall yield. The heuristically most appealing approach to this substance is a biomimetic formal synthesis reported by Johnson *et al.* in 1982.[21] In the central step of this synthesis, a rather specialized set of reaction conditions was found necessary to induce a bis tertiary allyl cation to engage a trisubstituted alkene in a cascade cyclization terminated by a hindered isopropylveratrole moiety.

As we have shown in the preceding studies, BF_3 in CH_3NO_2 is an unusually effective catalyst for promoting "H^+ initiated" cascade cyclizations of various 9-arylnona-2,6-dienes and related systems. Herein we describe the successful application of a $BF_3 \cdot CH_3NO_2$ cascade cyclization in a practical, highly convergent total synthesis of (±)-taxodione (1).

Reduction of 3,4-dimethoxy-5-isopropylbenzoic acid **19**[22] with BMS ($BH_3 \cdot SMe_2$) followed by treatment of the resultant alcohol with $SOCl_2$ provided benzylic chloride **20** in 90% overall yield. Sequential lithiation of (*E*)-4,8-dimethyl-3,7-nonadienonitrile (LDA-THF, −78 °C) followed by alkylation with **20** (−78 °C → 20 °C) furnished the precyclization substrate **21** in 88% isolated yield. The key bicyclization was subsequently effected by exposure of this sterically hindered substrate to gaseous BF_3 (4.2 equiv.) dissolved in CH_3NO_2 (12 h, 25 °C). In this manner, the essential tricyclic intermediate **22** could be reproducibly prepared in quantity as the *exclusive stereoisomer* in 83% yield after recrystallization.

The oxidative decyanation of **22** was effected by a variation of the procedure described by Watt.[23] Accordingly, lithiation of **22** followed by oxygenation of the resultant anion with O_2 at −78 °C and final hydroperoxide cleavage *in situ* [$SnCl_2$–HCl(aq)] gave a mixture containing ketone **24** (58% yield by GLC) and unsaturated nitrile **23** along with several other impurities that were difficult to separate. As a consequence, the crude material obtained in this way was reduced with $LiAlH_4$ to provide the readily purifiable axial alcohol **25** directly in 54% chromatographed yield from **22**. Reoxidation of **25** to **24** [PDC (2.2 equiv.), CH_2Cl_2, 25 °C] proceeded without incident in 88% yield. Direct demethylation of **24** prepared in this manner (BBr_3)[20b] followed by oxidation of the crude catechol by stirring in benzene with silica gel under an atmosphere of O_2 (2 h, 25 °C) in a modification of the procedure described by Matsumoto[20b] delivered (±)-taxodione (1) in 68% yield

from the intermediate **24**. The synthetic (±)-taxodione (1) prepared in this manner was identical to an authentic sample in all respects (mass spectrum, 300 MHz ^1H and 75 MHz ^{13}C NMR spectra).



a. BMS, THF; b. $SOCl_2$, CH_2Cl_2; c. $BF_3 \cdot CH_3NO_2$ (4.20 equiv), CH_3NO_2, 25 °C, 12h;
d. (i) LDA, THF, (ii) O_2, (iii) $SnCl_2$, HCl (aq.);
e. $LiAlH_4$, THF; f. PDC, CH_2Cl_2; g. BBr_3, CH_2Cl_2; h. O_2, silica gel.

This eminently practical synthesis of (±)-taxodione (1), which proceeded in seven steps and 21% overall yield, serves to illustrate the utility that $BF_3 \cdot CH_3NO_2$ promoted cationic cascade annulations possess for the elaboration of moderately complex polycyclic ring systems. The future

utilization of this synthetic method should greatly facilitate the accessibility of a variety of intermediates that were previously only available via more circuitous routes.

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EXPERIMENTAL SECTION

General experimental details: Nuclear magnetic resonance (NMR) spectra (^1H and ^{13}C) were recorded on a Bruker AC 300 MHz spectrometer. ^1H NMR chemical shifts are reported in ppm relative to the residual proton in chloroform-d_1 assigned at 7.24 ppm. ^{13}C NMR chemical shifts are reported in ppm relative to the center line in chloroform-d_1 assigned at 76.90 ppm. The descriptors: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), dt (doublet of triplets), td (triplet of doublets), tt (triplet of triplets), m (multiplet), cm (complex multiplet), and br (broad) were used for assigning the multiplicities of ^1H NMR spectra. Where appropriate, axially and equatorially disposed protons are designated $-H_a$ and $-H_e$ respectively immediately following the corresponding systematically numbered carbon atoms. DEPT experiments were performed on all compounds to identify the number of protons attached to each carbon. Infrared spectra were obtained on a Perkin-Elmer Model 1800, dual beam, FT-IR spectrometer. Electron impact mass spectra (70-eV) were recorded with a VG Instruments MM16-F spectrometer. High resolution mass spectra were recorded on a VG Instruments 70E-HF spectrometer. Gas chromatographs were obtained with a Varian Model 3700 gas chromatograph equipped with a flame ionization detector and a Hewlett-Packard 3390A Reporting Integrator. Either an Alltech Econocap SE-54 bonded phase; 15 m length, 0.54 mm id, and 1.2 μ film size column or a J and W Scientific DB-5 bonded phase 15 m megabore, 0.53 mm id. column were utilized for obtaining GLC's. Thin layer chromatography (TLC) analyses were performed with MN Polygram Sil G/UV_{254} 0.25 mm silica gel plates purchased from Alltech Associates. Flash and medium pressure liquid chromatography (MPLC) were performed with Merck 230-400 ASTM mesh, 0.040-0.063 mm particle size, silica gel 60 purchased from EM Science. Beckman-Altex glass columns, Fluid Metering Inc. Model R431 pumps, and Perkin-Elmer Model LC75 variable wavelength UV detector were used for MPLC separations. Melting points were determined with an Electrothermal melting point apparatus and are uncorrected. Combustion analyses were performed by Desert Analytics, Tucson, AZ.

Tetrahydrofuran (THF) and diethyl ether were freshly distilled from potassium metal and sodium benzophenone ketyl, respectively, prior to use. All other solvents and N,N-diisopropylamine were freshly distilled from CaH_2 (unless specified otherwise) prior to use. Molar solutions of $BF_3 \cdot CH_3NO_2$ were routinely prepared by passing BF_3 gas (3-4 g) via a syringe needle (6 cm, 20 gauge) into a preweighed 50 mL volumetric flask containing a rubber septum and 35-40 mL of CH_3NO_2 at 0 °C, reweighing, then diluting to the mark with additional CH_3NO_2. These solutions were stored in the dark at −20 °C for up to three weeks. Solutions of *n*-BuLi (2-3 M) were routinely prepared by diluting commercially available (Aldrich Chemical Co.) *n*-BuLi (10.0 M in hexane) with freshly distilled heptane (Na), and were titrated against (±)-2-butanol (2.0 M in toluene) using 1,10-phenanthroline as the indicator prior to use. LDA·THF complex was prepared by dropwise addition of *n*-BuLi (5.0 mL, 50 mmol, 10.0 M in hexanes) to a 0 °C solution of N,N-diisopropylamine (7.0 mL, 50 mmol) and THF (4 mL, 50 mmol) in methylcyclohexane (34 mL). This complex was titrated by the method of Vedejs[24] prior to use.

(3,4-Dimethoxyphenyl)acetonitrile, phenylacetonitrile, and (*E*)-1-bromo-3,7-dimethyl-2,6-octadiene (geranyl bromide) were purchased from Aldrich Chemical Co. and used without further purification. The allylic chlorides: (*E*)-1-chloro-3,7-dimethyl-2,6-octadiene (geranyl chloride), (*Z*)-1-chloro-3,7-dimethyl-2,6-octadiene (neryl chloride), and (2*E*,6*E*)-1-chloro-3,7,11-trimethyl-2,6,10-dodecatriene (farnesyl chloride) were prepared from the parent alcohols (purchased from Aldrich Chemical Co.) by the method of Meyers,[13] and gave satisfactory analysis. All reactions were carried out under an atmosphere of argon or nitrogen in oven-dried vessels. Concentrations were performed under reduced pressure with a Büchi rotary evaporator.

(E)-4,8-Dimethyl-3,7-nonadienonitrile.

A flame-dried, 500 mL, round-bottomed flask equipped with a magnetic stirring bar, rubber septum and N_2 inlet was flushed with N_2 then charged with (*E*)-1-chloro-3,7-dimethyloctadiene (15.0 g, 86.9 mmol), dry DMSO (250 mL) and anhydrous KCN (6.79 g, 0.104 mol). The reaction mixture was stirred overnight at room temperature and diluted with H_2O (1000 mL). The aqueous phase was extracted with hexane (6 x 100 mL) and the combined hexane extracts were washed with H_2O (3 x 100 mL), brine (2 x 100 mL) and then dried over anhydrous $MgSO_4$. The solution was filtered through neutral alumina and the solvent was evaporated *in vacuo*. The crude product was purified by vacuum distillation to afford 12.0 g (85%) of (*E*)-4,8-dimethyl-3,7-nonadieneonitrile as a colorless liquid: ^{1}H NMR ($CDCl_3$) δ 5.10 (dt, 1 H, J = 1.2, 7.0 Hz, =C*H*), 5.00 (dt, 1 H, J = 1.2, 6.1 Hz, =C*H*), 2.98 (d, 2 H, J = 7.0 Hz, CH_2CN), 2.00 (m, 4 H, 2 CH_2), 1.62 (s, 3 H, CH_3), 1.61 (s, 3 H, CH_3), 1.54 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 141.8 (*C*), 131.3 (*C*), 123.0 (*C*H), 117.8 (*C*N), 111.5 (*C*H), 38.7 (*C*H_2), 25.7 (*C*H_2), 25.0 (*C*H_2), 17.0 (*C*H_3), 15.7 (*C*H_3), 15.6 (*C*H_3) ppm; IR (neat) 2965-2858 (CH envelope), 2253 (CN), 1668, 1447, 1380, 1111, 916, 822 cm^{-1}; high resolution mass spectrum calcd for $C_{11}H_{17}N$ (M^+) 163.1392, found 163.1361.

General Procedure for the Alkylation of Nitriles

A flame-dried, 250-mL, round-bottomed flask equipped with a magnetic stirring bar, rubber septum, and N_2 inlet was flushed with N_2, and charged with dry diisopropylamine (2.80 mL, 20.0 mmol) and dry THF (20 mL). The solution was cooled to 0 °C, and *n*-BuLi (6.7 mL, 20.0 mmol, 3.0 M in heptane) was added dropwise via syringe. Stirring was continued for 15 min at 0 °C then a solution of the nitrile (20.0 mmol) in THF (5 mL) was added over 2 min via syringe. The resulting solution was stirred for 45 min at 0 °C then cooled to -78 °C. A solution of the appropriate halide (20.0 mmol) in THF (10 mL) was added in one portion via syringe, and the reaction mixture was stirred overnight while warming to room temperature. The reaction was quenched with saturated aqueous NH_4Cl (50 mL) and diluted with (1:1) ethyl acetate: hexane (50 mL). The organic phase was washed with H_2O (50 mL) and brine (50 mL), and the combined aqueous layers were back extracted with (1:1) ethyl acetate:hexane (3 x 50 mL). The combined organic layers were dried over anhydrous $MgSO_4$, and the solution was filtered through florisil. The solvents were evaporated *in vacuo* to give the crude product which was purified by flash chromatography (2.5-10% ethyl acetate in hexane for elution).

1. *(E)-2-(3,4-Dimethoxyphenyl)-5,9-dimethyl-4,8-decadienonitrile (2a).*

Aryldiene **2a** was prepared as a colorless oil in 67% yield from (3,4-dimethoxyphenyl)acetonitrile (1.655 g, 15.0 mmol) and (*E*)-1-bromo-3,7-dimethyloctadiene (2.255 g, 15.0 mmol): ^{1}H NMR ($CDCl_3$) δ 6.78 (m, 3 H, Ar*H*), 5.12 (t, 1 H, J = 7.2 Hz, =C*H*), 5.01 (t, 1 H, J = 6.7 Hz, =C*H*), 3.82 (s, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 3.67 (t, 1 H, J = 7.2 Hz, C*H*CN), 2.52 (m, 2 H, CH_2), 1.97 (m, 4 H, 2 CH_2), 1.62 (s, 3 H, CH_3), 1.53 (s, 3 H, CH_3), 1.49 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 148.9 (*C*), 148.4 (*C*), 139.7 (*C*), 131.2 (*C*), 127.8 (*C*), 123.6 (*C*H), 120.6 (*C*N), 119.4 (*C*H), 118.2 (*C*H), 111.0 (*C*H), 110.1 (*C*H), 55.6 (2 O*C*H_3), 39.3 (*C*H_2), 37.0 (*C*H), 34.0 (*C*H_2), 26.2 (*C*H_2), 25.3 (*C*H_3), 17.3 (*C*H_3), 15.9 (*C*H_3) ppm; IR (thin film) 3068-2818 (CH envelope), 2240 (CN), 1668, 1594,

1518, 1266, 1240, 1146, 1028 cm^{-1}; high-resolution mass spectrum calcd for $C_{20}H_{27}NO_2$ (M^+) 313.2042, found 313.2026.

2. *(E)-2-(3,4-Dimethoxyphenyl)methyl-4,8-dimethyl-3,7-nonadienonitrile (4).*

Aryldiene **4** was prepared as a white solid: mp 57-59 °C (recrystallized from hexane) in 81% yield from (*E*)-4,8-dimethyl-3,7-nonadienonitrile (8.668 g, 53.1 mmol) and 1-(chloromethyl)-3,4-dimethoxybenzene (9.907 g, 53.1 mmol): ^1H NMR ($CDCl_3$) δ 6.78 (m, 3 H, Ar*H*), 5.09 (dd, 1 H, J = 1.0, 7.7 Hz, =C*H*), 5.02 (t, 1 H, J = 6.7 Hz, =C*H*), 3.86 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 3.52 (q, 1 H, J = 7.7 Hz, C*H*CN), 2.92 (dd, 1 H, J = 7.7, 13.6 Hz, CH_2Ar), 2.79 (dd, 1 H, J = 6.7, 13.6 Hz, CH_2Ar), 2.01 (m, 4 H, 2 CH_2), 1.66 (s, 3 H, CH_3), 1.58 (s, 3 H, CH_3), 1.55 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 148.9 (*C*), 148.2 (*C*), 141.1 (*C*), 131.8 (*C*), 129.2 (*C*), 123.2 (*C*H), 121.2 (*C*H), 120.7 (*C*N), 118.0 (*C*H), 112.4 (*C*H), 111.3 (*C*H), 55.7 (2 OCH_3), 39.1 (CH_2), 38.9 (CH_2), 32.0 (*C*H), 26.1 (CH_2), 25.4 (CH_3), 17.4 (CH_3), 16.3 (CH_3) ppm; IR (KBr) 3064-2851 (CH envelope), 2233 (CN), 1643, 1608, 1592, 1467, 1444, 1264, 1241, 1163, 1030, 803, 764 cm^{-1}; high-resolution mass spectrum calcd for $C_{20}H_{27}NO_2$ (M^+) 313.2042, found 313.2047.

3. *(Z)-2-(3,4-Dimethoxyphenyl)-5,9-dimethyl-4,8-decadienenitrile (3).*

Aryldiene **3** was prepared as a colorless oil in 58% yield from (3,4-dimethoxyphenyl)acetonitrile (2.710 g, 15.0 mmol) and (*Z*)-1-chloro-3,7-dimethyloctadiene (2.604 g, 15.0 mmol): ^1H NMR ($CDCl_3$) δ 6.83 (m, 3 H, Ar*H*), 5.17 (t, 1 H, J = 7.2 Hz, =C*H*), 5.05 (br s, 1 H, =C*H*), 3.87 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 3.68 (t, 1 H, J = 6.8 Hz, C*H*CN), 2.55 (m, 2 H, CH_2), 1.96 (m, 4 H, 2 CH_2), 1.71 (s, 3 H, CH_3), 1.66 (s, 3 H, CH_3), 1.57 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 149.0 (*C*), 148.5 (*C*), 139.3 (*C*), 131.3 (*C*), 127.8 (*C*), 123.5 (*C*H), 120.4 (*C*N), 119.2 (*C*H), 119.0 (*C*H), 111.2 (*C*H), 110.3 (*C*H), 55.5 (2 OCH_3), 37.0 (*C*H), 33.8 (CH_2), 31.6 (CH_2), 25.9 (CH_2), 25.2 (CH_3), 22.9 (CH_3), 17.1 (CH_3) ppm; IR (thin film) 3075-2832 (CH envelope), 2240 (CN), 1594, 1518, 1266, 1146, 1028 cm^{-1}; high-resolution mass spectrum calcd for $C_{20}H_{27}NO_2$ (M^+) 313.2042, found 313.2054.

4. *(E)-5,9-Dimethyl-2-phenyl-4,8-decadienenitrile (2b).*

Aryldiene **2b** was prepared as a colorless oil in 72% yield from phenylacetonitrile (5.032 g, 43.0 mmol) and (*E*)-1-bromo-3,7-dimethyloctadiene (10.6 mL, 53.7 mmol); $LiN(TMS)_2$ (8.624 g, 51.7 mmol) was used as the base: ^1H NMR ($CDCl_3$) δ 7.25 (m, 5 H, Ar*H*), 5.09 (t, 1 H, J = 7.2 Hz, =C*H*), 4.97 (t, 1 H, J = 6.8 Hz, =C*H*), 3.68 (t, 1 H, J = 7.2 Hz, C*H*CN), 2.50 (m, 2 H, CH_2), 1.93 (m, 4 H, 2 CH_2), 1.59 (s, 3 H, CH_3), 1.50 (s, 3 H, CH_3), 1.43 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 139.7 (*C*), 135.5 (*C*), 131.0 (*C*), 128.5 (2 *C*H), 127.5 (*C*H), 127.0 (2 *C*H), 123.7 (*C*H), 120.2 (*C*N), 118.2 (*C*H), 39.3 (CH_2), 37.3 (*C*H), 34.0 (CH_2), 26.1 (CH_2), 25.2 (CH_3), 17.2 (CH_3), 15.7 (*C*H) ppm; IR (thin film) 3089-2846 (CH envelope), 2242 (CN), 1454, 1376, 700 cm^{-1}; high-resolution mass spectrum calcd for $C_{18}H_{23}N$ (M^+) 253.1830, found 253.1780.

5. *(4E,8E)-2-(3,4-Dimethoxyphenyl)-5,9-13-trimethyl-4,8,12-tetradecatrienenitrile (5).*

Aryltriene **5** was prepared as a colorless oil in 79% yield from (3,4-dimethoxyphenyl)acetonitrile (0.318 g, 1.79 mmol) and (*E,E*)-1-chloro-3,7,11-trimethyl-2,6,10-dodecatriene (0.418 g, 2.00 mmol): ^1H NMR ($CDCl_3$) δ 6.81 (m, 3 H, Ar*H*), 5.16 (t, 1 H, J = 7.5 Hz, =C*H*), 5.06 (t, 2 H, J = 6.8 Hz, 2 =C*H*), 3.86 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 3.69 (t, 1 H, J = 7.5 Hz, C*H*CN), 2.57 (m, 2 H, J = 7.2 Hz, CH_2), 2.04-1.92 (m, 8 H, 4 CH_2), 1.65 (s, 3 H, CH_3), 1.57 (s, 6 H, 2 CH_3), 1.53 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 149.1 (*C*), 148.6 (*C*), 140.0 (*C*), 135.1 (*C*), 131.1 (*C*), 128.0 (*C*), 124.2 (*C*H), 123.6 (*C*H), 120.8 (*C*N), 119.5 (*C*H), 118.3 (*C*H), 111.2 (*C*H), 110.3 (*C*H), 55.8 (2 OCH_3), 39.5 (2 CH_2), 37.2 (*C*H), 34.2 (CH_2), 26.0 (CH_2), 25.5 (CH_3), 17.5 (CH_3), 16.1 (CH_3), 15.8 (CH_3) ppm; IR (thin film) 3061-2832 (CH envelope), 2240 (CN), 1594, 1518 cm^{-1}; high-resolution mass spectrum calcd for $C_{25}H_{35}NO_2$ (M^+) 381.2668, found 381.2671.

General Procedure for Li/NH_3 Reductions: *(E)-1-(3,4-Dimethoxyphenyl)-4,8-dimethyl-3,7-nonadiene (2c).*

A 250-mL, three-necked, flask equipped with a magnetic stirring bar and dry-ice condenser was cooled to -78 °C. NH_3 (100 mL) was distilled from sodium and condensed into the flask. To the NH_3 was added Li (65.0 mg, 9.37 mmol) and *t*-BuOH (0.44 mL, 4.65 mmol), and the resulting solution was stirred for 10 min at -78 °C. A solution of nitrile **2a** (1.324 g, 4.22 mmol) in THF (2 mL) was added dropwise via syringe[25] and the reaction mixture was stirred for 5 min at -78 °C. The reaction was then quenched with approximately 2 g of solid NH_4Cl. The reaction flask was removed from the Dry-ice bath, and the NH_3 was allowed to evaporate overnight at room temperature. The residue was diluted with H_2O (50 mL) and the aqueous phase was extracted with diethyl ether (3 x 25 mL). The ether was washed with brine (25 mL) and dried over anhydrous $MgSO_4$. The solvent was removed *in vacuo* to yield the crude product which was purified by MPLC [ethyl acetate:hexane (1:99) for elution] to afford 0.803 g (66%) of **2c** as a colorless oil: ^1H NMR ($CDCl_3$) δ 6.74 (m, 3 H, Ar*H*), 5.16 (dt, 1 H, J = 1.0, 7.1 Hz, =C*H*), 5.07 (dt, 1 H, J = 1.0, 7.1 Hz, =C*H*), 3.85 (s, 3 H, OCH_3), 3.84 (s, 3 H, OCH_3), 2.57 (t, 2 H, J = 7.1 Hz, CH_2), 2.27 (q, 2 H, J = 7.1 Hz, CH_2), 2.00 (m, 4 H, 2 CH_2), 1.67 (s, 3 H, CH_3), 1.59 (s, 3 H, CH_3), 1.55 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 148.4 (*C*), 146.8 (*C*), 134.9 (*C*), 134.5 (*C*), 130.4 (*C*), 123.8 (*C*H), 123.2 (*C*H), 119.8 (*C*H), 111.7 (*C*H), 111.0 (*C*H), 55.2 (O*C*H_3), 55.1 (O*C*H_3), 39.2 (*C*H_2), 35.1 (*C*H_2), 29.5 (*C*H_2), 26.2 (*C*H_2), 25.0 (*C*H_3), 17.0 (*C*H_3), 15.3 (*C*H_3) ppm; IR (thin film) 3057-2823 (CH envelope), 1590, 1516, 1464, 1418, 1262, 1236, 1156, 1032 cm^{-1}; high-resolution mass spectrum calcd for $C_{19}H_{28}O_2$ (M^+) 288.2090, found 288.2094.

General Procedure for $BF_3 \cdot CH_3NO_2$ Promoted Cyclizations

A flame-dried, 25 x 150 mm, test tube equipped with a magnetic stirring bar, rubber septum and N_2 inlet was flushed with N_2, charged with dry CH_3NO_2 (4.8 mL) and cooled to -20 °C. $BF_3 \cdot CH_3NO_2$ (1.34 mL, 1.34 mmol, 1.0 M in CH_3NO_2) was added in one portion via syringe, and the resulting solution was stirred for 15 min at -20 °C. A solution of the substrate (0.32 mmol) in dry CH_3NO_2 (1.00 mL) was added in one portion via syringe, and the resulting mixture was stirred for 1 h at -20 °C. The reaction was quenched (at -20 °C) with saturated aqueous $NaHCO_3$ (5 mL) and the mixture was allowed to warm to room temperature. The layers were separated, and the organic phase was washed with H_2O (2 x 5 mL). The combined aqueous layers were back extracted with CH_2Cl_2 (3 x 5 mL), and the combined organic phase was dried over anhydrous $MgSO_4$. The solvents were evaporated *in vacuo* to furnish the crude products which were purified by MPLC (2.5-10% ethyl acetate in hexane for elution).

1. *10-Cyano-6,7-dimethoxy-1,2,3,4,4aβ,9,10β,10aα-octahydro-1,1,4a-trimethylphenanthrene (8).*

Cyclization of aryldiene **4** (1.032 g, 3.29 mmol) with $BF_3 \cdot CH_3NO_2$ (10.40 mL, 13.83 mmol, 1.33 M) in CH_3NO_2 (49.0 mL) afforded 0.975 g (95%) of **8** as a single diastereomer. For **8** as a white solid: mp 174-175 °C [recrystallized from (1:9) toluene:heptane]; ^1H NMR ($CDCl_3$) δ 6.73 (s, 1 H, Ar*H*), 6.60 (s, 1 H, Ar*H*), 3.84 (s, 6 H, 2 OCH_3), 3.30 (dd, 1 H, J = 7.0, 14.8 Hz, ArCH_a), 3.05 (m, 2 H, ArCH_e, CHCN), 2.18 (br d with fine structure, 1 H, J = 11.8 Hz, C(4)-H_e), 1.76 (dt, 1 H, J = 3.2, 13.3 Hz, C(3)-*H*), 1.66 (m, 2 H, C*H* ring junction, C(3)-*H*'), 1.54 (m, 2 H, C(2)-H_e, C(4)-H_a), 1.31 (dd, 1 H, J = 4.3, 13.3 Hz, C(2)-H_a), 1.21 (s, 3 H, CH_3), 1.17 (s, 3 H, CH_3), 1.09 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 147.7 (*C*), 147.0 (*C*), 141.0 (*C*), 124.9 (*C*), 123.7 (*C*), 111.3 (*C*H), 107.0 (*C*H), 56.1 (O*C*H_3), 55.7 (O*C*H_3), 53.3 (*C*H), 42.1 (*C*H_2), 38.6 (*C*H_2), 38.0 (*C*), 34.5 (*C*), 33.7 (*C*H_3), 33.7 (*C*H_2), 24.7 (*C*H), 22.6 (*C*H_3), 21.4 (*C*H_3), 18.4 (*C*H_2) ppm; IR (KBr) 3075-2832 (CH envelope), 2232 (CN), 1608, 1524, 1511, 1458, 1444, 1358, 1266, 1248, 1226, 1198, 1152, 1076, 864 cm^{-1}; high-resolution mass spectrum calcd for $C_{20}H_{27}NO_2$ (M^+) 313.2042, found 313.2053. Anal. Calcd for $C_{20}H_{27}NO_2$: C, 76.63; H, 8.69. Found: C, 76.24; H, 8.64.

2. *9-Cyano-6,7-dimethoxy-1,2,3,4,4aβ,9α,10,10aα-octahydro-1,1,4a-trimethylphenanthrene (9a) and 9-cyano-6,7-dimethoxy-1,2,3,4,4aβ,9β,10,10aα-octahydro-1,1,4a-trimethylphenanthrene (9b).*

Cyclization of aryldiene **2a** (0.237 g, 0.76 mmol) with $BF_3 \cdot CH_3NO_2$ (2.07 mL, 3.18 mmol, 1.54 M) in CH_3NO_2 (11.3 mL) afforded 0.229 g (97%) of **9a** and **9b** as a 1.0:1.3 mixture of diastereomers.

For **9a** as a white solid: mp 164-166 °C [recrystallized from (1:9) toluene:heptane]; ^{1}H NMR ($CDCl_3$) δ 6.74 (s, 1 H, Ar*H*), 6.64 (s, 1 H, Ar*H*), 3.98 (dd, 1 H, J = 6.9, 11.8 Hz, C*H*CN), 3.86 (s, 3 H, OCH_3), 3.84 (s, 3 H, OCH_3), 2.29 (ddd, 1 H, J = 1.6, 6.9, 12.5 Hz, C(10)-H_e), 2.22 (br d with fine structure, 1 H, J = 12.8 Hz, C(4)-H_e), 2.00 (apparent q, 1 H, J = 12.5 Hz, C(10)-H_a), 1.72 (dt, 1 H, J = 3.4, 13.9 Hz, C(3)-*H*), 1.62 (tt, 1 H, J = 3.4, 13.9 Hz, C(3)-*H'*), 1.48 (br d with fine structure, 1 H, J = 13.4 Hz, C(2)-H_e), 1.33 (dd, 1 H, J = 3.8, 12.8 Hz, C(4)-H_a), 1.26 (dd, 1 H, J = 1.6, 12.5 Hz, C*H* ring junction), 1.22 (s, 3 H, CH_3), 1.16 (dd, 1 H, J = 4.2, 13.4 Hz, C(2)-H_a), 0.95 (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 148.8 (*C*), 147.5 (*C*), 142.0 (*C*), 122.2 (*C*), 119.7 (*C*), 110.8 (*C*H), 108.5 (*C*H), 55.8 (2 OCH_3), 49.9 (*C*H), 41.2 (CH_2), 38.6 (CH_2), 37.4 (*C*), 33.2 (*C*), 32.9 (CH_3), 32.1 (*C*H), 24.8 (CH_3), 24.2 (CH_2), 21.3 (CH_3), 18.9 (CH_2) ppm; IR (KBr) 3082-2825 (CH envelope), 2232 (CN), 1608, 1518, 1460, 1440, 1262, 1212, 1198, 1158, 1140, 1042, 868 cm^{-1}; high-resolution mass spectrum calcd for $C_{20}H_{27}NO_2$ (M^+) 313.2042, found 313.2041.

For **9b** as a white solid: mp 132-134 °C [recrystallized from (1:9) toluene:heptane]; ^{1}H NMR ($CDCl_3$) δ 6.74 (s, 1 H, Ar*H*), 6.64 (s, 1 H, Ar*H*), 4.01 (d, 1 H, J = 6.4 Hz, C*H*CN), 3.84 (s, 6 H, 2 OCH_3), 2.20 (br d with fine structure, 1 H, J = 13.4 Hz, C(4)-H_e), 2.12 (br d, 1 H, J = 13.8 Hz, C(10)-H_e), 1.98 (td, 1 H, J = 6.4, 12.4, 13.8 Hz, C(10)-H_a), 1.74 (dt, 1 H, J = 3.3, 13.7 Hz, C(3)-*H*), 1.66 (buried m, 1 H, C(3)-*H'*), 1.63 (dd, 1 H, J = 1.7, 12.4 Hz, C*H* ring junction), 1.51 (br d with fine structure, 1 H, J = 13.4 Hz, C(2)-H_e), 1.43 (td, 1 H, J = 3.7, 13.4 Hz, C(4)-H_a), 1.28 (td, 1 H, J = 4.2, 13.4 Hz, C(2)-H_a), 1.15 (s, 3 H, CH_3), 1.02 (s, 3 H, CH_3), 0.91 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 148.8 (*C*), 147.2 (*C*), 142.2 (*C*), 122.2 (*C*), 119.6 (*C*), 111.2 (*C*H), 107.9 (*C*H), 55.7 (2 OCH_3), 47.7 (*C*H), 40.9 (CH_2), 38.3 (CH_2), 37.3 (*C*), 32.8 (*C*), 32.5 (CH_3), 31.5 (*C*H), 24.3 (CH_3), 23.1 (CH_3), 21.4 (CH_3), 18.9 (CH_2) ppm; IR (KBr) 3089-2832 (CH envelope), 2230 (CN), 1610, 1514, 1446, 1356, 1255, 1230, 1206, 1152, 1070, 1042, 856, 694 cm^{-1}; high-resolution mass spectrum calcd for $C_{20}H_{27}NO_2$ (M^+) 313.2042, found 313.2046. Anal. Calcd for $C_{20}H_{27}NO_2$: C, 76.63; H, 8.69. Found: C, 77.03; H, 8.68.

3. *9-Cyano-6,7-dimethoxy-1,2,3,4,4aβ,9α,10,10aβ-octahydro-1,1,4a-trimethylphenanthrene (10a) and 9-cyano-6,7-dimethoxy-1,2,3,4,4aβ,9β,10,10aβ-octahydro-1,1,4a-trimethylphenanthrene (10b).*

Cyclization of aryldiene **3** (0.100 g, 0.32 mmol) with $BF_3 \cdot CH_3NO_2$ (1.11 mL, 1.34 mmol, 1.21 M) in CH_3NO_2 (4.8 mL) afforded, in order of elution, 83 mg (83%) of **10a** and **10b** as a 1.0:1.0 mixture of diastereomers and 15 mg (15%) of **9b**.

For **10a** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 6.96 (s, 1 H, Ar*H*), 6.79 (s, 1 H, Ar*H*), 4.04 (dd, 1 H, J = 7.4, 9.9 Hz, C*H*CN), 3.88 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 2.57 (m, 1 H, C(10)-*H*), 2.18 (m, 2 H, C(10)-*H'*, C(4)-H_e), 1.53-1.42 (cm, 4 H, C(3)H_2, C(4)-H_a, C*H* ring junction), 1.35-1.21 (cm, 2 H, C(2)H_2), 1.15 (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3), 0.36 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 148.4 (*C*), 147.1 (*C*), 135.4 (*C*), 122.5 (*C*), 121.6 (*C*), 109.9 (*C*H), 108.4 (*C*H), 55.9 (OCH_3), 55.8 (OCH_3), 49.2 (*C*H), 40.6 (CH_2), 37.6 (CH_2), 37.0 (*C*), 34.1 (*C*), 32.0 (CH_3), 31.3 (CH_3), 28.0 (*C*H), 24.8 (CH_2), 24.0 (CH_3), 18.8 (CH_2) ppm; IR (thin film) 3082-2839 (CH envelope), 2227 (CN), 1610, 1518, 1464, 1260, 1218, 1168, 1078, 1030 cm^{-1}; high-resolution mass spectrum calcd for $C_{20}H_{27}NO_2$ (M^+) 313.2042, found 313.2043.

For **10b** as a white solid: mp 133-134 °C [recrystallized from (1:9) toluene:heptane]; ^{1}H NMR ($CDCl_3$) δ 6.80 (s, 1 H, Ar*H*), 6.74 (s, 1 H, Ar*H*), 4.09 (apparent t, 1 H, J = 9.0 Hz, CHCN), 3.88 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 2.50-2.29 (cm, 3 H, C(10)H_2, C(4)-H_e), 1.57 (dd, 1 H, J = 3.0, 6.0 Hz, C*H* ring junction), 1.47-1.15 (cm, 5 H, C(2)H_2, C(3)H_2, C(4)-H_a), 1.27 (s, 3 H, CH_3), 0.98 (s, 3 H, CH_3), 0.37 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 148.7 (*C*), 147.2 (*C*), 136.0 (*C*), 128.8 (*C*), 128.0 (*C*), 122.9 (*C*), 121.3 (*C*), 111.4 (*C*H), 107.7 (*C*H), 55.8 (OCH_3), 55.7 (OCH_3), 49.2 (*C*H), 42.3 (CH_2), 37.7 (CH_2), 36.6 (*C*), 35.0 (CH_3), 33.9 (*C*), 32.1 (CH_3), 28.1 (*C*H), 23.5 (CH_3), 23.4 (CH_2),

18.9 (CH_2) ppm; IR (KBr) 3075-2811 (CH envelope), 2228 (CN), 1606, 1516, 1456, 1394, 1235, 1158, 1104, 1076, 1029, 864, 784 cm^{-1}; high-resolution mass spectrum calcd for $C_{20}H_{27}NO_2$ (M^+) 313.2042, found 313.2040.

4. *9-Cyano-1,2,3,4,4aβ,9α,10,10aα-octahydro-1,1,4a-trimethylphenanthrene (11a) and 9-cyano-1,2,3,4,4aβ,9β,10,10aα-octahydro-1,1,4a-trimethylphenanthrene (11b).*

Cyclization of aryldiene **2b** (0.241 g, 0.95 mmol) with $BF_3 \cdot CH_3NO_2$ (2.60 mL, 4.00 mmol, 1.54 M) in CH_3NO_2 (14.3 mL) afforded 0.183 g (76%) of **11a** and **11b** as a 1.4:1.0 mixture of diastereomers.

For **11a** as a colorless oil: ^1H NMR ($CDCl_3$) δ 7.28 (m, 4 H, Ar*H*), 4.06 (dd, 1 H, J = 7.0, 12.6 Hz, C*H*CN), 2.32 (m, 2 H, C(10)-H_e, C(4)-H_e), 2.05 (apparent q, 1 H, J = 12.6 Hz, C(10)-H_a), 1.76 (dt, 1 H, J = 3.4, 13.6 Hz, C(3)-*H*), 1.65 (tt, 1 H, J = 3.4, 13.6 Hz, C(3)-*H'*), 1.51 (br d with fine structure, 1 H, J = 13.5 Hz, C(2)-H_e), 1.37 (dd, 1 H, J = 3.9, 13.2 Hz, C(4)-H_a), 1.31 (dd, 1 H, J = 1.6, 12.6 Hz, C*H* ring junction), 1.24 (s, 3 H, CH_3), 1.18 (dd, 1 H, J = 4.3, 13.5 Hz, C(2)-H_a), 0.97 (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 149.3 (*C*), 128.4 (*C*H), 128.0 (*C*H), 127.7 (*C*), 126.1 (*C*H), 125.0 (*C*H), 122.2 (*C*), 49.5 (*C*H), 41.1 (CH_2), 38.3 (CH_2), 37.6 (*C*), 33.3 (*C*), 32.9 (CH_3), 32.4 (*C*H), 25.0 (CH_3), 24.1 (CH_2), 21.4 (CH_3), 18.3 (CH_2) ppm; IR (thin film) 3061-2839 (CH envelope), 2238 (CN), 1488, 1458, 1378, 1028, 764, 732 cm^{-1}; high-resolution mass spectrum calcd for $C_{18}H_{23}N$ (M^+) 253.1831, found 253.1830.

For **11b** as a colorless oil: ^1H NMR ($CDCl_3$) δ 7.23 (m, 4 H, Ar*H*), 4.10 (d, 1 H, J = 6.4 Hz, C*H*CN), 2.28 (br d with fine structure, 1 H, J = 13.0 Hz, C(4)-H_e), 2.18 (br d, 1 H, J = 13.7 Hz, C(10)-H_e), 2.02 (td, 1 H, J = 6.4, 12.4, 13.7 Hz, C(10)-H_a), 1.76 (dt, 1 H, J = 3.4, 13.6 Hz, C(3)-*H*), 1.71 (buried m, 1 H, C(3)-*H'*), 1.65 (dd, 1 H, J = 2.0, 12.4 Hz, C*H* ring junction), 1.52 (br d with fine structure, 1 H, J = 13.4 Hz, C(2)-H_e), 1.41 (td, 1 H, J = 3.9, 13.0 Hz, C(4)-H_a), 1.29 (td, 1 H, J = 3.5, 13.4 Hz, C(2)-H_a), 1.17 (s, 3 H, CH_3), 1.03 (s, 3 H, CH_3), 0.93 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 149.8 (*C*), 129.3 (*C*H), 128.3 (*C*H), 127.8 (*C*), 126.1 (*C*H), 125.4 (*C*H), 122.3 (*C*), 47.6 (*C*H), 41.0 (CH_2), 38.2 (CH_2), 37.7 (*C*), 32.9 (*C*), 32.6 (CH_3), 31.8 (*C*H), 24.5 (CH_3), 23.2 (CH_2), 21.5 (CH_3), 18.9 (CH_2) ppm; IR (thin film) 3068-2853 (CH envelope), 2234 (CN), 1444, 1378, 1040, 760 cm^{-1}; high-resolution mass spectrum calcd for $C_{18}H_{23}N$ (M^+) 253.1831, found 253.1831. Anal. Calcd for $C_{18}H_{23}N$: C, 85.31; H, 9.15. Found: C, 84.94; H, 9.27.

5. *6,7-Dimethoxy-1,2,3,4,4aβ,9,10,10aα-octahydro-1,1,4a-trimethylphenanthrene (12).*

Cyclization of aryldiene **2c** (0.186 g, 0.65 mmol) with $BF_3 \cdot CH_3NO_2$ (2.53 mL, 2.71 mmol, 1.069 M) in CH_3NO_2 (9.6 mL) afforded 0.136 g (73%) of **12** as a single isomer. For **12** as a white solid: mp 86-87 °C [recrystallized from (1:9) toluene:heptane]; ^1H NMR ($CDCl_3$) δ 6.75 (s, 1 H, Ar*H*), 6.51 (s, 1 H, Ar*H*), 3.82 (s, 3 H, OCH_3), 3.81 (s, 3 H, OCH_3), 2.80 (m, 2 H, $ArCH_2$), 2.21 (br d with fine structure, 1 H, J = 12.5 Hz, C(4)-H_e), 1.84-1.56 (cm, 4 H, C(3)H_2, C(10)H_2), 1.47 (br d with fine structure, 1 H, J = 13.4 Hz, C(2)-H_e), 1.40 (dd, 1 H, J = 3.9, 12.5 Hz, C(4)-H_a), 1.31 (dd, 1 H, J = 2.1, 12.3 Hz, C*H* ring junction), 1.22 (dd, 1 H, J = 4.1, 13.4 Hz, C(2)-H_a), 1.17 (s, 3 H, CH_3), 0.94 (s, 3 H, CH_3), 0.91 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 146.9 (*C*), 146.6 (*C*), 142.1 (*C*), 127.2 (*C*), 111.3 (*C*H), 107.9 (*C*H), 55.9 (OCH_3), 55.6 (OCH_3), 50.6 (*C*H), 41.5 (CH_2), 31.0 (CH_2), 37.4 (*C*), 33.3 (CH_3), 33.2 (*C*), 30.1 (CH_2), 24.7 (CH_3), 21.5 (CH_3), 19.2 (CH_2), 19.0 (CH_2) ppm; IR (KBr) 3075-2818 (CH envelope), 1608, 1513, 1455, 1398, 1360, 1222, 1146, 1118, 1073, 1042, 1018, 854 cm^{-1}; high resolution mass spectrum calcd for $C_{19}H_{28}O_2$ (M^+) 288.2089, found 288.2073.

2-Chloromercurio-9-cyano-6,7-dimethoxy-1,2α,3,4,4aβ,9α,10,10aα-octahydro-1,1,4a-trimethyl phenanthrene (9c) and 2-chloromercurio-9-cyano-6,7-dimethoxy-1,2α,3,4,4aβ,9β,10,10aα-octahydro-1,1,4a-trimethyl phenanthrene (9d).

An oven dried, 25 mL, round-bottomed flask equipped with a magnetic stirring bar, rubber septum and N_2 inlet was flushed with N_2, charged with HgO (0.146 g, 0.67 mmol) and dry CH_3NO_2 (10 mL). Vigorous stirring was initiated and the orange suspension was cooled to 0 °C. Trifluoro-

methanesulfonic anhydride (113 μL, 0.67 mmol) was added dropwise *via* syringe and the resultant milky white solution was stirred for 18 h as it warmed to room temperature. Freshly distilled N,N-dimethylaniline (90 μL, 0.72 mmol) was added in one portion *via* syringe and the resulting brownish solution was cooled to −20 °C. A solution of aryldiene **2a** (0.169 g, 0.54 mmol) in CH_3NO_2 (2 mL) was added dropwise *via* syringe and the reaction mixture was stirred for 2 h at −20 °C. Saturated NaCl was added (5 mL), and the resulting solution was stirred for 24 h at room temperature. The reaction mixture was diluted with ether (20 mL), and the layers were separated. The ether layer was washed with 1 M HCl (10 mL), H_2O (2 x 20 mL), brine (20 mL) and then dried over anhydrous $MgSO_4$. The solvents were evaporated *in vacuo*, and the crude product was purified by flash chromatography [(1:4) ethyl acetate:hexane for elution] to yield 0.091 g (31%) of **9c** and **9d** as an unseparated mixture of diastereomers. Reduction of this mixture with $NaBH_4$ in absolute EtOH provided **9a** and **9b** (*vide supra*) as a 1.0:1.0 mixture of diastereomers following separation by MPLC. Partial ^1H NMR ($CDCl_3$) data from the spectrum of the chromatographed mixture of **9c** and **d**: δ 6.79, 6.78, 6.67, 6.63 (s, 4H, Ar*H*), 4.01 (dd, 1H, J = 6.5, 12.0 Hz, C*H*CN), 3.86, 3.83 (s, 3H, OCH_3), 2.75-2.63 (cm, 1H, C*H*HgCl).

Formation of Chrysene Derivatives

1. *6-Cyano-8,9-dimethoxy-1,2,3,4,4aβ,4bα,5,6α,10bβ,11,12,12aα-dodecahydro-1,1,4a,10b-tetramethylchrysene (13A) and 6-cyano-8,9-dimethoxy-1,2,3,4,4aβ,4bα,5,6β,10bβ,11,12,12aα-dodecahydro-1,1,4a,10b-tetramethylchrysene (13b).*

Cyclization of aryltriene **5** (98 mg, 0.26 mmol) with $BF_3 \cdot CH_3NO_2$ (1.10 mL, 1.079 mmol, 0.988 M) in CH_3NO_2 (3.9 mL), (*vide infra*), afforded 90 mg (92%) of **13**. Attempted separation of the reaction mixture by MPLC [ethyl acetate:hexane (1:99) for elution] gave two fractions A and B (1.0:1.3) each containing a 2:1 mixture of two compounds by GLC (uncorrected).

For fraction **13A** as a white solid: mp 195-205 °C [recrystallized from (1:9) toluene:heptane]; IR (KBr) 3089-2832 (CH envelope), 2232 (CN), 1514, 1460, 1248, 1228, 1204 cm^{-1}; high-resolution mass spectrum calcd for $C_{25}H_{35}NO_2$ (M^+) 381.2668, found 381.2669. For the major compound in *fraction A*; ^1H NMR ($CDCl_3$) δ 6.79 (s, 1 H, Ar*H*), 6.73 (s, 1 H, Ar*H*), 3.95 (dd, 1 H, J = 6.8, 11.9 Hz, C*H*CN), 3.84 (2 s, 6 H, 2 OCH_3), 1.23 (s, 3 H, CH_3), 0.91 (s, 3 H, CH_3), 0.85 (s, 3 H, CH_3), 0.83 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 110.8 (*C*H), 107.9 (*C*H), 55.8 (2 O*C*H$_3$), 54.4 (*C*H), 41.7 (*C*H$_2$), 40.4 (*C*H$_2$), 39.6 (*C*H$_2$), 33.1 (*C*H$_3$), 32.5 (*C*H), 26.0 (*C*H$_3$), 23.2 (*C*H$_2$), 21.2 (*C*H$_3$), 18.8 (*C*H$_2$), 18.3 (*C*H$_2$), 16.1 (*C*H$_3$) ppm. For the minor component in *fraction A*; ^1H NMR ($CDCl_3$) δ 6.84 (s, ArH), 6.76 (s, ArH), 3.85 (s, OCH$_3$) ppm; ^{13}C NMR ($CDCl_3$) δ 110.6 (*C*H), 108.8 (*C*H), 56.0 (O*C*H$_3$), 48.1 (*C*H), 42.2 (*C*H$_2$), 38.1 (*C*H$_2$), 37.4 (*C*H$_2$), 33.6 (*C*H), 33.1 (*C*H$_3$), 30.9 (*C*H$_3$), 26.7 (*C*H$_2$), 25.5 (*C*H$_3$), 22.6 (*C*H$_2$), 21.8 (*C*H$_3$), 19.7 (*C*H$_2$) ppm.

For fraction **13B** as a white solid: mp 184-202 °C [recrystallized from (1:9) toluene:heptane]; IR (KBr) 3075-2832 (CH envelope), 2234 (CN), 1518, 1458, 1260, 1240, 1154 cm^{-1}; high-resolution mass spectrum calcd for $C_{25}H_{35}NO_2$ (M^+) 381.2668, found 381.2677. For the major compound in *fraction B*; ^1H NMR ($CDCl_3$) δ 6.73 (s, 1 H, Ar*H*), 6.62 (s, 1 H, Ar*H*), 3.99 (d, 1 H, J = 5.8 Hz, C*H*CN), 3.83 (s, 6 H, 2 OCH_3), 1.16 (s, 3 H, CH_3), 0.90 (s, 3 H, CH_3), 0.86 (s, 3 H, CH_3), 0.83 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 111.0 (*C*H), 108.1 (*C*H), 55.8 (2 O*C*H$_3$), 52.4 (*C*H), 48.2 (*C*H), 41.6 (*C*H$_2$), 40.2 (*C*H$_2$), 39.1 (*C*H$_2$), 33.0 (*C*H$_3$), 32.0 (*C*H), 25.6 (*C*H$_3$), 22.2 (*C*H$_2$), 21.2 (*C*H$_3$), 18.8 (*C*H$_2$), 18.2 (*C*H$_2$), 16.4 (*C*H$_3$) ppm.

2. *Structural simplification of 13a and 13b. 8,9-Dimethoxy-1,2,3,4,4aβ,4bα,5,6α,10bβ,11,12,12aα-dodecahydro-1,1,4a,10b-tetramethylchrysene (14).*

Reduction of the crude cyclization reaction mixture containing **13a** and **b** (68 mg, 0.18 mmol) with Li (3 mg, 0.39 mmol) and *t*-BuOH (19 μL, 0.20 mmol) in NH_3 (20 mL), (*vide infra*), afforded 36 mg (57% from **5**) of **14** as a single compound after MPLC [(1:99) ethyl acetate:hexane was used for elution] and recrystallization. For **14** as a white solid: mp 113-114 °C [recrystallized from (1:9)

toluene:heptane]; ^{1}H NMR ($CDCl_3$) δ 6.74 (s, 1 H, Ar*H*), 6.48 (s, 1 H, Ar*H*), 3.82 (s, 3 H, O*CH*$_3$), 3.80 (s, 3 H, O*CH*$_3$), 2.85-0.90 (cm, 14H, C*H* envelope), 1.21 (s, 3 H, C*H*$_3$), 0.90 (s, 3 H, C*H*$_3$), 0.85 (s, 3 H, C*H*$_3$), 0.83 (s, 3 H, C*H*$_3$) ppm; ^{13}C NMR ($CDCl_3$) δ 147.0 (*C*), 146.6 (*C*), 142.4 (*C*), 127.2 (*C*), 111.2 (*C*H), 108.0 (*C*H), 56.2 (*C*H), 56.0 (O*CH*$_3$), 55.6 (O*CH*$_3$), 55.4 (*C*H), 42.0 (*CH*$_2$), 40.8 (*CH*$_2$), 39.7 (*CH*$_2$), 37.8 (*C*), 37.5 (*C*), 33.2 (*CH*$_3$), 30.5 (*CH*$_2$), 21.3 (*CH*$_3$), 19.0 (*CH*$_2$), 18.5 (*CH*$_2$), 18.0 (*CH*$_2$), 16.2 (*CH*$_3$) ppm; IR (KBr) 3082-2818 (CH envelope), 2234 (CN), 1518, 1458, 1260, 1240, 1154 cm^{-1}; high-resolution mass spectrum calcd for $C_{24}H_{36}O_2$ (M^+) 356.2715, found 356.2707.

Preparation and BF_3•CH_3NO_2 Mediated Cyclizations of β-Ketoester 6 and Enol Derivatives 7a-c

1. *Methyl (E)-7,11-dimethyl-3-oxo-6,10-dodecadieneoate (6).*

A flame-dried, 250-mL, round-bottomed flask equipped with a magnetic stirring bar, rubber septum and N_2 inlet was flushed with N_2, charged with dry diisopropylamine (16.7 mL, 0.12 mol) and dry THF (125 mL), and cooled to 0 °C. *n*-BuLi (25.7 mL, 0.12 mol, 4.64 M in heptane) was added dropwise via syringe, and the resulting solution was stirred for 15 min at 0 °C. A solution of methyl acetoacetate (6.587 g, 0.057 mol) in dry THF (10 mL) was added dropwise via syringe, and the reaction mixture was stirred for 1 h at 0 °C. HMPA (29.6 mL, 0.17 mol) was added in one portion via syringe, and the resulting solution was immediately cooled to -78 °C. (*E*)-1-bromo-3,7-dimethyl-octadiene (11.8 mL, 0.059 mol) was added in one portion via syringe, and the reaction mixture was stirred overnight while it warmed to room temperature. The reaction was quenched with saturated aqueous NH_4Cl (100 mL), and the organic phase was washed with H_2O (50 mL) and brine (50 mL). The combined aqueous layers were back extracted with (1:1) ethyl acetate: hexane (3 x 100 mL), and the combined organic phase was dried over anhydrous $MgSO_4$. The solvents were evaporated *in vacuo* and the crude product was initially purified by flash chromatography [ethyl acetate:hexane (1:9) for elution]. Final purification of the chromatographed material by bulb-to-bulb distillation afforded 12.167 g (85%) of **6** as a colorless liquid: ^{1}H NMR ($CDCl_3$) δ 5.04 (m, 2 H, 2 =C*H*), 3.71 (s, 3 H, O*CH*$_3$), 3.42 (s, 2 H, C*H*$_2$), 2.53 (t, 2 H, J = 7.3 Hz, C*H*$_2$), 2.26 (q, 2 H, J = 7.3 Hz, C*H*$_2$), 1.99 (m, 4 H, 2 C*H*$_2$), 1.64 (s, 3 H, C*H*$_3$), 1.58 (s, 3 H, C*H*$_3$), 1.56 (s, 3 H, C*H*$_3$) ppm; ^{13}C NMR ($CDCl_3$) δ 202.3 (*C*=O ketone), 166.9 (*C*=O ester), 136.7 (*C*), 131.3 (*C*), 124.0 (*C*H), 121.9 (*C*H), 52.1 (O*CH*$_3$), 49.0 (*CH*$_2$), 42.9 (*CH*$_2$), 39.5 (*CH*$_2$), 26.5 (*CH*$_2$), 25.5 (*CH*$_3$), 22.0 (*CH*$_2$), 17.5 (*CH*$_3$), 15.9 (*CH*$_3$) ppm; IR (neat) 3033-2839 (CH envelope), 1750 (C=O), 1718 (C=O), 1654, 1630, 1438, 1238 cm^{-1}; high-resolution mass spectrum calcd for $C_{15}H_{24}O_3$ (M^+) 252.1725, found 252.1729.

2. *Methyl (2Z,6E)-3-[dimethyl-(1,1-dimethylethyl)siloxy]-7,11-dimethyl-2,6,10-dodecatrieneoate (7a).*

A flame-dried, 50-mL, round-bottomed flask equipped with a magnetic stirring bar, rubber septum and N_2 inlet was flushed with N_2, charged with oil-free NaH (414 mg, 17.26 mmol), dry THF (15 mL) and cooled to 0 °C. A solution of β-ketoester **6** (1.089 g, 4.32 mmol) in dry THF (4 mL) was added dropwise via syringe, and the resulting solution was stirred for 1 h at 0 °C then cooled to −78 °C. *t*-Butyldimethylsilyl trifluoromethanesulfonate (1.04 mL, 4.53 mmol) was added dropwise via syringe. The Dry-ice bath was removed and the reaction mixture was stirred for 1 h while the solution was allowed to warm to room temperature. The reaction was quenched with saturated aqueous NH_4Cl (20 mL) and the organic phase was washed with brine (2 x 25 mL). The combined aqueous layers were back extracted with ether (3 x 25 mL) and the organic phase was dried over anhydrous $MgSO_4$. The solvents were evaporated *in vacuo* and the crude product was initially purified by flash chromatography [ethyl acetate:hexane (1:9) for elution]. Final purification of the chromatographed material by bulb-to-bulb distillation afforded 0.601 g (38%) of **7a** as a colorless liquid: ^{1}H NMR ($CDCl_3$) δ 5.06 (br s with fine structure, 3 H, 3 =C*H*), 3.62 (s, 3 H, O*CH*$_3$), 2.23-1.96 (cm, 8 H, 4 C*H*$_2$), 1.65 (s, 3 H, C*H*$_3$), 1.58 (s, 6 H, 2 C*H*$_3$), 0.96 (s, 9 H, 3 C*H*$_3$), 0.20 (s, 6 H, 2 C*H*$_3$) ppm; ^{13}C NMR ($CDCl_3$) δ 167.6 (*C*), 165.7 (*C*), 136.3 (*C*), 131.1 (*C*), 124.0 (*C*H), 122.3 (*C*H), 98.6 (*C*H), 50.2 (O*CH*$_3$), 39.5 (*CH*$_2$), 38.2 (*CH*$_2$), 26.5 (*CH*$_2$), 25.6 (3 *CH*$_3$), 25.5 (*CH*$_3$), 25.4 (*CH*$_2$), 18.4 (*C*), 17.5 (*CH*$_3$), 15.9 (*CH*$_3$), -4.2 (2 *CH*$_3$) ppm; IR (neat) 3068-2853 (CH envelope), 1718 (C=O

ester), 1620, 1436, 1256, 1134, 1046, 840, 784 cm^{-1}; high-resolution mass spectrum calcd for $C_{21}H_{38}O_3Si$ (M^+) 366.2590, found 366.2598.

3. *Methyl (2E,6E)-3-[dimethyl-(1,1-dimethylethyl)siloxy]-7,11-dimethyl-2,6,10-dodecatrieneoate (7c).*

A flame-dried, 50-mL, round-bottomed flask equipped with a magnetic stirring bar, rubber septum and N_2 inlet was flushed with N_2, charged with β-ketoester **6** (1.349 g, 5.35 mmol), imidazole (0.765 g, 11.24 mmol) and dry DMF (20 mL). The solution was cooled to 0 °C and *t*-butyldimethylsilyl chloride (0.848 g, 5.62 mmol) was added in one portion as a solid. The reaction mixture was stirred overnight and then allowed to warm to room temperature. The reaction was quenched with H_2O (20 mL) and extracted with diethyl ether (3 x 25 mL). The combined ethereal layers were washed with 5% aqueous HCl (10 mL), H_2O (10 mL), saturated $NaHCO_3$ (10 mL), H_2O (10 mL) and brine (2 x 10 mL). The combined aqueous layers were back extracted with diethyl ether (3 x 25 mL) and the organic phase was dried over anhydrous $MgSO_4$. The solvents were removed *in vacuo* to give the crude product which was initially purified by MPLC [ethyl acetate:hexane (1:19) for elution]. Final purification of the chromatographed material by bulb-to-bulb distillation afforded 1.595 g (81%) of **7c** as a colorless liquid: ^1H NMR ($CDCl_3$) δ 5.15 (dt, 1 H, J = 1.0, 6.9 Hz, =C*H*), 5.07 (m, 1 H, =C*H*), 5.06 (s, 1 H, =C*H*), 3.63 (s, 3 H, OCH_3), 2.73 (t, 2 H, J = 7.5 Hz, CH_2), 2.22 (q, 2 H, J = 7.5 Hz, CH_2), 1.98 (m, 4 H, 2 CH_2), 1.66 (s, 3 H, CH_3), 1.59 (s, 3 H, CH_3), 1.58 (s, 3 H, CH_3), 0.93 (s, 9 H, 3 CH_3), 0.21 (s, 6 H, 2 CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 173.2 (*C*), 167.9 (*C*), 135.8 (*C*), 131.3 (*C*), 124.3 (*C*H), 123.0 (*C*H), 98.5 (*C*H), 50.5 (O*C*H_3), 39.6 (*C*H_2), 33.3 (*C*H_2), 26.7 (*C*H_2), 25.5 (*C*H_3), 25.5 (*C*H_2), 25.4 (3 *C*H_3), 18.0 (*C*), 17.5 (*C*H_3), 15.9 (*C*H_3), -4.8 (2 *C*H_3) ppm; IR (neat) 3068-2853 (CH envelope), 1718 (C=O ester), 1620, 1436, 1256, 1134, 1046, 840, 784 cm^{-1}; high-resolution mass spectrum calcd for $C_{21}H_{38}O_3Si$ (M^+) 366.2590, found 366.2578.

4. *Methyl (2Z,6E)-3-Acetoxy-7,11-dimethyl-2,6,10-dodecatrieneoate (7b).*

A flame-dried, 50-mL, round-bottomed flask equipped with a magnetic stirring bar, reflux condenser and N_2 inlet was flushed with N_2, and charged with β-ketoester **6** (2.241 g, 8.88 mmol), 2-acetoxypropene (4.3 mL, 38.37 mmol) and TsOH (125 mg). The mixture was heated to reflux overnight, cooled to room temperature and diluted with diethyl ether (20 mL). The ethereal solution was washed with saturated $NaHCO_3$ (5 mL), H_2O (5 mL), and brine (5 mL), and dried over anhydrous $MgSO_4$. The volatile materials were evaporated *in vacuo* and the crude product was initially purified by flash chromatography [(1:19) ethyl acetate:hexane for elution]. Final purification of the chromatographed material by bulb-to-bulb distillation afforded 2.267 g (87%) of **7b** as a colorless liquid: ^1H NMR ($CDCl_3$) δ 5.55 (s, 1 H, =C*H*), 5.04 (m, 2 H, 2 =C*H*), 3.61 (s, 3 H, OCH_3), 2.20- (cm, 4 H, 2 CH_2), 2.19 (s, 3 H, C(O)CH_3), 1.97 (m, 4 H, 2 CH_2), 1.62 (s, 3 H, CH_3), 1.55 (s, 3 H, CH_3), 1.54 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 167.7 (*C*), 164.1 (*C*), 163.2 (*C*), 136.7 (*C*), 131.2 (*C*), 123.9 (*C*H), 121.8 (*C*H), 106.7 (*C*H), 51.0 (*C*H_3), 39.4 (*C*H_2), 35.3 (*C*H_2), 26.4 (*C*H_2), 25.4 (*C*H_3), 24.2 (*C*H_2), 20.7 (*C*H_3), 17.4 (*C*H_3), 15.8 (*C*H_3) ppm; IR (neat) 3080-2856 (CH envelope), 1772 (C=O), 1728 (C=O), 1668, 1368, 1234, 1170, 1138, 1036 cm^{-1}; high-resolution mass spectrum calcd for $C_{17}H_{26}O_4$ (M^+) 294.1831, found 294.1814.

5. *1-Carbomethoxy-2-oxo-1α,2,3,4,4aα,5,6,7,8,8aβ-perhydro-5,5,8a-trimethylnaphthalene (15).*

Cyclization of the (2*Z*)-silyl enol ether **7a** (0.11 g, 0.30 mmol) with $BF_3 \cdot CH_3NO_2$ (1.29 mL, 1.27 mmol, 0.988 M) in CH_3NO_2 (4.5 mL) (*vide supra*) for 3 h at −20 °C, afforded 53 mg (69%) of **15** as a white solid: mp 85-86 °C [following recrystallization from (1:99) ethyl acetate: hexane]; lit.[16] mp 85.5-87 °C; ^1H NMR ($CDCl_3$) δ 3.65 (s, 3 H, OCH_3), 3.18 (s, 1 H, C*H*), 2.47 (dd, 1 H, J = 5.0, 14.2 Hz, C(O)C-*H*), 2.30 (m, 1 H, C(O)C-*H'*), 2.02 (m, 1 H, CH'-*H*), 1.78-1.15 (cm, 8 H, 3 CH_2, CH-*H'*, C*H* ring junction), 1.12 (s, 3 H, CH_3), 0.93 (s, 3 H, CH_3), 0.85 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 205.3 (*C*=O ketone), 168.5 (*C*=O ester), 69.9 (*C*H), 53.1 (*C*H), 51.2 (O*C*H_3), 41.7 (*C*H_2), 41.1 (*C*H_2), 39.0 (*C*H_2), 33.3 (*C*H_3), 22.7 (*C*H_2), 21.6 (*C*H_3), 18.4 (*C*H_3), 14.6 (*C*H_2) ppm; IR (KBr)

3020-2832 (CH envelope), 1746 (C=O), 1716 (C=O), 1438, 1428, 1370, 1348, 1200, 1172, 1144, 1114 cm^{-1}; high-resolution mass spectrum calcd for $C_{15}H_{24}O_3$ (M^+) 252.1725, found 252.1727.

6. *1-Carbomethoxy-2-oxo-1β,2,3,4,4aα,5,6,7,8,8aβ-perhydro-5,5,8a-trimethylnaphthalene (16).*

Cyclization of the (2*E*)-silyl enol ether **7c** (0.129 g, 0.35 mmol) with $BF_3 \cdot CH_3NO_2$ (1.42 mL, 1.48 mmol, 1.044 M) in CH_3NO_2 (5.0 mL) (*vide supra*) for 3 h at -20 °C, afforded 80 mg (90%) of **16** as a white solid: mp 105-106 °C [following recrystallization from petroleum ether (bp = 30-60 °C)]; ^1H NMR ($CDCl_3$) δ 3.62 (s, 3 H, OCH_3), 2.90 (apparent d, 1 H, J = 1.5 Hz, C*H*), 2.89 (m, 1 H, J = 7.4 Hz, C(O)C-*H*), 2.37 (dm, 1 H, J = 2.3, 14.6 Hz, C(O)C-*H'*), 2.11 (dd, 1 H, J = 3.2, 12.8 Hz, C*H* ring junction), 1.96 (m, 1 H, C(4)-*H*), 1.63-1.34 (cm, 5 H, C(7)H_2, C(8)-*H*, C(6)-*H*, C(4)-*H'*), 1.25 (dd, 1 H, J = 3.7, 13.3 Hz, C(8)-*H'*), 1.16 (dd, 1 H, J = 3.7, 13.1 Hz, C(6)-*H'*), 0.94 (s, 3 H, CH_3), 0.91 (s, 3 H, CH_3), 0.81 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 206.9 (*C*=O ketone), 169.3 (*C*=O ester), 70.7 (*C*H), 51.7 (OCH_3), 44.0 (*C*H), 41.6 (CH_2), 39.8 (CH_2), 37.9 (CH_2), 33.1 (CH_3), 22.7 (CH_2), 21.9 (CH_3), 20.8 (CH_3), 18.5 (CH_2) ppm; IR (KBr) 3006-2852 (CH envelope), 1726 (C=O), 1708 (C=O), 1424, 1190, 1156, 1004 cm^{-1}; high-resolution mass spectrum calcd for $C_{15}H_{24}O_3$ (M^+) 252.1725, found 252.1722.

7. *Cyclization of Enol Acetate 7b.*

Cyclization of enol acetate **7b** (0.105 g, 0.36 mmol) with $BF_3 \cdot CH_3NO_2$ (1.52 mL, 1.50 mmol, 0.988 M) in CH_3NO_2 (12.6 mL) (*vide supra*) followed by stirring overnight at -20 °C, afforded, in order of elution, 6 mg (7%) of **16** and 30 mg (33%) of **15**.

8. *3,4,4aβ,5,6,7,8β,9,10,10aα-Decahydro-4a,8-epoxy-3-oxo-1,1,8-trimethyl-1H-cycloocta[c]pyran (18).*

Cyclization of β-ketoester **6** (0.103 g, 0.41 mmol) with $BF_3 \cdot CH_3NO_2$ (1.64 mL, 1.71 mmol, 1.044 M) in CH_3NO_2 (5.8 mL) for 3 h at -20 °C (*vide supra*) afforded 82 mg (84%) of **18** as a white solid: mp 122-124 °C (following recrystallization from hexane); ^1H NMR ($CDCl_3$) δ 2.43 (AB q, 2 H, J = 16.5 Hz, C(O)CH_2), 2.10-1.95 (cm, 4 H, C(A)-*H*, C(B)-*H*, C(C)-*H*, C*H* ring junction), 1.80 (dd, 1 H, J = 5.0, 12.9 Hz, C(E)-*H*), 1.69-1.47 (cm, 6 H, C(A)-*H'*, C(B)-*H'*, C(C)-*H'*, C(D)H_2, C(E)-*H'*), 1.40 (s, 3 H, CH_3), 1.34 (s, 3 H, CH_3), 1.13 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 169.3 (*C*=O lactone), 84.8 (*C*), 70.8 (*C*), 69.7 (*C*), 50.1 (*C*H), 47.6 (CH_2), 36.5 (CH_2), 34.7 (CH_2), 31.9 (CH_3), 31.6 (CH_3), 31.5 (CH_2), 24.0 (CH_3), 22.2 (CH_2), 19.6 (CH_2) ppm; IR (KBr) 3006-2839 (CH envelope), 1718 (C=O), 1392, 1322, 1288, 1152, 1134, 1104, 1096, 1040, 982 cm^{-1}; high-resolution mass spectrum calcd for $C_{14}H_{22}O_3$ (M^+) 238.1569, found 238.1570.

Total Synthesis of (±)-Taxodione (1)

3,4-Dimethoxy-5-(1-methylethyl)phenylmethanol.

A flame-dried, 250-mL, round-bottomed flask equipped with a magnetic stirring bar, rubber septum and N_2 inlet was flushed with N_2, charged with acid **19**[20] (7.13 g, 31.8 mmol), dry THF (50 mL) and cooled to 0 °C. $BH_3 \cdot DMS$ (5.0 mL, 50.0 mmol, 10 M) was added dropwise via syringe and the resulting solution was stirred overnight and allowed to warm to room temperature. The reaction was quenched by careful addition of H_2O (50 mL - caution, vigorous gas evolution) and the resulting solution was diluted with diethyl ether (100 mL). The ether layer was separated, washed with brine (50 mL) and dried over anhydrous $MgSO_4$. The solvents were evaporated *in vacuo* to give the crude product which was purified by bulb-to-bulb distillation to afford 6.25 g (94%) of the corresponding alcohol as a white solid: mp 38-39 °C; ^1H NMR ($CDCl_3$) δ 6.79 (d, 1 H, J = 1.6 Hz, Ar*H*), 6.77 (d, 1 H, J = 1.6 Hz, Ar*H*), 4.60 (s, 2 H, CH_2), 3.83 (s, 3 H, OCH_3), 3.78 (s, 3 H, OCH_3), 3.33 (m, 1 H, J = 6.9 Hz, C*H*), 1.95 (br s, 1 H, O*H*), 1.19 (d, 6 H, J = 6.9 Hz, 2 CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 152.5 (*C*), 145.5 (*C*), 142.3 (*C*), 136.6 (*C*), 116.7 (*C*H), 108.4 (*C*H), 65.4 (CH_2), 60.7 (OCH_3), 55.5 (OCH_3), 26.6 (*C*H), 23.3 (2 CH_3) ppm; IR (KBr) 3310 (br OH), 3020-2818 (CH envelope), 1588,

1488, 1466, 1432, 1310, 1142, 1066, 1010, 842 cm^{-1}; high-resolution mass spectrum calcd for $C_{12}H_{18}O_3$ (M^+) 210.1256, found 210.1249.

1-Chloromethyl-3,4-dimethoxy-5-(1-methylethyl)benzene (20).

A flame-dried, 200 mL, round-bottomed flask equipped with a magnetic stirring bar, 60 mL pressure equalizing addition funnel fitted with a rubber septum and a N_2 inlet was charged with the above alcohol (6.01 g, 26.6 mmol), dry CH_2Cl_2 (44 mL) and then cooled to 0 °C. $SOCl_2$ (2.33 mL, 31.9 mmol) [freshly distilled from $(PhO)_3P$] was added over 30 min via the addition funnel. Stirring was continued at 0 °C until gas evolution had ceased and then the reaction mixture was stirred at room temperature for 2 h. The reaction was quenched by careful addition of $NaHCO_3$ (25 mL) and the CH_2Cl_2 layer was washed with H_2O (25 mL), brine (25 mL) and then dried over anhydrous $MgSO_4$. Evaporation of the solvent *in vacuo* afforded the crude product which was purified by bulb-to-bulb distillation to yield 5.76 g (95%) of **20**. For **20** as a colorless oil: ^1H NMR ($CDCl_3$) δ 6.86 (d, 1 H, J = 1.7 Hz, Ar*H*), 6.82 (d, 1 H, J = 1.7 Hz, Ar*H*), 4.57 (s, 2 H, CH_2), 3.88 (s, 3 H, OCH_3), 3.83 (s, 3 *H*, OCH_3), 3.36 (d, 1 H, J = 6.9 Hz, C*H*), 1.23 (d, 6 H, J = 6.9 Hz, 2 CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 152.5 (*C*), 146.3 (*C*), 142.4 (*C*), 132.9 (*C*), 118.5 (*C*H), 109.9 (*C*H), 60.6 (OCH_3), 55.5 (OCH_3), 46.6 (CH_2), 26.7 (*C*H), 23.2 (2 CH_3) ppm; IR (thin film) 3061-2818 (CH envelope), 1590, 1488, 1464, 1430, 1314, 1068, 1010, 710 cm^{-1}; high-resolution mass spectrum calcd for $C_{12}H_{17}ClO_2$ (M^+) 228.0940, found 228.0917.

(E)-4,8-Dimethyl-2-[3,4-dimethoxy-5-(1-methylethyl)-phenyl]methyl-3,7-nonadienenitrile (21).

Aryldiene **21** was prepared as a colorless oil in 88% yield from (*E*)-4,8-dimethyl-3,7-nonadienonitrile (1.486 g, 9.10 mmol) and benzyl chloride **20** (2.035 g, 8.98 mmol) (*vide supra*): ^1H NMR ($CDCl_3$) δ 6.68 (d, 1 H, J = 1.7 Hz, Ar*H*), 6.65 (d, 1 H, J = 1.7 Hz, Ar*H*), 5.13 (d, 1 H, J = 8.8 Hz, =C*H*), 5.06 (t, 1 H, J = 5.4 Hz, =C*H*), 3.85 (s, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 3.55 (q, 1 H, J = 8.8 Hz, C*H*CN), 3.34 (m, 1 H, J = 6.9 Hz, C*H*), 2.96 (dd, 1 H, J = 7.5, 13.5 Hz, CH_2Ar), 2.80 (dd, 1 H, J = 6.9, 13.5 Hz, CH_2Ar), 2.03 (m, 4 H, 2 CH_2), 1.68 (s, 3 H, CH_3), 1.60 (s, 3 H, CH_3), 1.54 (s, 3 H, CH_3), 1.21 (d, 6 H, J = 6.9 Hz, 2 CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 152.0 (*C*), 145.0 (*C*), 141.5 (*C*), 140.5 (*C*), 131.9 (*C*), 131.2 (*C*), 123.0 (*C*H), 120.2 (*C*N), 118.6 (*C*H), 117.9 (*C*H), 110.5 (*C*H), 60.0 (OCH_3), 55.1 (OCH_3), 39.0 (CH_2), 38.7 (CH_2), 31.4 (*C*H), 26.3 (*C*H), 25.8 (CH_2), 25.0 (CH_3), 22.9 (2 CH_3), 17.0 (CH_3), 15.8 (CH_3) ppm; IR (thin film) 3057-2823 (CH envelope), 2236 (CN), 1588, 1488, 1464, 1432, 1308, 1226, 1146, 1068, 1012 cm^{-1}; high-resolution mass spectrum calcd for $C_{23}H_{33}NO_2$ (M^+) 355.2512, found 355.2514.

10-Cyano-5,6-dimethoxy-7-(1-methyethyl)-1,2,3,4,4aβ,9,10β,10aα-octahydro-1,1,4a-trimethylphenanthrene (22).

Cyclization of aryldiene **21** (0.556 g, 1.56 mmol) with $BF_3 \cdot CH_3NO_2$ (6.70 mL, 6.57 mmol, 0.977 M) in CH_3NO_2 (23.5 mL), (*vide supra*), by stirring 5 min at -20 °C then overnight at room temperature, afforded 0.460 g (83%) of **22** as a single diastereomer following recrystallization from ethyl acetate:hexane (1:99). For **22** as a white solid: mp 118-120 °C; ^1H NMR ($CDCl_3$) δ 6.63 (s, 1 H, Ar*H*), 3.79 (s, 3 H, OCH_3), 3.74 (s, 3 H, OCH_3), 3.26-3.05 (cm, 3 H, CH, ArCH_2), 3.00-2.89 (cm, 2 H, C(4)-H_e, C*H*CN), 1.69 (d, 1 H, J = 9.8 Hz, C*H* ring junction), 1.65-1.43 (cm, 4 H, C(4)-H_a, C(2)-H_e, (C(3)H_2), 1.34 (s, 3 H, CH_3), 1.29 (s, 3 H, CH_3), 1.25 (buried m, 1 H, C(2)-H_a), 1.20 (s, 3 H, CH_3), 1.16 (d, 6 H, J = 6.9 Hz, 2 CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 151.6 (*C*), 150.0 (*C*), 140.7 (*C*), 138.6 (*C*), 128.1 (*C*), 124.2 (*C*), 120.8 (*C*H), 60.0 (OCH_3), 59.8 (OCH_3), 53.6 (*C*H), 41.8 (CH_2), 40.9 (*C*), 37.7 (CH_2), 36.5 (CH_2), 34.3 (*C*), 33.9 (CH_3), 26.5 (*C*H), 25.0 (*C*H), 23.4 (CH_3), 23.1 (CH_3), 22.5 (CH_3), 22.4 (CH_3), 18.8 (CH_2) ppm; IR (KBr) 3075-2825 (CH envelope), 2230 (CN), 1472, 1400, 1330, 1316, 1302, 1252, 1064, 1048, 1020 cm^{-1}; high-resolution mass spectrum calcd for $C_{23}H_{33}NO_2$ (M^+) 355.2511, found 355.2496. Anal. Calcd for $C_{23}H_{33}NO_2$: C, 77.69; H, 9.36. Found: C, 77.82; H, 9.32.

5,6-Dimethoxy-7-(1-methylethyl)-1,2,3,4,4aβ,9,10,10aα-octahydro-9-oxo-1,1,4a-trimethylphenanthrene (24); and 10-Cyano-5,6-dimethoxy-7-(1-methylethyl)-1,2,3,4,4aβ,10aα-hexahydro-1,1,4a-trimethylphenanthrene (23).

A flame-dried, 25-mL, round-bottomed flask equipped with a magnetic stirring bar, rubber septum, and argon inlet was swept with argon, charged with cyclized nitrile **22** (0.210 g, 0.59 mmol), dry THF (8 mL) and cooled to 0 °C. LDA•THF complex (3.36 mL, 2.95 mmol, 0.879 M in methylcyclohexane) was added dropwise via syringe, and the resulting solution was stirred for 1 h at 0 °C. The reaction mixture was cooled to -78 °C and dry oxygen was bubbled through the solution for 30 min. The reaction was quenched (at -78 °C) with acidic $SnCl_2$ (2 mL, 1 M in 2 M HCl), and the resulting solution was stirred at 0 °C for 30 min. The solution was diluted with H_2O (5 mL), diethyl ether (10 mL) and then filtered through a pad of celite to remove inorganic salts. The layers were separated and the ether layer was washed with H_2O (5 mL), 10% aqueous NaOH (2 x 5 mL), H_2O (5 mL) and brine (5 mL). The aqueous layers were back extracted with diethyl ether (3 x 5 mL) and the combined organic phases were dried over anhydrous $MgSO_4$. Evaporation of the solvents *in vacuo* afforded 0.248 g of the crude product which contained 58% of **24**, and 38% of **23** by GLC. For **23** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.25 (d, 1 H, J = 2.8 Hz, =C*H*), 6.75 (s, 1 H, Ar*H*), 3.79 (s, 3 H, OCH_3), 3.77 (s, 3 H, OCH_3), 3.24 (m, 1 H, J = 6.9 Hz, C*H*), 2.99 (br d with fine structure, 1 H, J = 10.5 Hz, C(4)-H_e), 2.37 (d, 1 H, J = 2.8 Hz, C*H* ring junction), 1.71-1.47 (cm, 4 H, C(3)H_2, C(2)-H_e, C(4)-H_a), 1.30 (s, 3 H, CH_3), 1.28 (s, 3 H, CH_3), 1.20 (d, 3 H, J = 6.9 Hz, CH_3), 1.15 (d, 3 H, J = 6.9 Hz, CH_3), 1.14 (buried m, 1 H, C(2)-H_a), 1.14 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 153.7 (*C*), 150.9 (*C*), 146.3 (*C*H), 141.0 (*C*), 139.3 (*C*), 127.3 (*C*), 122.2 (*C*H), 109.5 (*C*), 60.2 (O*C*H_3), 59.9 (O*C*H_3), 51.5 (*C*H), 42.6 (*C*H_2), 41.6 (*C*), 35.9 (*C*H_2), 33.5 (*C*H_3), 33.1 (*C*), 26.5 (*C*H), 23.4 (*C*H_3), 22.8 (*C*H_3), 22.1 (*C*H_3), 19.3 (*C*H_3), 18.7 (*C*H_2) ppm; IR (thin film) 3033-2825 (CH envelope), 2200 (CN), 1610, 1440, 1400, 1300, 1262, 1096, 1020, 800 cm^{-1}; high-resolution mass spectrum calcd for $C_{23}H_{31}NO_2$ (M^+) 353.2355, found 353.2354.

5,6-Dimethoxy-10-hydroxy-7-(1-methylethyl)-1,2,3,4,4aβ,9,10α,10aα-octahydro-1,1,4a-trimethyl-phenanthrene (25).

The crude product (0.248 g) from the oxidative decyanation reaction was dissolved in dry diethyl ether (5 mL) and lithium aluminum hydride (67 mg, 1.77 mmol) was added as a solid. The reaction mixture was stirred for 3 h at room temperature and then carefully quenched with 5% HCl (5 mL - caution, vigorous gas evolution). The reaction mixture was diluted with H_2O (10 mL), diethyl ether (10 mL) and then filtered through a pad of celite to remove inorganic salts. The layers were separated and the ether layer was washed with saturated aqueous $NaHCO_3$ (10 mL), H_2O (10 mL) and brine (10 mL). The combined aqueous layers were back extracted with diethyl ether (3 x 10 mL) and the combined organic phases were dried over anhydrous $MgSO_4$. The solvents were evaporated *in vacuo* and the crude alcohol was purified by MPLC [ethyl acetate:hexane for (1:19) elution] to afford 110 mg (54% from **22**) of **25** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 6.63 (s, 1 H, Ar*H*), 4.61 (br s, 1 H, C*H*OH), 3.84 (s, 3 H, OCH_3), 3.75 (s, 3 H, OCH_3), 3.23 (m, 1 H, J = 6.9 Hz, C*H*), 3.08 (dd, 1 H, J = 4.3, 17.1 Hz, ArCH_a), 2.89 (br d with fine structure, 1 H, J = 12.7 Hz, C(4)-H_e), 2.84 (d, 1 H, J = 17.1 Hz, ArCH_e), 1.81 (dt, 1 H, J = 3.9, 12.7 Hz, C(3)-*H*), 1.69 (s, 3 H, CH_3), 1.56 (t, 1 H, J = 3.9 Hz, C(3)-*H'*), 1.47 (br d with fine structure, 1 H, J = 15.3 Hz, C(2)-H_e), 1.40 (s, 1 H, C*H* ring junction), 1.38 (buried s, 1 H, O*H*), 1.34 (dd, 1 H, J = 3.5, 12.7 Hz, C(4)-H_a), 1.27 (s, 3 H, CH_3), 1.24 (buried m, 1 H, C(2)-H_a), 1.19 (apparent t, 6 H, J = 6.9 Hz, 2 CH_3), 1.02 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 152.2 (*C*), 149.4 (*C*), 140.2 (*C*), 138.9 (*C*), 127.7 (*C*), 122.2 (*C*H), 65.7 (*C*H), 59.9 (O*C*H_3), 59.7 (O*C*H_3), 54.1 (*C*H), 42.3 (*C*H_2), 42.1 (*C*H_2), 39.8 (*C*H_2), 39.0 (*C*), 34.3 (*C*), 34.1 (*C*H_3), 26.5 (*C*H), 24.0 (*C*H_3), 23.5 (*C*H_3), 23.3 (*C*H_3), 23.2 (*C*H_3), 19.5 (*C*H_2) ppm; IR (thin film) 3464 (br, OH), 3047-2818 (CH envelope), 1470, 1446, 1404, 1328, 1304, 1070, 1054, 1028 cm^{-1}; high-resolution mass spectrum calcd for $C_{22}H_{34}O_3$ (M^+) 346.2508, found 346.2508.

PDC Oxidation of Alcohol 25 to Ketone 24.

A flame-dried, 25-mL, round-bottomed flask equipped with a magnetic stirring bar and rubber septum was charged with alcohol **25** (0.110 g, 0.32 mmol) and dry CH_2Cl_2 (5 mL). Pyridinium dichromate (0.263 g, 0.70 mmol) was added as a solid and the reaction mixture was stirred for 2 h at room temperature. The mixture was then filtered through a plug of silica gel to remove the inorganic salts. The solvents were evaporated *in vacuo* and the crude product was purified by flash chromatography [ethyl acetate:hexane (1:39) for elution] to afford 87 mg (88%) of **24** as a white solid: mp 102-103 °C (lit[18b] mp 102-103.5 °C); ^{1}H NMR ($CDCl_3$) δ 6.60 (s, 1 H, Ar*H*), 3.83 (s, 3 H, OCH_3), 3.77 (s, 3 H, OCH_3), 3.67 (d, 1 H, J = 20.3 Hz, ArC*H*), 3.37 (d, 1 H, J = 20.3 Hz, ArC*H'*), 3.25 (m, 1 H, J = 7.0 Hz, C*H*), 3.10 (br d with fine structure, 1 H, J = 12.4 Hz, C(4)-H_e), 2.59 (s, 1 H, C*H* ring junction), 1.80-1.55 (cm, 4 H, C(2)-H_e, C(3)H_2, C(4)-H_a), 1.34 (s, 3 H, CH_3), 1.25 (s, 3 H, CH_3), 1.19 (apparent t, 6 H, J = 7.0 Hz, 2 CH_3), 1.10 (dd, 1 H, J = 3.0, 12.5 Hz, C(2)-H_a), 1.01 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 210.0 (*C*=O), 151.6 (*C*), 149.7 (*C*), 141.0 (*C*), 138.9 (*C*), 128.7 (*C*), 121.0 (*C*H), 63.0 (*C*H), 60.1 (O*C*H$_3$), 59.9 (O*C*H$_3$), 46.3 (*C*H$_2$), 44.6 (*C*), 42.3 (*C*H$_2$), 37.9 (*C*H$_2$), 32.9 (*C*H$_3$), 32.7 (*C*), 26.5 (*C*H), 23.5 (*C*H$_3$), 23.1 (*C*H$_3$), 22.4 (*C*H$_3$), 21.8 (*C*H$_3$), 19.1 (*C*H$_2$) ppm; IR (thin film) 3075-2818 (CH envelope), 1722 (C=O), 1466, 1442, 1402, 1316, 1066, 1020 cm^{-1}; high-resolution mass spectrum calcd for $C_{22}H_{32}O_3$ (M^+) 344.2351, found 344.2356.

6,9-Dioxo-5-hydroxy-7-(1-methylethyl)-1,2,3,4,4aβ,6,10,10aα-octahydro-1,1,4a-trimethyl-phenanthrene [(±)-Taxodione] (1).

A flame-dried, 10-mL, round-bottomed flask equipped with a magnetic stirring bar, rubber septum and argon inlet was flushed with argon, charged with ketone **24** (42 mg, 0.12 mmol), dry CH_2Cl_2 and cooled to -78 °C. BBr_3 (1.22 mL, 1.22 mmol, 1 M in CH_2Cl_2) was added dropwise via syringe, and the resulting solution was stirred for 10 min at -78 °C and then 30 min at room temperature. The solvents and excess BBr_3 were evaporated and ice (1 g), H_2O (5 mL) and ethyl acetate (10 mL) were added to the residue. The layers were separated, and the organic phase was washed with saturated aqueous $NaHCO_3$ (5 mL) and brine (5 mL). The combined aqueous layers were back extracted with ethyl acetate (3 x 5 mL) and the combined organic phases were dried over anhydrous $MgSO_4$. The solvents were evaporated *in vacuo* and the crude dihydroxy compound was dissolved in dry benzene (20 mL). Silica gel (5 g) was added and the resultant slurry was stirred under an atmosphere of oxygen for 2 h at room temperature. The reaction mixture was filtered through a pad of celite and the silica gel was eluted with an additional 50 mL of benzene. Evaporation of the solvent *in vacuo* afforded 26 mg (68%) of **1** as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 7.55 (s, 1 H, O*H*), 6.85 (s, 1 H, C(1)-*H*), 6.18 (s, 1 H, C(10)-*H*), 3.05 (m, 1 H, J = 6.9 Hz, C*H*), 2.91 (br d with fine structure, 1 H, J = 11.9 Hz, C(4)-H_e), 2.57 (s, 1 H, C*H* ring junction), 1.74-1.18 (cm, 5 H, C(2)H_2, C(3)H_2, C(4)-H_a), 1.24 (s, 6 H, 2 CH_3), 1.15 (apparent t, 6 H, J = 6.9 Hz, 2 CH_3), 1.09 (s, 3 H, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 200.8 (*C*), 181.6 (*C*), 145.2 (*C*), 144.9 (*C*), 139.8 (*C*), 136.0 (*C*H), 133.9 (*C*H), 125.5 (*C*), 62.9 (*C*H), 42.8 (*C*), 42.5 (*C*H$_2$), 36.9 (*C*H$_2$), 33.1 (*C*H$_3$), 32.7 (*C*), 27.0 (*C*H), 22.0 (*C*H$_3$), 21.7 (*C*H$_3$), 21.5 (*C*H$_3$), 21.1 (*C*H$_3$), 18.4 (*C*H$_2$) ppm; IR (thin film) 3324 (br, OH), 3026-2839 (CH envelope), 1674, 1642, 1628, 1616, 1352 cm^{-1}; high-resolution mass spectrum calcd for $C_{20}H_{26}O_3$ (M^+) 314.1882, found 314.1881.

LITERATURE CITED AND FOOTNOTES

†This article is dedicated to Professor William S. Johnson on the occasion of his 81st birthday.

1. Fellow of the Alexander von Humboldt Foundation 1993-1995.
2. Johnson, W. S. *Stud. Org. Chem.* (Amsterdam) **1981**, 6 (New Synth. Methodol. Bio. Act. Subst.), 1.
3. Johnson, W. S. *Bioorg. Chem.* **1976**, *5*, 51 and references therein.
4. Johnson, W. S.; Fletcher, V. R.; Chenera, B.; Bartlett, W. R.; Tham, F. S.; Kullnig, R. K. *J. Am. Chem. Soc.* **1993**, *115*, 497.
5. Johnson, W. S.; Plummer, M. S.; Reddy, S. P.; Barlett, W. R. *J. Am. Chem. Soc.* **1993**, *115*, 515.
6. (a) Harring, S. R.; Edstrom, E. D.; Livinghouse, T. *Adv. Heterocycl. Nat. Prod. Synth.*, *2*, 299-376 (1992). (b) McMurry, J. E.; Erion, M. D. *J. Am. Chem. Soc.* **1985**, *107*, 2712. (c) White, J. D.; Avery, M. A.; Carter, J. P. *J. Am. Chem. Soc.* **1982**, *104*, 3923. (d) Hoye, T. R.; Caruso, A. J.; Dellaria, J. F.; Kurth, M. *J. Am. Chem. Soc.* **1982**, *104*, 6704. (e) Nishizawa, M.; Yamada, H.; Hayashi, Y. *Tetrahedron Lett.* **1987**, *28*, 3255.
7. Bartlett, P. A. in "Asymmetric Synthesis" vol. *3*, J. D. Morrison, ed., Academic Press, New York, 1984, pp. 341-409 ("H^+" induced cyclizations), pp. 411-454 (heteroatom initiated cyclizations).
8. Semenovskii, A. V.; Smit, V. A.; Kucherov, V. F. *Izv. Akad. Nauk, SSSR Ser. Khim.* **1965**, 1424.
9. Muntyan, G. E.; Kurbanov, M.; Smit, V. A.; Semenovskii, A. V.; Kucherov, V. F. *Izv. Akad. Nauk. SSSR Ser. Khim.* **1973**, 633.
10. (a) Stork, G.; Burgstahler, A. W. *J. Am.Chem. Soc.* **1955**, *77*, 5068. (b) Sadler, P. A.; Eschenmoser, A.; Schinz, H.; Stork, G. *J. Am. Chem. Soc.* **1957**, *40*, 2191.
11. Saito, A.; Matsushita, H.; Kaneko, H. *Chem. Lett.* **1984**, 591.
12. Nasipuri, D.; Das, G. *J. Chem. Soc. Perkin Trans. I.* **1979**, 2776. For instance, the example described in this paper proceeds in only *52% isolated* yield.
13. Collington, E. W.; Meyers, A. I. *J. Org. Chem.* **1971**, *36*, 3044.
14. Casey, C. P.; Marten, D. F. *Synth. Comm.* **1973**, *3*, 321.
15. We have previously reported that the sulfenylative cyclization of **2c** gives rise to the corresponding bicyclization product in 51% yield together with 8% of the monocyclization product resulting from initiation at the *internal* alkene.[6a]
16. White, J. D.; Skeean, R. W.; Trammell, G. L. *J. Org. Chem.* **1985**, *50*, 1939.
17. Harring, S. R.; Livinghouse, T. *J. Chem. Soc. Chem. Commun.* **1992**, 503.
18. An abbreviated account of this synthesis has appeared previously: Harring, S. R.; Livinghouse, T. *J. Chem. Soc. Chem. Commun.* **1992**, 502.
19. (a) Kupchan, S. M.; Karim, A.; Marcks, C. J. *J. Am. Chem. Soc.* **1968**, *90*, 5923. (b) Kupchan, S. M.; Karim, A.; Marcks, C. J. *J. Org. Chem.* **1969**, *34*, 3912.
20. (a) Mori, K.; Matsui, M. *Tetrahedron* **1970**, *26*, 3467. (b) Matsumoto, T.; Tachibana, T.; Uchida, J.; Fukui, K. *Bull. Soc. Chem. Jpn.* **1971**, *44*, 2766; (c) Matsumoto, T.; Ohsuga, T.; Haranda, S.; Fukui, K. *Bull. Soc. Chem. Jpn.* **1977**, *50*, 266. (d) Matsumoto, T.; Usui, S.; Morimoto, T. *Bull. Soc. Chem. Jpn.* **1977**, *50*, 1575. (e) Himmelsbach, R. J.; Haltiwanger, R. C.; Snitman, D. L.; Watt, D. S. *Tetrahedron Lett.* **1979**, *20*, 2477. (f) Stevens, R. V.; Bisacchi, G. S. *J. Org. Chem.* **1982**, *47*, 2396. (g) Engler, T. A.; Sampath, U.; Naganathan, S.; Vander Velde, D.; Takusagawa, F. *J. Org. Chem.* **1989**, *54*, 5712.
21. Johnson, W. S.; Shenvi, A. B.; Boots, S. G. *Tetrahedron*, **1982**, *38*, 1397.
22. (a) The acid **19** was prepared by a high yielding (e.g. 73%) modification of the literature procedure[20b] in which acetyl chloride was substituted for propionyl chloride in the acylation of 2-isopropylveratrole. (b) Edwards, J.D.; Cashaw, J.L. *J. Am. Chem. Soc.* **1956**, *78*, 3821.
23. Selikson, S. J.; Watt, D. S. *J. Org. Chem.* **1975**, *40*, 267.
24. Vedejs, E.; Engler, D. A.; Telschow, J. E. *J. Org. Chem.* **1978**, *43*, 188.
25. On some occasions additional Li was added to maintain the blue color of the solution during the addition of the nitrile.

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