(31) (a) All melting points were determined using a calibrated hot-stage apparatus. Mass spectra were obtained using an AEI MS-902 mass spectrometer at 70 eV. Proton nuclear magnetic resonance spectra were obtained using a JEOL MH-100, Varian T-60, or Bruker WH-270 spectrometer. High-pressure liquid chromatography was performed on a Waters Model ALC-100 liquid chromatograph employing a LDC 254-nm UV detector which was calibrated for the relative responses of detected compounds and standards. Vapor phase chromatography was performed on a Varian Aerograph Series 2100 instrument employing a flame ionization detector which was calibrated for the relative responses of the detected compound and standard. Column chromatography was performed on either silica gel (Matheson Coleman and Bell, grade 62, 60–200 mesh) or basic alumina (Fisher Scientific, adsorption grade, 80–200 mesh) packings mixed with Sylvania 2282 phosphor and slurry packed into Vycor columns such that band elution could be monitored by a hand-held UV lamp. Preparative thin layer chromatography was performed using MN-Kieselgel G-UV-254 silica gel. (b) For preparations which are similar to one another, the first example is given in detail. For full details in the related cases see ref 31c. (c) D. R. Diehl, Ph.D. Thesis, University of Wisconsin, Madison, 1978.
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(45) (a) A preliminary photolysis of this molecule was performed by Gary E. Keck while in this research group. (b) G. E. Keck private communication.
(46) (a) Quantum yields checked by 100-MHz NMR integration agreed with those determined by vapor phase chromatography. (b) Additionally, the quantum yield for run 4 was checked by high-pressure liquid chromatography using one 8 × 1/4 in. column packed with 5–10-μ porous silica gel beads and eluted with 0.02% anhydrous ether in anhydrous hexane. The quantum yield value was 0.044.
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(55) (a) S_0 energies before configuration interaction are used to obtain excitation energies since calculations using only singly and doubly excited configurations tend to give excessive ground-state stabilization.[30b,c] (b) Note the same finding by E. W. Thulstrup and J. Michl, *J. Am. Chem. Soc.*, **98**, 4533 (1976). (c) See also ref 18d,e.

Regiochemical Control in Dihydrophenanthrene Synthesis. A Photochemical Total Synthesis of Juncusol

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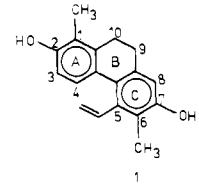
Abstract: Three approaches are described toward the total synthesis of juncusol, 1,6-dimethyl-5-vinyl-2,7-dihydroxy-9,10-dihydrophenanthrene (**1**), a cytotoxic constituent of the needlerush *Juncus roemerianus*. Wittig condensation of the phosphonium salt derived from 2-methyl-3-methoxybenzyl bromide with 3-methoxy-4-methyl-5-cyanobenzaldehyde gave the mixture of *E* and *Z* cyanostilbenes **13**. Reduction of this mixture gave the corresponding diarylethane, which failed to undergo oxidative aryl–aryl cyclization. Photocyclization of the above stilbenes proceeded readily to give a 7:1 ratio of the two expected phenanthrenes in which the unwanted 7-cyano regioisomer **17** predominated. The Ziegler modification of the Ullmann coupling was used to prepare the symmetrical dialydehyde **43**, which was converted by Wittig reagent to the vinyl aldehyde **44** and ultimately reduced to key intermediate **47**. Photocyclization of the latter gave the dihydrophenanthrene alcohol **48** which was converted via the aldehyde **46**, Wittig homologation, and demethylation to juncusol. The overall yield of the latter from 2-methyl-3-methoxybenzaldehyde is 18% over ten steps; the route provides the first total synthesis of this natural product.

Introduction

During their search for antileukemic constituents of the extract of the needlerush (*Juncus roemerianus*), Miles et al. isolated a crystalline $C_{18}H_{18}O_2$ phenol, juncusol, having cytotoxic activity against the NCI 90 KB human epidermoid carcinoma of the nasopharynx test system (ED_{50} = 0.3 μg/mL).[1] The structure of juncusol was established by these investigators as the 9,10-dihydrophenanthrene **1** by single-crystal X-ray diffraction analysis of its diacetate.



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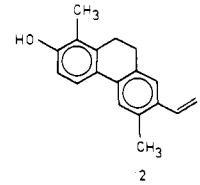

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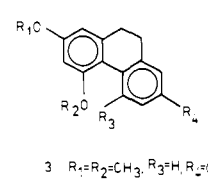

3 $R_1=R_2=CH_3$, $R_3=H$, $R_4=OH$
4 $R_1=R_2=CH_3$, $R_3=OH$, $R_4=H$
5 $R_1=R_4=H$, $R_2=CH_3$, $R_3=OH$

Juncusol (**1**), like its congener juncunol (**2**),[2] differs from most other 9,10-dihydrophenanthrene phytoalexins[3] such as orcinol (**3**), logoglossol (**4**), and hircinol (**5**) in having alkyl and vinyl substituents on the carbocyclic nucleus. For this reason the efficient and regioselective total synthesis of juncusol is not a trivial exercise. Although substances **3**, **4**, and **5** are synthetically accessible through conventional phenanthrene chemistry followed by catalytic reduction of the 9,10 double bond,[4] such an approach may not be feasible for juncusol. Thus the selective catalytic hydrogenation of the 9,10 double bond is often

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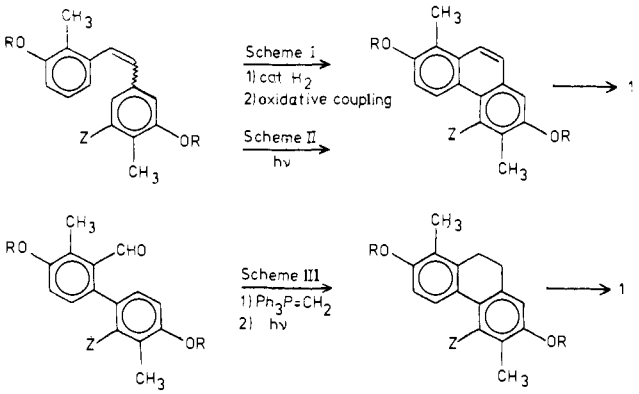
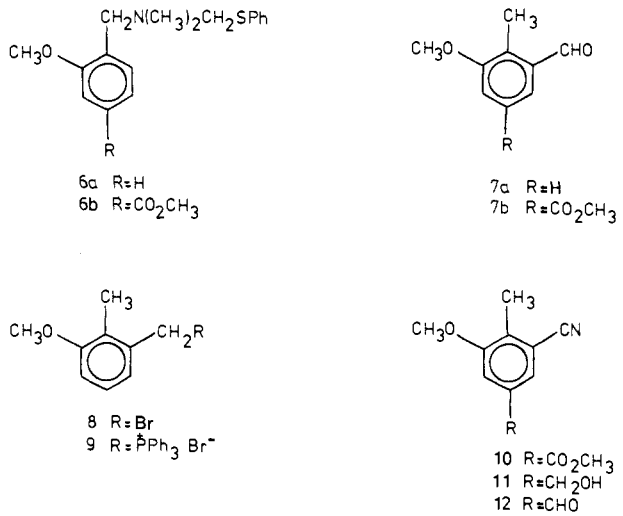
Schemes I–III



Scheme IV



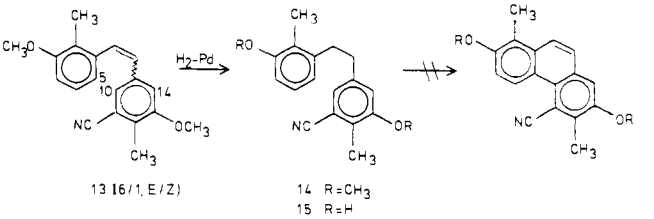
unexpectedly difficult and indiscriminate reduction of the aromatic A and C rings has been observed.[4b] Moreover, the regioselective construction of the requisite phenanthrene could prove impractical, and late introduction of the vinyl group would be required. This paper reports approaches explored in our laboratories designed to achieve a simple and practical total synthesis of juncusol.

Three alternative strategies were formulated to reach the desired target. The first, reminiscent of our recent synthesis of steganacin,[5] envisioned the initial formation of a bibenzyl intermediate followed by oxidative aryl–aryl coupling (Scheme I). The second would proceed by initial construction of a stilbene followed by photochemical phenanthrene cyclization and subsequent double bond reduction (Scheme II). The third plan would differ from the two preceding schemes by first forming the biaryl bond, followed by a photochemical 2-vinylbiphenyl closure as depicted in Scheme III. In each of these strategies the substituent Z would be a convenient precursor of the vinyl group, selected for its compatibility with the early steps of the synthetic sequence. As will be shown below, certain of the intermediates prepared during our study proved to be useful in more than one synthetic scheme.

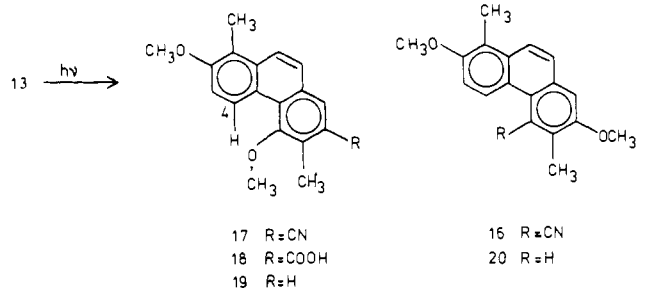
Oxidative Aryl–Aryl Coupling

The A-ring precursor required for each of the three strategies was prepared from *o*-methoxybenzyl bromide[6] and dimethylaminothiophenylmethane[7] by a modified Sommelet–Hauser rearrangement.[8] Thus reaction of the ammonium salt **6a** with potassium *tert*-butoxide in dry 1,2-dimethoxyethane followed by acid hydrolysis gave the expected aldehyde **7a** in 87% yield. Reduction of **7a** with $LiAlH_4$ followed by treatment

Scheme V



Scheme VI



with HBr gas in chloroform gave bromide **8** in 97% yield. This was converted by triphenylphosphine in boiling benzene to the crystalline phosphonium salt **9** in 92% yield (Scheme IV).

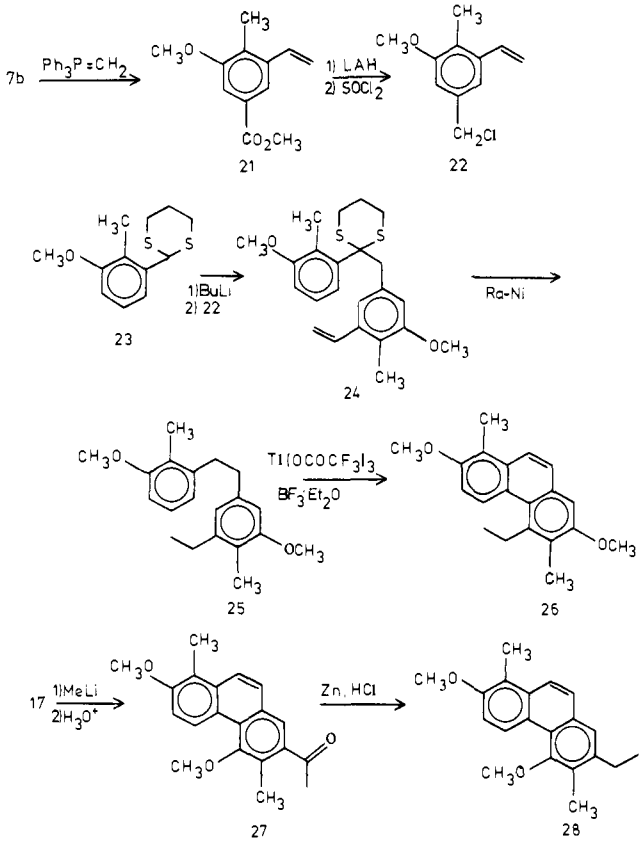
The C-ring unit for Schemes I and II was prepared by a similar Sommelet–Hauser sequence now starting with the commercially available 3-methoxy-4-methylbenzoic acid. Esterification with CH_2N_2 and bromination with NBS in CCl_4 (AIBN initiator) gave 95% of the corresponding benzyl bromide. Reaction of the latter with dimethylaminothiophenylmethane to give the salt **6b** and subsequent Sommelet–Hauser rearrangement[8] with potassium *tert*-butoxide gave the aldehyde ester **7b** in 41% overall yield. The aldehyde was converted to nitrile **10** in 90% yield with sodium formate and hydroxylamine in refluxing formic acid.[9] Selective reduction with $LiBH_4$ in boiling tetrahydrofuran gave in 81% yield the cyano alcohol **11** which was oxidized with activated manganese dioxide in chloroform to the cyano aldehyde **12** in 93% yield.

Reaction of the Wittig reagent, generated from phosphonium salt **9** with *n*-butyllithium–tetrahydrofuran, with cyano aldehyde **12** gave 67% of the key intermediate, cyanostilbene **13**, as a 6:1 *E*/*Z* mixture. To implement the oxidative aryl–aryl coupling strategy of Scheme I, cyanostilbene **13** was reduced in quantitative yield over Pd in ethyl acetate to give the diarylethane **14** (Scheme V). This compound was demethylated at 200 °C by pyridine hydrochloride to give 93% of the bisphenol **15**. Repeated attempts to achieve oxidative cyclization of either dimethoxy compound **14** or bisphenol **15** using $Tl(OCOCF_3)_3$ or VOF_3 under a variety of conditions were entirely unsuccessful. In general only starting material could be recovered even after prolonged reaction times at elevated temperatures. These observations were somewhat surprising in view of the wide variety of phenolic and nonphenolic aryl–aryl couplings known to be mediated by these reagents.[10] Apparently the cyano group provides enough deactivation to halt this particular intramolecular coupling process.

Stilbene Photocyclization

We thus returned to cyanostilbene **13** to explore its utility in Scheme II chemistry. Irradiation of stilbenes in the presence of a mild oxidant is well known to give phenanthrenes.[11] In the case of compound **13** two regioisomers are possible, and, in fact, upon irradiation with >290-nm light in benzene containing 5% I_2, two regioisomeric phenanthrenes were formed in a 7:1 ratio in 70% total yield. Unambiguous assignment of the desired structure **16** or the unwanted structure **17** to either

Scheme VII

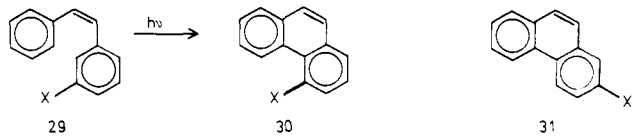


product could not be achieved by NMR or other spectroscopic means. However, chemical methods established the major product as the unwanted isomer **17**. Thus the major product was hydrolyzed to a carboxylic acid (**18**) which could be decarboxylated with Cu-quinoline to a single dimethoxydimethylphenanthrene (**19**). The six aromatic protons of the latter all showed up as parts of overlapping AB quartets in the NMR of **19**. This was consistent with the structural formulations **17** → **18** → **19**, whereas the alternative **20** should exhibit two one-proton singlets. Moreover, the chemical shift of the downfield proton H-4 remained virtually constant at δ 9.5–9.6 throughout the series **17** → **18** → **19**. This is consistent with an unchanged magnetic environment near H-4, but not with the hypothetical replacement of CN by H as in the conversion **16** → **20** (Scheme VI).

Additional support for structure **17** as the major photocyclization product was obtained by an independent chemical correlation as outlined in Scheme VII. Dithiane **23**, formed from aldehyde **7a**, was condensed with chloride **22** using *n*-butyllithium in tetrahydrofuran to give the coupling product **24** in 58% yield. Attempts to selectively desulfurize this substance proved fruitless; however, reduction of both the dithioketal and the vinyl group was accomplished in 97% yield employing either W-4 or W-7 Raney nickel. Oxidation of the resulting diarylethane **25** with $Tl(OCOCF_3)_3$ in the presence of $BF_3{\cdot}Et_2O$ according to the procedure of Taylor and McKillop[12] gave a single phenanthrene which was expected to have the structure **26** based on the para–para coupling normally observed in these oxidative reactions.[13] Comparison of the ^1H NMR spectra of phenanthrene **26** with its immediate precursor **25** showed that this expectation was correct. The diarylethane **25** shows an ethyl group appearing as a quartet at δ 2.6 and a triplet at δ 1.2. In contrast, the strongly deshielded ethyl group of phenanthrene **26** appears at δ 3.3 (q) and 1.6 (t).

Phenanthrene **26** was related to the major photocyclization product **17** as follows. Treatment of **17** with methyllithium in THF followed by acid hydrolysis gave 90% of the methyl ketone **27**. Reduction of the latter under anhydrous Clemmensen conditions[14] gave phenanthrene **28** in 75% yield. Compounds **26** and **28** had virtually identical mass spectra but were quite distinct by TLC and NMR. The ^1H NMR of **28** showed normal ethyl resonances at δ 2.6 (q) and 1.3 (t), consistent with the designated structure.

The 7:1 ratio of photocyclization isomers **20** and **16** derived from cyanostilbene **13** was unexpected. Several studies have shown that isomer ratios from meta-substituted stilbenes are usually of the order 1:1 to 2:1, and are relatively insensitive to the electron donor or acceptor properties of the substituent(s). For example, Mallory[15] has shown that, for the stilbene **29**,

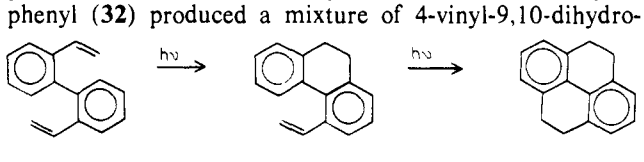


varying the substituent X from CH_3 to Cl to CF_3 does not influence the nearly 1:1 ratio of photoproducts **30** and **31**, while roughly similar results have been observed by others from F, Ph, and OCH_3 substituent effects.[16]

Although the nature and geometry of the product-determining state in the above photocyclization are uncertain, as is the molecular orbital model to be employed to predict product ratios, the predominance of isomer **17** from cyanostilbene **13** is consistent with either the Güsten-Klasinc[17] ground-state model or with simple frontier MO considerations. HMO calculations[18] on stilbene **13** show a higher π-electron density (1.011) on C-14, ortho to OCH_3, than on C-10 (0.988), ortho to CN, suggesting preferred closure to the former site according to the Güsten-Klasinc[17] model. Alternatively, the LUMO Hückel coefficients for atoms C-5, C-10, and C-14 in the cyanostilbene were respectively +0.1828, +0.0419, and −0.4126, favoring C-5 to C-14 bonding in the expected conrotatory excited state closure.

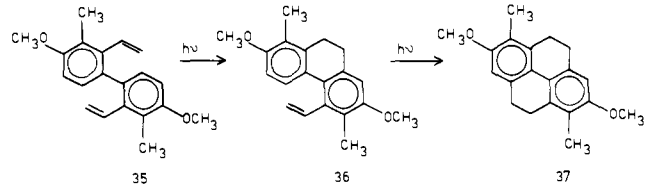
Vinylbiphenyl Cyclization Route

Since the stilbene photocyclization had proceeded with unfavorable regiochemistry our efforts next focused on Scheme III strategy whereby a suitable biaryl would first be prepared. The target biaryl was envisioned as the symmetrical dialdehyde **43**. This choice greatly simplifies the synthesis since both halves of the dialdehyde can be formed from an intermediate already in hand, namely, the methoxytolualdehyde **7a**. Moreover, ample precedent exists for the photochemical cyclization of vinylbiphenyl hydrocarbons to the corresponding dihydrophenanthrenes, obviating a difficult reduction step. In particular, Morgan et al. discovered that photolysis of 2-vinylbiphenyl produced 9,10-dihydrophenanthrene even in the presence of oxygen; no phenanthrene was produced.[19] More to the point, Padwa et al. had recently observed that 2,2′-divinylbiphenyl (**32**) produced a mixture of 4-vinyl-9,10-dihydro-

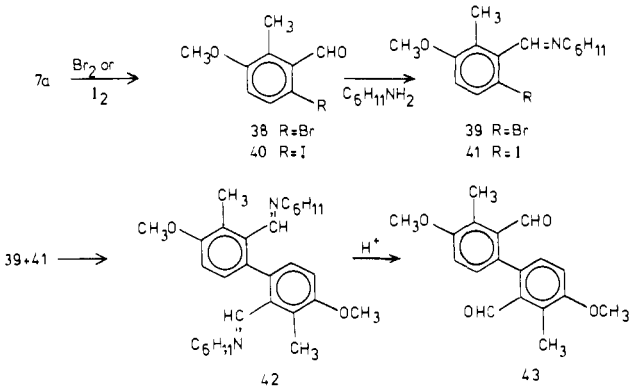


phenanthrene (**33**) and 4,5,9,10-tetrahydropyrene (**34**) upon brief irradiation.[20] Prolonged irradiation gave only **34**.

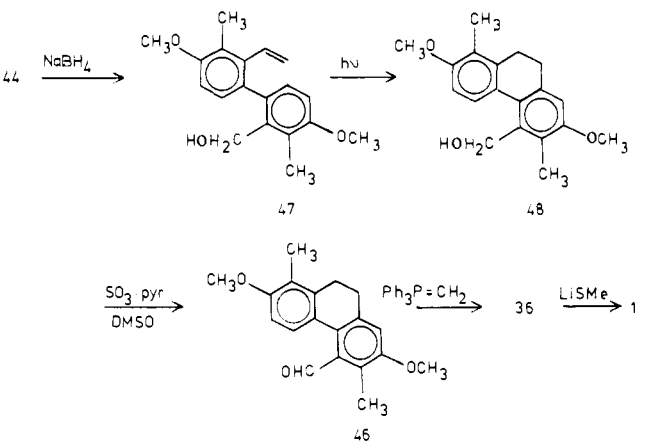
Our initial photochemical substrate thus became the bis-



Scheme VIII



Scheme IX

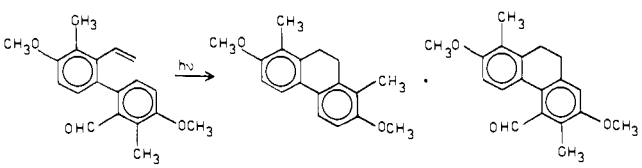


styrene **35**. It was hoped that photolysis of this compound for short times would give predominantly juncusol dimethyl ether (**36**) rather than the secondary photolysis product **37**.

The synthesis of bisstyrene **35** is outlined in Scheme VIII. Bromination of aldehyde **7a** in acetic acid regiospecifically[21] produced bromo aldehyde **38** in 93% yield. Attempted Ullmann coupling (Cu, DMF, reflux or Cu, 200°C) of **38** gave only starting material and reduction product **7a**. Bromo aldehyde **38** did self-condense using Ni(0),[22] but the yields of dialdehyde **43** were only about 15%. The iodo aldehyde **40** was next prepared in 77% yield by reaction of **7a** with iodine and silver trifluoroacetate in CH_2Cl_2.[23] Classical Ullmann condensation of iodo aldehyde (Cu, DMF, reflux) gave dialdehyde **43** in 41% yield along with 45% yield of **7a**. The most successful coupling was carried out using the cyclohexylimines **39** and **41** as pioneered by Ziegler.[24] Lithiation of bromo imine **39** with butyllithium, conversion to the cuprate with CuI·P(OEt)$_3$, and addition of iodo imine **41** produced the coupled diimine **42** in 93% yield after recrystallization. Hydrolysis with saturated oxalic acid gave dialdehyde **43** (95% yield), which was converted to the desired bisstyrene **35** in 89% yield with excess methylenetriphenylphosphorane.

Careful irradiation of bisstyrene **35** in benzene, as monitored by NMR, showed only starting material and tetrahydropyrene **37** as the reaction proceeded. Even during short photolysis times no juncusol dimethyl ether (**36**) could be detected by NMR or after workup. Apparently in this instance the rate of the second photocyclization is much greater than the first, and no detectable concentration of the intermediate 9,10-dihydrophenanthrene **36** builds up in the reaction mixture.

To circumvent the above failure, dialdehyde **43** was reacted with 0.9 equiv of methylenetriphenylphosphorane to give the vinyl monoaldehyde **44** in 55% isolated yield, along with 29% recovered dialdehyde **43** and 11% bisstyrene **35**. As anticipated from the results of Padwa,[20] photolysis of vinyl aldehyde **44**



produced only a little of the desired **46**, giving mainly the decarbonylated 9,10-dihydrophenanthrene **45**. Compound **45** is formed by cyclization of the vinyl terminus to the formyl-substituted carbon atom followed by photochemical α-cleavage of the formyl group.

This synthetic impasse was finally solved by reduction of vinyl aldehyde **44** to vinyl alcohol **47** with $NaBH_4$ in quantitative yield (Scheme IX). Photolysis of alcohol **47** proceeded smoothly to give the desired dihydrophenanthrene alcohol **48** in 60–65% yield. Alcohol **48** was selectively oxidized with SO_3-pyridine and Et_3N in Me_2SO[25] to give the dihydrophenanthrene aldehyde **46**. Direct reaction of this crude aldehyde with methylenetriphenylphosphorane cleanly gave juncusol dimethyl ether (**36**), mp 149–150°C, in 70% overall yield from **48**. The ^{13}C NMR spectrum of synthetic **36** was indistinguishable from that recorded for natural **36** by Pelletier.[26] Careful demethylation of synthetic **36** with lithium thiomethoxide in HMPA[27] produced juncusol (**1**) in 81% yield. Our synthetic juncusol **1** gave mp 174.5–175.5°C (lit. mp 176°C) and was identical with a natural sample of juncusol by mixture melting point, ^1H NMR, and TLC. The synthetic and natural diacetate derivatives were also indistinguishable.[28]

The above synthesis of juncusol proceeds in ten steps from the simple aldehyde **7a** in about 18% yield. It bypasses the serious limitations encountered in the two alternative strategies discussed, and may offer a precedent for convenient syntheses of other 9,10-dihydrophenanthrene plant constituents.

Experimental Section

General. All reaction mixtures were stirred with a magnetic stirrer. Glassware was dried by flaming. Solvents were dried as follows: THF, Na/benzophenone; DME, Na; Me_2SO and HMPA, CaH_2. Triethylamine and cyclohexylamine were distilled from KOH prior to use. Potassium *tert*-butoxide was used from a fresh bottle without further purification. Benzene for the photolyses was purified by washing with concentrated H_2SO_4, water, and KOH and distilled from Na prior to use.

All melting and boiling points are uncorrected. NMR spectra were run on a JEOL-MH 100 using Me_4Si as an internal standard. IR spectra were run on a Perkin-Elmer 137 or a Perkin-Elmer 467. Mass spectra were run on a Du Pont 490B. Analyses were performed by Chemalytics Inc.

Reaction of *o*-Methoxybenzyl Bromide with Dimethylaminothiophenylmethane. Salt 6a. *o*-Methoxybenzyl bromide (3.5 g, 18.7 mmol) was dissolved in acetonitrile (20 mL), placed under nitrogen, and cooled to 0 °C. Dimethylaminothiophenylmethane (2.92 g, 18.7 mmol) was added dropwise and the reaction mixture was allowed to warm to room temperature and stirred for 22 h. The reaction mixture was then diluted with dry benzene and the white solid was filtered, washed with benzene, and pumped dry to yield 5.8 g of **6a** (90%): mp 159–162 °C; NMR ($CDCl_3$) δ 3.21 (6 H, s), 3.87 (3 H, s), 4.96 (2 H, s), 5.48 (2 H, s), 6.99 (2 H, m), 7.38 (4 H, m), 7.76 (3 H, m).

Anal. ($C_{17}H_{22}BrNOS$) C, H.

3-Methoxy-2-methylbenzaldehyde (7a). Ammonium salt **6a** (4.5 g, 12.2 mmol) was suspended in dry DME (50 mL) in a round-bottom flask, placed under nitrogen, and cooled to −20 °C in a dry ice-carbon tetrachloride bath. Potassium *tert*-butoxide (2.06 g, 18.3 mmol) was added in small portions over 2 h at −20 °C. The mixture was then stirred for 1 h at 0 °C and 1.5 h at room temperature and poured into brine. The aqueous layer was extracted with ether. The ether layer was then washed with 2 N H_2SO_4 and the acid layer was allowed to stand for 1 h, during which time an oily layer appeared. This was extracted with ether, washed with water, dried over Na_2SO_4, and con-

centrated in vacuo to give 1.3 g of **7a**. Chromatography of the residue in the original ether layer (SiO_2, $CHCl_3$) gave an additional 300 mg of **7a**: total yield 1.6 g (87%); bp 63–65 °C (0.5 mm); IR ($CHCl_3$) 1680 cm^{-1}; NMR ($CDCl_3$) δ 2.52 (3 H, s), 3.84 (3 H, s), 7.16 (3 H, m); MS *m/e* 150 (M^+).

Anal. ($C_9H_{10}O_2$) C, H.

Ammonium Salt 6b. Methyl-2-methoxy-3-methylbenzoic acid (1.9 g, 10.6 mmol), NBS (2.0 g, 11.1 mmol), and a spatula tip of AIBN (catalyst) were refluxed in carbon tetrachloride (50 mL) for 4 h. The succinimide was filtered and the filtrate was washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo to give 2.57 g (95%) of crude methyl-2-methoxy-3-bromomethylbenzoic acid, mp 69–74 °C. Recrystallization of a small sample from cyclohexane gave mp 80–82.5 °C; IR ($CHCl_3$) 1705 cm^{-1}; NMR ($CDCl_3$) δ 3.90 (3 H, s), 3.93 (3 H, s), 4.52 (2 H, s), 7.38 (3 H, m); MS *m/e* 260, 258 (M^+), 179.

The crude bromide (1 g, 3.9 mmol) and dimethylaminothiophenylmethane (0.65 g, 3.9 mmol) were reacted in acetonitrile (10 mL) using the procedure for **6a** to give 1.25 g (75%) of ammonium salt **6b** as a white solid: mp 161.5–162.5 °C; NMR ($CDCl_3$) δ 3.24 (6 H, s), 3.91 (3 H, s), 3.97 (3 H, s), 5.07 (2 H, s), 5.53 (2 H, s), ~7.5 (8 H, m).

Anal. ($C_{19}H_{24}BrNO_3S$) C, H.

Methyl-2-formyl-4-methoxy-3-methylbenzoic Acid (7b). Ammonium salt **6b** (21.2 g, 49.8 mmol) was treated with potassium *tert*-butoxide (8.4 g, 74.6 mmol) in DME (500 mL) following the above procedure for salt **6a**. After the acid layer was allowed to stand for 1 h the white solid was filtered to yield 4.3 g of aldehyde **7b**. Concentration of the ether layer followed by trituration with isopropyl ether gave an additional 1.3 g of **7b**, total 5.6 g (54%). The aldehyde **7b** was recrystallized from isopropyl ether: mp 128–130 °C; IR ($CHCl_3$) 1710, 1700 cm^{-1}; NMR ($CDCl_3$) δ 2.58 (3 H, s), 2.93 (6 H, s), 7.59 (1 H, d, J = 2 Hz), 8.06 (1 H, d, J = 2 Hz), 10.28 (1 H, s); MS *m/e* 208 (M^+), 177.

Anal. ($C_{11}H_{12}O$) C, H.

Methyl-3-cyano-5-methoxy-4-methylbenzoic Acid (10). Aldehyde **7b** (3.50 g, 17.0 mmol), sodium formate (2.14 g, 19.6 mmol), and hydroxylamine hydrochloride (1.4 g, 34 mmol) were refluxed for 1 h in 97% formic acid (100 mL). The reaction mixture was cooled and diluted with 100 mL of cold water. The white precipitate was filtered, washed with water, and dried in vacuo to yield 3.1 g of **10** (90%): mp 92–94 °C (aqueous MeOH); IR ($CHCl_3$) 2225, 1715 cm^{-1}; NMR ($CDCl_3$) δ 2.44 (3 H, s), 3.88 (3 H, s), 3.90 (3 H, s), 7.55 (1 H, d, J = 2 Hz), 7.77 (1 H, d, J = 2 Hz); MS *m/e* 205 (M^+), 174.

Anal. ($C_{11}H_{11}NO_3$) C, H.

3-Methoxy-5-hydroxymethyl-2-methylbenzonitrile (11). Ester **10** (2.5 g, 12.2 mmol) was dissolved in THF (50 mL). To this was slowly added lithium borohydride (2.5 g, 12.5 mmol). The resulting suspension was refluxed for 18 h, cooled, and poured into cold water. The aqueous layer was extracted with chloroform and the organic layer was washed with water and brine and dried over Na_2SO_4. Concentration in vacuo gave 1.74 g of **11** (81%): mp 71–72 °C (benzene); IR ($CHCl_3$) 3600 broad, 2225 cm^{-1}; NMR ($CDCl_3$) δ 1.96 (1 H, broad s), 2.39 (3 H, s), 3.88 (3 H, s), 4.67 (2 H, s), 7.07 (1 H, broad s), 7.14 (1 H, broad s); MS *m/e* 177 (M^+).

Anal. ($C_{10}H_{11}NO_2$) C, H.

3-Methoxy-2-methylbenzyl Alcohol. $LiAlH_4$ (130 mg, 3.61 mmol) was suspended in dry THF (30 mL), cooled to 0 °C, and placed under nitrogen. To this was added aldehyde **7a** (500 mg, 3.33 mmol) in THF (10 mL) and the reaction mixture was stirred at 0 °C for 30 min. Then water (130 μL) was added followed by 15% NaOH (130 μL) and water (390 μL). The solution was filtered and the filtrate concentrated in vacuo to give 490 mg (97%) of analytically pure 3-methoxy-2-methylbenzyl alcohol: mp 51–54 °C; IR ($CHCl_3$) 3600 cm^{-1} broad; NMR ($CDCl_3$) δ 2.13 (3 H, s), 2.62 (1 H, broad s), 2.76 (3 H, s), 4.52 (2 H, s), ~6.9 (3 H, m); MS *m/e* 152 (M^+), 134.

Anal. ($C_9H_{12}O_2$) C, H.

(3-Methoxy-2-methylbenzyl)triphenylphosphonium Bromide (9). HBr gas was bubbled through a solution of 3-methoxy-2-methylbenzyl alcohol (4.60 mg, 3.03 mmol) in chloroform (15 mL) for 30 min. This solution was then washed with water, saturated $NaHCO_3$, and brine. The organic layer was dried over Na_2SO_4 and concentrated in vacuo to give 650 mg (100%) of bromide **8**, which was used directly in the next reaction: IR ($CHCl_3$) no hydroxyl; NMR ($CDCl_3$) δ 2.26 (3 H, s), 3.80 (3 H, s), 4.48 (2 H, s), ~6.9 (3 H, m).

Bromide **8** (2.7 g, 12.6 mmol) and triphenylphosphine (3.6 g, 13.7 mmol) were refluxed in benzene (50 mL) for 24 h. The reaction mixture was cooled and the precipitate was filtered and washed with benzene to give 5.8 g (92%) of phosphonium salt **9**: mp 231–232 °C; NMR ($CDCl_3$) δ 1.5 (3 H, s), 3.73 (3 H, s), 5.08 (1 H, broad s), 5.81 (1 H, broad s), 6.9 (3 H, m), 7.75 (15 H, m).

Anal. ($C_{27}H_{26}BrOP$) C, H.

2-Cyano-4,2′-dimethoxy-3,1′-dimethylstilbene (13) (*E* and *Z*). Activated MnO_2 (4.5 g, 56 mmol) was added to alcohol **11** (500 mg, 28 mmol) in chloroform (40 mL). The resulting suspension was refluxed for 3.5 h, cooled, filtered and concentrated in vacuo to give 464 mg (93%) of aldehyde **12**: mp 107–110 °C; IR ($CHCl_3$) 2220, 1705 cm^{-1}; NMR ($CDCl_3$) δ 2.50 (3 H, s), 3.98 (3 H, s) 7.54 (1 H, d, J = 1 Hz), 7.68 (1 H, d, J = 1 Hz), 9.94 (1 H, s); MS *m/e* 175 (M^+).

n-Butyllithium (0.97 mL, 2.2 M in hexanes, 2.13 mmol) was added dropwise to phosphonium salt **9** (970 mg, 2.04 mmol) suspended in THF (25 mL) under nitrogen. The resulting orange-red solution was stirred for 20 min at room temperature and the aldehyde **12** (325 mg, 1.85 mmol) was added dropwise in THF (5 mL). The solution was stirred at room temperature for 12 h, poured into water, and extracted with chloroform. The organic layer was washed with water and brine, dried over Na_2SO_4 and concentrated in vacuo to give 370 mg (67%) of a mixture of *cis*- and *trans*-stilbenes **13** (1:6, cis:trans). The stilbene **13** was generally used as a cis/trans mixture. Trituration with methanol gave 250 mg of *trans*-stilbene: mp 111–112.5 °C (MeOH, ether); IR ($CHCl_3$) 2225, 1605, 970 cm^{-1}; NMR ($CDCl_3$) δ 2.30 (3 H, s), 2.40 (3 H, s), 3.92 (3 H, s), 3.98 (3 H, s), ~7.2 (7 H, m); MS *m/e* 293 (M^+). Chromatography of the mother liquor from trituration (SiO_2, cyclohexane/ether, 2/1) gave 60 mg of *trans*-stilbene (more polar) and 60 mg of *cis*-stilbene (less polar): mp 80–83 °C (MeOH); IR ($CHCl_3$) 2225, 1600 cm^{-1}; NMR ($CDCl_3$) δ 2.13 (3 H, s), 2.35 (3 H, s), 3.42 (3 H, s), 3.92 (3 H, s), 6.9 (7 H, m); MS *m/e* 293 (M^+).

Anal. (for trans) ($C_{19}H_{19}NO_3$) C, H.

(2-Cyano-4,2′-dimethoxy-3,1′-dimethyl)-1,2-diphenylethane (14). Stilbene **13** (100 mg, 0.34 mmol) was catalytically hydrogenated in EtOAc with 10% palladium on charcoal (10 mg). The suspension was filtered through Celite and concentrated in vacuo to give 100 mg (99%) of diarylethane **14**: mp 98–101 °C (MeOH); IR ($CHCl_3$) 2225 cm^{-1}; NMR ($CDCl_3$) δ 2.14 (3 H, s), 2.26 (3 H, s), 2.85 (4 H, s), 3.77 (3 H, s), 3.81 (3 H, s), 6.8 (5 H, m); MS *m/e* 295 (M^+), 135.

Anal. Calcd for $C_{19}H_{21}NO_2$: C, 77.25; H, 7.16; N, 4.74. Found: C, 76.61; H, 7.41; N, 4.74.

(2-Cyano-4,2′-dihydroxy-3,1′-dimethoxy)-1,2-diphenylethane (15). Diarylethane **14** (100 mg, 0.34 mmol) and pyridine hydrochloride (600 mg, 5.1 mmol) were heated in a test tube immersed in an oil bath at 200 °C for 2 h. The mixture was diluted with water and the white precipitate was filtered and dried. Chromatography ($CHCl_3$/EtOAc, 4/1, SiO_2) gave 84 mg (93%) of bisphenol **15**: mp 184–186.5 °C; IR ($CHCl_3$) 3600, 2225 cm^{-1}; NMR ($CDCl_3$) δ 2.36 (3 H, s), 2.61 (3 H, s), 2.81 (4 H, s), 3.05 (2 H, broad s), ~6.8 (5 H, m); MS *m/e* 267 (M^+), 121.

Anal. ($C_{17}H_{17}NO_2$) N.

2-Cyano-4,7-dimethoxy-3,8-dimethylphenanthrene (17). Stilbene **13** (232 mg, 0.79 mmol) was dissolved in benzene (20 mL) along with two small crystals of iodine. The solution was irradiated for 48 h with a medium-pressure Hg lamp through a Pyrex filter with exposure to air. The solution was poured into $NaHSO_3$ and the layers were separated. The organic layer was washed with water and brine and dried over Na_2SO_4. Concentration in vacuo and chromatography (SiO_2, cyclohexane/ether, 4/1) gave 160 mg (70%) of a 7/1 mixture of phenanthrenes as determined by NMR. Recrystallization from MeOH gave 135 mg (59%) of the major isomer **17**: mp 159–160 °C; IR ($CHCl_3$) 2225 cm^{-1}; NMR ($CDCl_3$) δ 2.55 (3 H, s), 2.64 (3 H, s), 3.71 (3 H, s), 3.94 (3 H, s), 7.28 (1 H, d, J = 9 Hz), 7.54 (1 H, d, J = 10 Hz), 7.86 (1 H, s), 7.90 (1 H, d, J = 10 Hz), 9.42 (1 H, d, J = 9 Hz); MS *m/e* 291 (M^+).

Anal. ($C_{19}H_{17}NO_2$) C, H.

2,5-Dimethoxy-1,6-dimethylphenanthrene (19). Phenanthrene **17** (9 mg) and two pellets of KOH were refluxed in ethylene glycol (2 mL) for 75 min, cooled, and diluted with water. The aqueous layer was extracted with chloroform and then acidified to congo red with 5% HCl. The acid layer was extracted with ether and the organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo to give acid **18**. The crude acid **18** (MS 310 (M^+), 4.5 mg) was dissolved in quinoline (0.5 mL) and heated with a spatula tip of copper powder, at reflux for 2.5 h. The reaction mixture was

diluted with ether and filtered. The filtrate was washed with 5% HCl, saturated $NaHCO_3$, and brine. It was then dried over Na_2SO_4 and concentrated in vacuo. Chromatography of the residue (SiO_2, $CHCl_3$) gave 1.6 mg of phenanthrene **19** which was homogeneous by TLC and was identified by its spectral characteristics: IR ($CHCl_3$) no carbonyl, no nitrile; NMR ($CDCl_3$) δ 2.55 (3 H, s), 2.61 (3 H, s), 3.78 (3 H, s), 4.00 (3 H, s), ~7.6 (5 H, m), 9.52 (1 H, d, J = 9 Hz); MS *m/e* 266 (M^+), 251.

(3-Methoxy-2-methyl)-2-phenyl-1,3-dithiane (23). Aldehyde **7a** (100 mg, 0.67 mmol) and 1,3-propanedithiol (72 mg, 0.67 mmol) were dissolved in chloroform (5 mL) and stirred for 1 h at room temperature. The solution was cooled to −20 °C and $BF_3{\cdot}Et_2O$ (70 μL) was dropped in. The reaction mixture was allowed to warm to room temperature and stirred for 6 h. The chloroform was then washed with water, 10% KOH, water, and brine. Drying over Na_2SO_4 and concentration in vacuo gave 147 mg (93%) of dithiane **23**: mp 115–116 °C (EtOH); IR ($CHCl_3$) no carbonyl; NMR ($CDCl_3$) δ 1.96 (2 H, m), 2.28 (3 H, s), 2.88 (4 H, m), 3.74 (3 H, s), 5.29 (1 H, s), 6.65 (1 H, dd), 7.08 (2 H, m); MS *m/e* 240 (M^+), 208.

Anal. ($C_{12}H_{16}OS_2$) C, H.

3-Methoxy-5-hydroxymethyl-2-methylstyrene. *n*-Butyllithium (6 mL, 2.2 M in hexane, 13.2 mmol) was added dropwise to methyltriphenylphosphonium bromide (4.5 g, 12.6 mmol) suspended in dry THF (50 mL) under nitrogen. The resulting orange solution was stirred for 15 min at room temperature and then aldehyde **7b** (2.5 g, 12.0 mmol) was added dropwise in THF (15 mL). The reaction mixture was stirred for 4 h at room temperature and poured into dilute oxalic acid. The aqueous layer was extracted with chloroform and the organic layer was washed with water and brine. After drying over Na_2SO_4 and concentration in vacuo, the residue was passed through a short silica gel column eluting with 50% ether–cyclohexane. This gave 2.2 g (89%) of **21** as a white solid, mp 35.5–38 °C, which was used directly in the next reaction: IR ($CHCl_3$) 1710 cm^{-1}; NMR ($CDCl_3$) δ 2.24 (3 H, s), 3.87 (3 H, s), 3.91 (3 H, s), 5.26 (1 H, dd, J_{AX} = 10, J_{AB} = 2 Hz), 5.70 (1 H, dd, J_{BX} = 18, J_{AB} = 2 Hz), 6.95 (H, dd, J_{AX} = 10, J_{BX} = 18 Hz), 7.41 (1 H, d, J = 1 Hz), 7.78 (1 H, d, J = 1 Hz); MS *m/e* 206 (M^+), 175, 147.

Ester **21** (1.42 g, 6.89 mmol) was reduced with $LiAlH_4$ (525 mg, 13.8 mmol) following the procedure for compound **8** with stirring for 1 h at room temperature before workup. The yield of 3-methoxy-5-hydroxymethyl-2-methylstyrene was 1.27 g (91%), mp 61–61.5 °C (cyclohexane). An analytical sample was prepared by sublimation at 60 °C (1 mm): IR ($CHCl_3$) 3600 cm^{-1}, no carbonyl; NMR ($CDCl_3$) δ 1.82 (1 H, broad s), 2.19 (3 H, s), 3.82 (3 H, s), 4.62 (2 H, s), 5.28 (1 H, dd, J_{AX} = 11, J_{AB} = 2 Hz), 5.92 (1 H, dd, J_{BX} = 18, J_{AB} = 2 Hz), 6.80 (1 H, s), 6.92 (1 H, dd, J_{AX} = 11, J_{BX} = 18 Hz), 7.05 (1 H, s); MS *m/e* 178 (M^+).

Anal. ($C_{11}H_{14}O_2$) C, H.

(3-Methoxy-2-methyl)-2-phenyl(3-vinyl-5-methoxy-4-methyl)-2-benzyl-1,3-dithiane (24). Thionyl chloride (86 μL, 1.18 mmol) was added dropwise to a solution of 3-methoxy-5-hydroxymethyl-2-methylstyrene (200 mg, 1.12 mmol) and pyridine (96 μL, 1.18 mmol) in dry THF (10 mL). The reaction mixture was stirred overnight at room temperature and poured into ether. The organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. Distillation of the residue in a Kugelrohr (~100 °C, 2 mm) gave 160 mg (75%) of chloride **22** which turned black upon standing for several days and was used directly in the next reaction: IR ($CHCl_3$) no hydroxyl; NMR ($CDCl_3$) δ 2.20 (3 H, s), 3.82 (3 H, s), 4.54 (2 H, s), 5.30 (1 H, dd, J_{AX} = 11, J_{AB} = 2 Hz), 5.60 (1 H, dd, J_{BX} = 18, J_{AB} = 2 Hz), 6.78 (1 H, s), 6.92 (1 H, dd, J_{AX} = 11, J_{BX} = 18 Hz), 7.06 (1 H, s); MS *m/e* 196 (M^+), 161.

n-Butyllithium (0.45 mL, 1.8 M in hexane, 0.81 mmol) was added to dithiane **23** (186 mg, 0.78 mmol) in dry THF (15 mL) at −40 °C. The resulting green solution was stirred for 2 h at ~−15 °C and then cooled to −78 °C. Chloride **22** (152 mg, 0.78 mmol) was added dropwise in THF (5 mL). The reaction mixture was stirred for 12 h at −50 °C, warmed to 0 °C, and poured into ice water. The aqueous layer was extracted with chloroform and this was washed with water and brine. The organic layer was dried over Na_2SO_4 and concentrated in vacuo. Trituration of the residue with ethanol gave 180 mg of analytically pure dithiane **24**: mp 151–152 °C; NMR ($CDCl_3$) δ 1.95 (2 H, m), 2.08 (3 H, s), 2.62 (3 H, s), 2.72 (4 H, m), 3.58 (3 H, s), 3.62 (2 H, s), 3.81 (3 H, s), ~5.2 (2 H, m), 6.09 (1 H, s), ~6.9 (5 H, m); MS *m/e* 400 (M^+), 239.

Anal. ($C_{23}H_{28}O_2S_2$) C, H.

2,7-Dimethoxy-3,8-dimethyl-4-ethylphenanthrene (26). Raney Ni (W-4) (~400 mg in 4 mL of EtOH) was added to dithiane **24** (40 mg, 0.10 mmol) in dioxane (15 mL). The suspension was refluxed overnight and filtered through Celite. Concentration in vacuo and preparative TLC on thick layer silica gel plates (cyclohexane–ether, 19/1) gave 28 mg (97%) of diarylethane **25** as a clear oil: NMR ($CDCl_3$) δ 1.16 (3 H, t), 2.14 (3 H, s), 2.20 (3 H, s), 2.60 (2 H, q), 2.95 (4 H, broad s), 3.88 (3 H, s), 3.92 (3 H, s), 6.8 (4 H, m), 7.16 (1 H, d); MS *m/e* 298 (M^+).

$Tl^{III}(OCOCF_3)_3$ (49 mg, 0.097 mmol) was weighed into a flame-dried flask and placed under nitrogen. To this was added carbon tetrachloride (4 mL) and the suspension was cooled to 0 °C. Diarylethane **25** (26 mg, 0.087 mmol) was added in 1 mL of carbon tetrachloride followed by $BF_3{\cdot}Et_2O$ (152 μL). The green-black solution was allowed to warm to room temperature and stirred for 12 h. The reaction mixture was then quenched with saturated KI (5 mL) and stirred for 30 min. To this were added a spatula tip of sodium metabisulfite and one of sodium bicarbonate. The solution was filtered and washed with chloroform. The layers were separated and the organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. An NMR of the residue showed an approximately 1:1 ratio of starting material **25** to phenanthrene **26.** Preparative chromatography on thick layer silica gel plates (94% cyclohexane, 6% ether) gave 15 mg of phenanthrene **26** (~85% pure by NMR), as the more polar, fluorescent band: NMR ($CDCl_3$) δ 1.59 (3 H, t), 2.44 (3 H, s), 2.58 (3 H, s), 3.32 (2 H, q), 3.92 (6 H, s), 7.01 (1 H, d, J = 9 Hz), 7.48 (1 H, d, J = 9 Hz), 7.73 (1 H, d, J = 9 Hz), 8.39 (1 H, d, J = 9 Hz); MS *m/e* 294 (M^+).

4,7-Dimethoxy-3,8-dimethyl-2-ethylphenanthrene (28). Methyllithium (46 μL, 1.7 M in ether, 0.08 mmol) was added to phenanthrene **17** (15 mg, 0.05 mmol) in dry THF (3 mL) under nitrogen at room temperature. After 1 h the mixture was diluted with 10% H_2SO_4 (4 mL) and stirred at room temperature for 6 h. This was diluted with water and extracted with methylene chloride. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo to give 15 mg (90%) of ketone **27** which was directly reduced in the next reaction: IR ($CHCl_3$) 1685 cm^{-1}; NMR ($CDCl_3$) δ 2.64 (3 H, s), 2.70 (3 H, s), 2.74 (3 H, s), 3.79 (3 H, s), 4.03 (3 H, s), 7.26 (1 H, dd, J = 9 Hz), 7.71 (1 H, d, J = 10 Hz), 7.99 (1 H, s), 7.99 (1 H, d, J = 10 Hz), 9.57 (1 H, d, J = 9 Hz); MS *m/e* 308 (M^+), 293, 278.

Methyl ketone **27** (12 mg, 0.04 mmol) was dissolved in ether (2 mL) and THF (2 mL). The solution was cooled to 0 °C and saturated with dry HCl gas. Several small spatula tips of activated zinc dust were added over 30 min at 0 °C and the reaction mixture was stirred for an additional 30 min at 0 °C. The solution was diluted with ether, washed with water, concentrated in vacuo, and pumped dry. Chromatography of the residue on silica gel (cyclohexane–ether, 3/1) gave 9 mg (75%) of phenanthrene **28** as a white solid: mp 75–81 °C; IR ($CHCl_3$) no carbonyl; NMR ($CDCl_3$) δ 1.30 (3 H, t), 2.48 (3 H, s), 2.60 (3 H, s), 2.82 (2 H, q), 3.74 (3 H, s), 3.98 (3 H, s), 7.37 (1 H, d, J = 9 Hz), 7.60 (1 H, d, J = 9 Hz), 7.84 (1 H, d, J = 9 Hz), 9.44 (1 H, d, J = 9 Hz) (integration accounted for another proton in the aromatic region); MS: *m/e* 294 (M^+), 279.

6-Bromo-3-methoxy-2-methylbenzaldehyde (38). Bromine (0.69 mL, 13.4 mmol) in acetic acid (5 mL) was added dropwise to aldehyde **7a** (2.008 g, 13.4 mmol) in acetic acid (40 mL) over 30 min at room temperature. The reaction mixture was stirred for 36 h, diluted with water, and filtered to give an off-white solid which was sublimed (0.5 mm, 60 °C bath temperature) to give 2.84 g of bromide **38** (93%): mp 65–67 °C (sealed tube); IR ($CHCl_3$) 1700 cm^{-1}; NMR ($CDCl_3$) δ 2.44 (3 H, s), 3.86 (3 H, s), 6.80 (1 H, d, J = 10 Hz), 7.47 (1 H, d, J = 10 Hz), 10. 48 (1 H, s); MS *m/e* 230, 228 (M^+), 149.

Anal. ($C_9H_9BrO_2$) C, H.

6-Bromo-3-methoxy-2-methylbenzaldehyde *N*-Cyclohexylimine (39). Bromo aldehyde **38** (11.5 g, 50.2 mmol), cyclohexylamine (4.66 mL, 55.2 mmol), and benzene (110 mL) were added to a 250-mL flask equipped with a Dean-Stark trap. The mixture was refluxed for 10 h, cooled, and concentrated in vacuo. Recrystallization of the residue from methanol gave 14.7 g (95%) of bromo imine **39** as white needles: mp 84–85 °C; IR ($CHCl_3$) 1650 cm^{-1}; NMR ($CDCl_3$) δ ~1.6 (10 H, m), 2.30 (3 H, s), 3.30 (1 H, broad s), 3.82 (3 H, s), 6.72 (1 H, d, J = 9 Hz), 8.47 (1 H, s); MS *m/e* 311, 309 (M^+).

Anal. ($C_{15}H_{20}BrNO$) C, H.

6-Iodo-3-methoxy-2-methylbenzaldehyde (40). To a 500-mL flask were added aldehyde **7a** (10.42 g, 69.5 mmol), silver trifluoroacetate (18.4 g, 76.4 mmol), and methylene chloride (200 mL). To this was

added iodine (17.7 g, 69.5 mmol) in methylene chloride (200 mL) with vigorous stirring. The reaction mixture was stirred for 36 h at room temperature, filtered through Celite, and concentrated in vacuo. Trituration of the residue with 95% ethanol and filtration gave 14.7 g (77%) of iodo aldehyde **40** as a white solid: mp 68–69 °C (MeOH); IR ($CHCl_3$) 1690 cm^{-1}; NMR ($CDCl_3$) δ 2.27 (3 H, s), 3.79 (3 H, s), 3.79 (3 H, s), 6.65 (1 H, d, J = 9 Hz), 7.63 (1 H, d, J = 9 Hz), 10.01 (1 H, s); MS *m/e* 276 (M^+), 149.

Anal. ($C_9H_9IO_2$) C, H.

6-Iodo-3-methoxy-2-methylbenzaldehyde *N*-Cyclohexylimine (41). Iodo imine **41** was prepared in the same manner as bromo imine **39** using 13.9 g (50.4 mmol) of iodo aldehyde **40**, 4.89 mL (55.4 mmol) of cyclohexylamine, and 200 mL of benzene. Recrystallization of the residue from methanol gave 16.5 g (92%) of iodo imine **41** as white needles: mp 88–89 °C; IR ($CHCl_3$) 1650 cm^{-1}; NMR ($CDCl_3$) δ ~1.6 (10 H, m), 2.03 (3 H, s), 2.69 (3 H, s), 3.04 (1 H, broad s), 3.68 (3 H, s), 6.42 (1 H, d, J = 9 Hz), 7.48 (1 H, d, J = 9 Hz), 8.14 (1 H, s); MS *m/e* 357 (M^+), 230.

Anal. ($C_{15}H_{20}INO$) C, H.

4,4′-Dimethoxy-3,3′-dimethylbiphenyl-2,2′-dialdehyde Di(*N*-cyclohexylimine) (42). Bromo imine **39** (0.955 g, 3.08 mmol) was dissolved in dry THF (10 mL) in a three-neck round-bottom flask, placed under nitrogen, and cooled to −78 °C. *n*-Butyllithium (1.4 mL, 2.33 M in hexane, 3.23 mmol) was added dropwise and the resulting yellow solution stirred at −78 °C for 15 min. Triethyl phosphite–copper iodide complex (1.65 g, 4.62 mmol) was added dropwise in THF (2 mL) at −78 °C and the resulting orange-red solution was stirred for 15 min at −78 °C. Iodo imine (1.1 g, 3.08 mmol) in THF (3 mL) was added dropwise at −78 °C and the reaction mixture was allowed to come slowly to room temperature overnight. The mixture was poured into water and extracted with methylene chloride. The organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. Recrystallization from methanol gave 1.32 g (93%) of diimine **42** as white needles: mp 103–103.5 °C; IR ($CHCl_3$) 1625 cm^{-1}; NMR ($CDCl_3$) δ ~1.6 (10 H, m), 2.31 (3 H, s), 2.92 (1 H, broad s), 3.80 (3 H, s), 6.78 (2 H, AB quartet, J = 9 Hz), 7.96 (1 H, s); MS *m/e* 460 (M^+), 377, 363.

Anal. ($C_{30}H_{40}N_2O_2$) C, H.

4,4′-Dimethoxy-3,3′-dimethylbiphenyl-2,2′-dialdehyde (43). To a 1-L round-bottom flask were added coupled imine **42** (14.2 g, 30.9 mmol), THF (400 mL), and saturated oxalic acid (400 mL). The mixture was stirred at room temperature for 16 h, diluted with water, and filtered to give 8.1 g (95%) of dialdehyde **43** as a white solid: mp 215–218 °C (EtOH–$CHCl_3$); IR ($CHCl_3$) 1695 cm^{-1}; NMR ($CDCl_3$) δ 2.54 (3 H, s), 3.94 (3 H, s), 7.14 (2 H, s), broadens to AB system on addition of benzene, 10.14 (1 H, s); MS *m/e* 298 (M^+), 283.

Anal. ($C_{18}H_{18}O_4$) C, H.

4,4′-Dimethoxy-3,3′-dimethyl-2,2′-divinylbiphenyl (35). Methyltriphenylphosphonium bromide (378 mg, 1.05 mmol) was suspended in dry THF (15 mL) in a round-bottom flask. This suspension was placed under nitrogen and *n*-butyllithium (453 μL, 2.33 M in hexane, 1.05 mmol) was dropped in at room temperature. The orange solution was stirred for 15 min and then aldehyde **43** (150 mg, 0.50 mmol) was added in THF (15 mL). The reaction mixture was stirred for 20 h at room temperature, poured into water, and extracted with methylene chloride. The organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. Chromatography (SiO_2 cyclohexane–ether, 3/1) of the residue gave 132 mg (89%) of bisstyrene **35**: mp 147.5–149 °C (EtOH); IR ($CHCl_3$) no carbonyl; NMR ($CDCl_3$) δ 2.24 (3 H, s), 280 (3 H, s), 4.88 (1 H, dd, J_{AX} = 17, J_{AB} = 2 Hz), 5.12 (1 H, dd, J_{BX} = 11, J_{AB} = 2 Hz), 6.35 (1 H, dd, J_{AX} = 17, J_{BX} = 11 Hz), 6.76 (2 H, AB quartet, J = 8 Hz); MS *m/e* 294 (M^+).

Anal. ($C_{20}H_{22}O_2$) C, H.

4,4′-Dimethoxy-3,3′-dimethyl-2′-vinylbiphenyl-2-aldehyde (44). Methyltriphenylphosphonium bromide (78 mg, 0.22 mmol) was suspended in THF (5 mL) in a round-bottom flask and placed under nitrogen. *n*-Butyllithium (98 μL, 2.33 M in hexane, 0.23 mmol) was added dropwise at room temperature. The resulting yellow solution was stirred for 15 min and then dialdehyde **43** (74 mg, 0.25 mmol) was added, suspended in THF (15 mL). The solution was stirred for 14 h at room temperature, poured into water, and extracted with methylene chloride. The organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was chromatographed on thick layer plates (SiO_2, $CHCl_3$) to give (in order of increasing polarity) bisstyrene **35** (8 mg, 11%), styrene aldehyde **47** (40 mg, 55%), and recovered dialdehyde **43** (21 mg, 28%). The styrene aldehyde **44** was recrystallized from methanol: mp 124–126 °C; IR ($CHCl_3$) 1700 cm^{-1}; NMR ($CDCl_3$) δ 2.27 (3 H, s), 2.50 (3 H, s), 3.87 (6 H, s), 4.93 (1 H, dd, J_{AX} = 18, J_{AB} = 2 Hz), 5.26 (1 H, dd, J_{BX} = 10, J_{AB} = 2 Hz), 6.42 (1 H, dd, J_{AX} = 18, J_{BX} = 10 Hz), 6.90 (2 H, AB quartet, J = 9 Hz), 7.11 (1 H, s), 9.92 (1 H, s); MS *m/e* 296 (M^+), 281.

Anal. ($C_{19}H_{20}O_3$) C, H.

4,4′-Dimethoxy-3,3′-dimethyl-2-hydroxymethyl-2′-vinylbiphenyl (47). Styrene aldehyde **44** (870 mg, 2.94 mmol) was dissolved in THF (30 mL) in a round-bottom flask. To this was added absolute ethanol (5 mL) and $NaBH_4$ (170 mg, 4.72 mmol). The reaction mixture was stirred for 1 h, poured into water, and extracted with methylene chloride. The organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo to give 885 mg of styrene alcohol **47** (100%) as a white solid: mp 112–114 °C (cyclohexane); IR ($CHCl_3$) 3600 cm^{-1}; NMR ($CDCl_3$) δ 1.52 (1 H, broad s), 2.29 (3 H, s), 2.34 (3 H, s), 3.89 (6 H, s), 4.40 (2 H, s), 5.02 (1 H, dd, J_{AX} = 17, J_{AB} = 2 Hz), 5.28 (1 H, dd, J_{BX} = 11, J_{AB} = 2 Hz), 6.48 (1 H, dd, J_{AX} = 7, J_{BX} = 11 Hz), 6.92 (4 H, 2 overlapping AB quartets); MS *m/e* 298 (M^+), 280.

Anal. ($C_{19}H_{22}O_3$) C, H.

5-Hydromethyl-2,7-dimethoxy-1,6-dimethyl-9,10-dihydrophenanthrene (48). Styrene alcohol **47** (500 mg, 1.68 mmol) was dissolved in purified, dry benzene (500 mL) and placed under nitrogen. This solution was irradiated for 3 h at room temperature in a photolysis well, through a Pyrex filter, with a medium-pressure Hg lamp. It was then concentrated in vacuo and chromatographed (SiO_2, $CHCl_3$) to give 326 mg of dihydrophenanthrene alcohol **48** as the most polar fraction: mp 191–193 °C (EtOH); IR ($CHCl_3$) 3600 cm^{-1}; NMR ($CDCl_3$) δ 1.90 (1 H, broad s), 2.25 (3 H, s), 2.37 (3 H, s), 2.71 (4 H, s), 3.89 (6 H, s), 4.79 (2 H, s), 6.83 (1 H, s), 6.88 (1 H, d, J = 9 Hz), 7.88 (1 H, d, J = 9 Hz); MS *m/e* 298 (M^+), 283.

Anal. ($C_{19}H_{22}O_3$) C, H.

2,7-Dimethoxy-1,6-dimethyl-9,10-dihydrophenanthrene-5-aldehyde (46). Dihydrophenanthrene alcohol **48** (44 mg, 0.15 mmol) and triethylamine (205 μL, 1.5 mmol) were dissolved in dry Me_2SO (2 mL) in a test tube and placed under nitrogen. To this was added sulfur trioxide–pyridine (117 mg, 75 mmol) in Me_2SO (1 mL) at room temperature. The reaction mixture was stirred for 3 h, acidified to pH ~4 with 5% HCl, diluted with water, and extracted with methylene chloride. The organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was chromatographed (SiO_2, $CHCl_3$) to give 32 mg (73%) of aldehyde **49**: mp 192–194 °C (EtOH–CH_2Cl_2); IR ($CHCl_3$) 1685 cm^{-1}; NMR ($CDCl_3$) δ 2.28 (3 H, s), 2.46 (3 H, s), 2.82 (4 H, s), 3.90 (3 H, s), 3.93 (3 H, s), 6.98 (2 H, AB quartet, J = 9 Hz), 7.06 (1 H, s), 10.15 (1 H, s); MS *m/e* 296 (M^+), 281.

Superior overall yields were obtained when crude **46** was directly converted into juncusol dimethyl ether (**36**) and then purified.

Juncusol Dimethyl Ether (36). Methyltriphenylphosphonium bromide (36 mg, 0.1 mmol) was suspended in dry THF (2 mL) in a test tube and placed under nitrogen. *n*-Butyllithium (47 μL, 2.33 M in hexane, 0.11 mmol) was dropped in at room temperature. The yellow solution was stirred for 15 min and then aldehyde **46** (25 mg, 0.085 mmol) was added in THF (1 mL). The reaction mixture was stirred for 16 h at room temperature, poured into water, and extracted with methylene chloride. The organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was chromatographed (SiO_2, $CHCl_3$) and the least polar band cut to give 18.5 mg of juncusol dimethyl ether: mp 149–150 °C (MeOH); NMR ($CDCl_3$, 100 MHz FT) δ 2.33 (3 H, s), 2.25 (3 H, s), 2.72 (4 H, s), 3.94 (3 H, s), 3.96 (3 H, s), 5.22 (1 H, dd, J_{AX} = 17, J_{AB} = 2 Hz), 5.50 (1 H, dd, J_{BX} = 12, J_{AB} = 2 Hz), ~6.75 (3 H, overlapping dd, s and d), 7.62 (1 H, d, J = 9 Hz); MS *m/e* 279; ^{13}C NMR ($CDCl_3$, ppm downfield from Me_4Si) δ 11.8, 13.4, 25.8, 30.9, 55.6, 55.8, 107.0, 109.0, 119.7, 122.7, 123.6, 127.3, 127.7, 128.4, 137.0, 135.5, 138.0, 139.5, 156.2, 156.5.

Anal. ($C_{20}H_{22}O_2$) C, H.

Juncusol (1). Juncusol dimethyl ether **36** (15 mg, 0.05 mmol) and LiSMe (15 mg, 0.28 mmol) were dissolved in dry HMPA (2 mL) in a test tube. The solution was placed under nitrogen and heated for 2 h in an oil bath at 160 °C. The reaction mixture was poured into cold water, acidified (pH ~4) with 5% HCl, and extracted with ether. The ether layer was washed with water and brine, dried over Na_2SO_4, and

concentrated in vacuo. The residue was chromatographed (SiO_2, $CHCl_3$) and then passed through a short Florisil column (Et_2O) to remove colored impurities. This gave 11 mg of juncusol (**1**) (81%): mp 174.5–175.5 °C (benzene); IR (KBr) 3350, 1600 cm^{-1}; NMR ($CDCl_3$) δ 2.22 (3 H, s), 2.26 (3 H, s), 2.64 (4 H, s), 5.17 (1 H, dd, J_{AX} = 17, J_{AB} = 2 Hz), 5.40 (1 H, dd, J_{BX} = 11, J_{AB} = 2 Hz), 6.68 (3 H, m), 7.50 (1 H, d, J = 9 Hz); MS *m/e* 266 (M^+), 251, 237.

Juncusol Diacetate. Synthetic juncusol (6 mg) was dissolved in dry pyridine (0.5 mL) and placed under nitrogen. Acetic anhydride (9 μL, 4 equiv) was added dropwise and the mixture was stirred for 12 h at room temperature and then poured into 1 N HCl. The acid was extracted with methylene chloride and the organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was chromatographed (SiO_2, $CHCl_3$) and filtered through Florisil (Et_2O) to yield 7 mg (88%) of juncusol diacetate, mp 189–191 °C (benzene). This was identical with a sample prepared by acetylation of natural juncusol: NMR ($CDCl_3$) δ 2.16 (3 H, s), 2.20 (3 H, s), 2.36 (6 H, s), 2.75 (4 H, s), 5.26 (1 H, dd, J_{AX} = 17, J_{AB} = 2 Hz), 5.55 (1 H, dd, J_{BX} = 11, J_{AB} = 2 Hz), 6.84 (3 H, m), 7.66 (1 H, d, J = 9 Hz); MS *m/e* 350, 308, 266.[28]

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The Complexation Chemistry of Cyclohexaamyloses. 3. Per-*O*-methylcyclohexaamylose Adducts with 4-Biphenylcarboxylate and *p*-Methylcinnamate Anions[1,2]

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Abstract: Conductometric and ^{13}C NMR spectrometric analyses of aqueous solutions containing 4-biphenylcarboxylate (BPC) or *p*-methylcinnamate (PMC) anions and per-*O*-methylcyclohexaamylose (MCy) indicate formation of MCy_2, MCy·BPC, MCy_2·BPC, MCy·PMC, and MCy_2·PMC complexes. Values of equilibrium constants for each complex formation reaction were estimated at 30 °C. Intrinsic ^{13}C chemical shifts of the various adducts were calculated as well. These are discussed in terms of (1) preferential binding of phenyl and *p*-tolyl terminals of BPC and PMC, respectively, in the binary complexes, (2) face to face orientations of the wide MCy apertures in the MCy_2 and ternary adducts, and (3) noncentered occlusion of the PMC anion within the cavity of its ternary complex.

Cyclohexaamylose, which we denote as Cy, forms complexes with a variety of molecules and ions in aqueous solutions. Among these we have studied the Cy complexes of 4-biphenylcarboxylate[1] (I) and *p*-methylcinnamate[2] (II) anions (Figure 1) (to be abbreviated BPC and PMC, respectively) and detected both Cy·PMC and Cy_2·PMC in solutions of Cy and PMC, but only the Cy_2·BPC complex in that system. ^{13}C NMR data indicate that the carboxylate terminal of PMC is preferentially bound in the wide rim of the Cy cavity. Other recent studies of Cy complexes with *p*-nitrophenolate[3] and

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