Enynones in Organic Synthesis. 8. Synthesis of the Antimicrobial-Cytotoxic Agent Juncusol and Members of the Effusol Class of Phenols

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Two new syntheses of phenols have been developed which have been utilized in an efficient preparation of the antimicrobial-cytotoxic agent juncusol (**22**) and several members of the effusol (**23**) class of phenols. These results complement our earlier studies with enynones of type **42** and provide for the highly efficient conversion of **42** to either methylenecyclopentenones **45** or phenols of type **47** or **54** with virtually 100% selectivity.

Introduction

In papers 6 and 7 of this series, we described a novel synthesis of methylenecyclopentenones of general structure **4**, which were prepared from enynones **1** by a two-step sequence involving enolization to dienols **2**, followed by electrocyclization (Figure 1).[1a,b] For nonactivated substrates **1** (B, C, R = H, alkyl), cyclization of **2** to **4** is slow under thermal conditions, but it is dramatically accelerated in the presence of suitable electron donors. In particular, α-tocopherol (vitamin E, **3**) is a highly effective catalyst, affording **4** in yields of up to 98% under conditions of either thermal (SET) or photoassisted single electron transfer (PET).[1a] Among other examples, this methodology was employed in efficient syntheses of methylenomycin B (**5**) and desepoxy-4,5-didehydromethylenomycin A (**6**) and in formal syntheses of methylenomycin A (**7**) and xanthocidin (**8**).[1b,g]

A useful variant of this methodology takes advantage of the high reactivity of bis-acetylenic alcohols of general structure **9**, themselves derived from the corresponding esters by reaction with excess lithium acetylides (Figure 2).[1a] Upon thermolysis (90–200 °C), alcohols **9** undergo a facile oxy-Cope rearrangement,[2] affording enynones **10** as mixtures of *(E)*- and *(Z)*-isomers. In practice these last materials need not be isolated but rather are directly converted to spirocyclic methylenecyclopentenones **11** by SET-catalyzed cyclization.[1a] Compounds of type **11** are of interest because they are attractive precursors to a wide range of spirocyclic compounds found in nature. For example, Martin et al. employed the closely related spirocycle **13** in a novel synthesis of acorone (**14**).[3] Our experience with transformations of the type **10** → **11** led us to anticipate that acorone precursor **13** might be

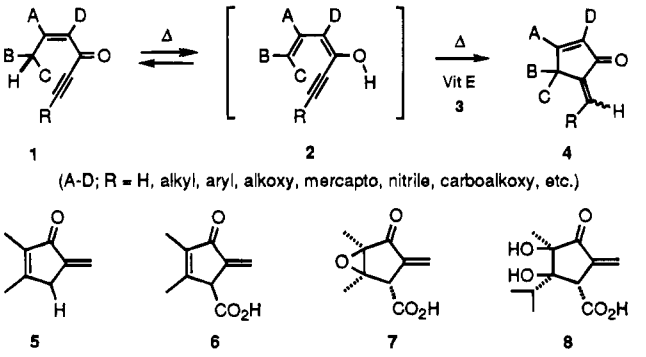

Figure 1.

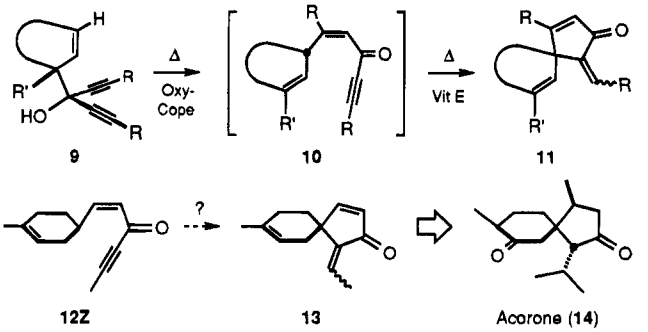

Figure 2.

prepared in a similar fashion by cyclization of enynone **12Z**.

In order to test this hypothesis, enynone **12Z** was prepared by the route outlined in Scheme 1, taking advantage of the high *(Z)*-selectivity of Wittig reagent **16** in its reaction with aldehyde **15**.[4,5] Following hydrolysis, the resultant enal **18Z** was converted in two steps to **12Z** by initial condensation with lithiopropyne (**19b**), followed by MnO_2 oxidation (64% overall yield). Surprisingly, however, **12Z** turned out to be a poor substrate for spirocyclization, affording at best a 15–20% yield of **13** upon catalysis with **3** under PET conditions (200 °C, 300 nm).[1a] In addition to decomposition, the major product in these reactions was the corresponding *(E)*-enynone **12E**, which was highly favored at equilibrium and

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(1) (a) Jacobi, P. A.; Armacost, L. M.; Brielmann, H. L.; Cann, R. O.; Kravitz, J. I.; Martinelli, M. J. *J. Org. Chem.* **1994**, *59*, 5292. (b) Jacobi, P. A.; Brielmann, H. L.; Cann, R. O. *J. Org. Chem.* **1994**, *59*, 5305. Preliminary communications: (c) Jacobi, P. A.; Armacost, L. M.; Kravitz, J. I.; Martinelli, M. J.; Selnick, H. G. *Tetrahedron Lett.* **1988**, *29*, 6865. (d) Jacobi, P. A.; Armacost, L. M.; Kravitz, J. I.; Martinelli, M. J. *Tetrahedron Lett.* **1988**, *29*, 6869. (e) Jacobi, P. A.; Kravitz, J. I. *Tetrahedron Lett.* **1988**, *29*, 6873. (f) Jacobi, P. A.; Zheng, W. *Tetrahedron Lett.* **1991**, *32*, 1279. (g) Jacobi, P. A.; Cann, R. O.; Skibbie, D. F. *Tetrahedron Lett.* **1992**, *33*, 2265.

(2) (a) Viola, A.; Collins, J. J.; Filipp, N. *Tetrahedron* **1981**, *37*, 3765. (b) Viola, A.; MacMillan, J. H. *J. Am. Chem. Soc.* **1970**, *92*, 2404. (c) Viola, A.; MacMillan, J. H.; Proverb, R. J.; Yates, B. L. *J. Chem. Soc., Chem. Commun.* **1971**, 936.

(3) Martin, S. F.; Chou, T. *J. Org. Chem.* **1978**, *43*, 1027. We are grateful to Professor S. F. Martin, of the University of Texas, for providing us with NMR spectra of **13Z,E**.

(4) Wittig reagent **16**: Cresp, T. M.; Sargent, M. V.; Vogel, P. *J. Chem Soc., Perkin Trans. I* **1974**, 37.

(5) Aldehyde **15**: (a) McCrae, D. A.; Dolby, L. *J. Org. Chem.* **1977**, *42*, 1607. (b) Fray, G. I.; Robinson, R. *J. Am. Chem. Soc.* **1961**, *83*, 249. (c) Lutz, E. F.; Bailey, G. M. *J. Am. Chem. Soc.* **1964**, *86*, 3899.

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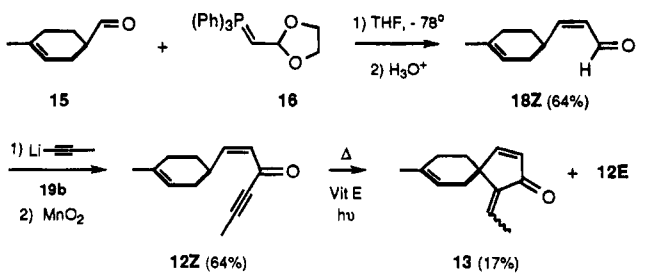
Scheme 1



completely unreactive toward spirocyclization (see also below).[1a]

Equilibration of **12Z** and **12E** occurred rapidly at 200 °C, and also at lower temperatures (83–125 °C) upon catalysis with weak acids such as RCO_2H (R = alkyl, CF_3) (Figure 3). These last reactions also afforded trace amounts of spirocycle **13** (<2%). With stronger acids, however, both **12Z** and **12E** were converted to an isomeric material whose structure was eventually determined to be that of dihydronapthol **21a**.[1e] Collidinium *p*-toluenesulfonate (CPTS) was a particularly effective catalyst, affording **21a** in 65% yield upon heating at 250 °C in mesitylene. Transformations of the type **12** → **21a** appear to be unprecedented, and they have considerable synthetic potential. In a future communication we will report on a general solution to the problem of *E,Z*-isomerization in enynones of type **12**, and their efficient transformation to spirocycles of type **13**.[6] In the present paper we describe our mechanistic studies of the cyclization leading from **12Z,E** to **21a**, which culminated in a novel synthesis of juncusol (**22**) and related materials.[1f] Juncusol has been found to possess interesting antimicrobial and cytotoxic properties,[7] which include action against human epidermoid carcinoma of the nasopharynx. In addition, we have uncovered a third class of enynone cyclization which provides access to phenols bearing the substitution pattern found in effusol (**23**).[1e,8]

Discussion and Results

Synthesis of Juncusol (22) and Related Materials. Our mechanistic studies began with the assumption that enolization of **12Z,E** to **24a** is the initial step leading to **21a** (Scheme 2). This postulate appeared reasonable in view of the ease of isomerization of **12Z** to **12E** under acid-catalyzed conditions (vide supra) and the fact that both **12Z** and **12E** were efficient substrates for cyclization (geometrical isomers of **24a** are also possible and are undoubtedly present in equilibrium). In principle, **24a** might be directly converted to allene **26a** via a concerted 1,7-hydrogen shift,[9] involving migration of H-3 (bold) to the terminus of the acetylenic π-bond (dashed arrow). Once formed, allene **26a** could afford dihydronapthol **21a**

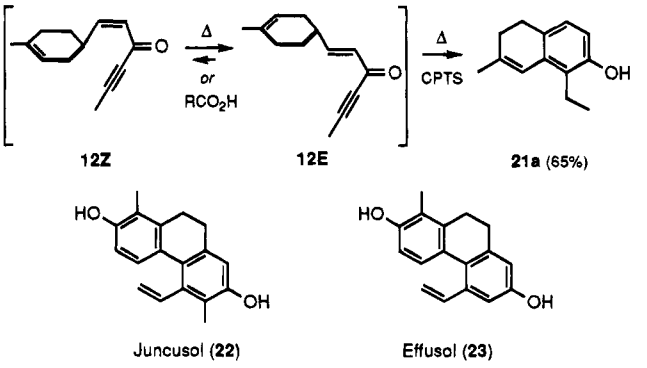
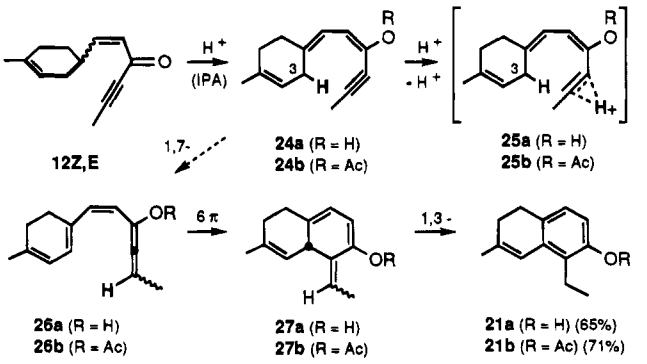


Figure 3.

Scheme 2



by 6π-electrocyclization (**26a** → **27a**) followed by aromatization. These last steps find excellent precedent in the work of Okamura *et al.*,[10] who have utilized similar allenyl diene electrocyclizations in the synthesis of drimatrienes. According to this mechanism, CPTS functions mainly as a catalyst for enolization of **12Z,E** to **24a**.

The feasibility of this mechanism was initially probed with the enol acetate **24b** (mixture of isomers), which was readily derived by treatment of **12Z,E** with Ac_2O/*p*-TsOH at 25 °C. Were a 1,7-hydrogen shift operative, **24b** should react under purely thermal conditions to afford allenol acetate **26b** (dashed arrow), and subsequently dihydronapthol acetate **21b** in analogous fashion to **24a** (cf. Scheme 2). However, this turned out not to be the case. Thus, in the absence of acid, **24b** was unreactive at the temperatures previously utilized for cyclization, being recovered unchanged after brief heating at 250 °C (prolonged heating leads to decomposition). Interestingly, however, with CPTS at 250 °C, **24b** was rapidly converted to the phenol acetate **21b**, which was identical with the material obtained by acetylation of **21a**. On the basis of these observations, we favor a protonation–deprotonation route leading from **24a,b** to **26a,b**, in which protonation occurs on the conjugated acetylene (cf. **25a,b**), followed by deprotonation at C-3. As before, electrocyclization and aromatization would then afford the observed products **21a,b**. In agreement with this hypothesis, phenol acetate **21b** was obtained in both higher yield (71%), and with faster rate, upon direct heating of enynone **12Z,E** with CPTS and isopropenyl acetate (IPA). This result is in accord with an expected stabilization of intermediates of type **24b**–**26b**, as compared with the corresponding protic derivatives **24a**–**26a**.

(6) Jacobi, P. A.; Lee, K, manuscript in preparation.

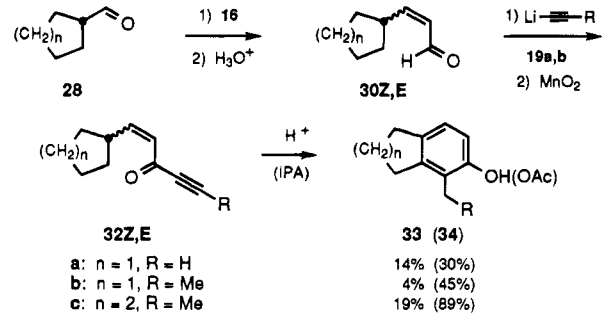
(7) Juncusol (**22**) isolation: (a) Miles, D. H.; Bhattacharyya, J.; Mody, N. V.; Atwood, J. L.; Black, S.; Hedin, P. A. *J. Am. Chem. Soc.* **1977**, *99*, 618. (b) Chapatwala, K. D.; De La Cruz, A. A.; Miles, D. H. *Life Sci.* **1981**, *29*, 1997. Synthesis: (c) Boger, D. L.; Mullican, M. D. *J. Org. Chem.* **1984**, *49*, 4045. (d) Schultz, A. G.; Shen, M.; *Tetrahedron Lett.* **1981**, *22*, 1775. (e) McDonald, E.; Martin, R. T. *Ibid.* **1978**, 4723. (f) Kende, A. S.; Curran, D. P. *Tetrahedron Lett.* **1978**, 3003; *J. Am. Chem. Soc.* **1979**, *101*, 1857.

(8) Effusol (**23**) isolation: (a) Bhattacharyya, J. *Experientia* **1980**, *36*, 27. (b) Mody, N. V.; Mahmoud, I. I.; Finer-Moore, J.; Pelletier, S. W. *J. Nat. Prod.* **1982**, *45*(6), 733. Synthesis: (c) Carvalho, C. F.; Sargent, M. V.; Stanojevic, E. *Aust. J. Chem.* **1984**, *37*, 2111.

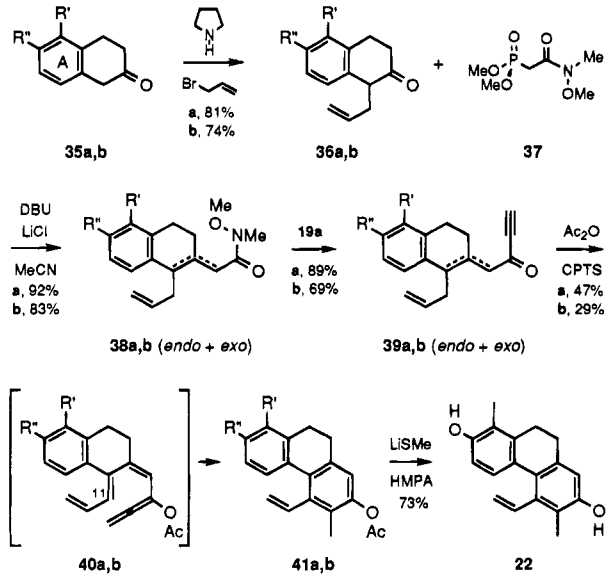
(9) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Verlag Chemie/Academic Press Inc.: New York, 1970.

(10) (a) Okamura, W. H.; Peter, R.; Reischl, W. *J. Am. Chem. Soc.* **1985**, *107*, 1034. (b) Okamura, W. H.; Elnagar, H. Y. *J. Org. Chem.* **1988**, *53*, 3060.

Scheme 3



Scheme 4



[a] **a**, R′ = Me, R″ = OMe; **b**, R′, R″ = H.

The scope of this reaction was first explored with the acetylenic enones **32a–c** (*Z*:*E* mixtures), which were prepared in analogous fashion to **12Z,E** beginning with the known aldehydes **28a,b** (n = 1, 2), or in the case of **32cZ,E**, from the known enals **30cZ,E** (Scheme 3).[11a–c] In each case modest yields of the phenols **33a–c** were obtained when only CPTS was employed as catalyst.[12] However, as with **12Z,E** (Scheme 2), we found that these conversions take place at a markedly enhanced rate in the presence of isopropenyl acetate (IPA) and yield the corresponding phenol acetates **34** in much improved yield. Acetate cleavage with $NaBH_4$ in MeOH then provided the parent phenols **33** in 85–100% yield.[13]

Application of this methodology to the synthesis of juncusol (**22**) required the preparation of enynone **39a**, which was readily accomplished as diagrammed in Scheme 4. The starting material for our synthesis of **39a** was the known β-tetralone derivative **35a**, which was prepared in multigram quantities following the procedure of Schultz *et al.*[14a] Attempted mono-alkylation of the sodium enolate of **35a** with allyl bromide invariably led to substantial amounts of bis-alkylated material.[14b] However, the pyrrolidine enamine of **35a** underwent smooth mono-alkylation to afford the desired intermediate **36a** in 81% yield.[15] Next, **36a** was directly converted to the unsaturated amide **38a** by reaction with the Wittig reagent **37**,[16] employing the general conditions of Masamune and Rousch (92% yield).[17] The material thus obtained consisted of an ~4.5:1 mixture of *endo* and *E-exo* isomers, which were initially separated and carried through the synthesis individually. However, it was subsequently found that separation at this stage was unnecessary since both sets of isomers reacted in nearly identical fashion. Thus, pure *endo* amide **38a***(endo)* afforded an 89% yield of *endo* enynone **39a***(endo)* upon condensation with lithium acetylide (**19a**),[18] and interestingly, pure *E-exo* amide **38a***(E-exo)* also gave predominantly (~6:1) *endo* enynone **39a***(endo)* under identical conditions. Furthermore, both **39a***(endo)* and **39a***(E-exo)* underwent cyclization to give the juncusol precursor **41a** under substantially the same conditions. In this case the most satisfactory results were obtained with neat acetic anhydride as the acylating reagent and collidinium *p*-toluenesulfonate (CPTS) as the acid catalyst. Thus, **39a** afforded a 47% yield of **41a** upon heating at 160 °C for 3 h with Ac_2O/CPTS. Finally, **41a** was converted to juncusol (**22**), mp 172.7–173.7 °C, in 73% yield with LiSMe in HMPA (23% overall yield from **35a**).[7f] The material thus obtained was identical in all respects with an authentic sample.[19]

Cyclizations of the type **39** → **41** are less favorable when ring A does not contain an electron-donating substituent. For example, enynone **39b** (R″ = H), prepared in analogous fashion to **39a** (R″ = OMe) from tetralone **35b**,[11b] reacted only very slowly to afford phenol acetate **41b** (29%) under the same conditions as employed for the conversion of **39a** to **41a**. This result is consistent with the intermediacy of allenol acetates **40a,b**, in which the methoxyl group in **40a** increases the nucleophilicity at C-11 by its resonance effect.

Ring Systems Related to Effusol (23). In view of the reactivity pattern exhibited by enynones **12**, **32**, and **39**, it was of interest to explore the effect of similar reaction conditions on substrates which could not be transformed to allenyl dienes of type **26** and **40** (cf. Schemes 2 and 4). One such example was the dibenzyl enynone **42a** (R = Ph), which in its protonated enol form **43a***(H+)* lacks the α-proton required for allenyl diene formation (Scheme 5). In this case we were interested to find that **42a** gave mixtures of the methylenecyclo-

(11) (a) Aldehyde **28a**: Dev, V. *J. Chem. Educ.* **1970**, *47*, 477. (b) Aldehyde **28b**; tetralone **35b**: Aldrich Chemical Co., Milwaukee, WI. (c) Enals **30cZ,E**: Gung, B. W.; Karipides, A.; Wolf, M. A. *Tetrahedron Lett.* **1992**, *33*, 713.

(12) (a) Phenol **33a** had identical spectral data and physical properties as that reported by Tius *et al.*[12b] (b) Tius, M. A.; Thurkauf, A.; Truesdell, J. W. *Tetrahedron Lett.* **1982**, 2823.

(13) Walker, E. H. R. *Chem. Soc. Rev.* **1976**, *5*, 23. Attempted acetate cleavage in the absence of $NaBH_4$ invariably led to highly colored reaction mixtures containing phenol oxidation products.

(14) (a) Shen, M.; Schultz, A. G. *Org. Prep. Proc. Int.* **1983**, *15*(3), 145. (b) Faust, J. A.; Jules, L. H.; Lee, L.; Sahyun, M. *J. Am. Pharm. Assoc.* **1957**, *46*, 118.

(15) (a) Stork, G.; Schulenberg, J. W. *J. Am. Chem. Soc.* **1962**, *84*, 284. (b) Murphy, J. G.; Ager, J. H.; May, E. L. *J. Org. Chem.* **1960**, *25*, 1386. (c) Allyl tetralone **36b**: Monkovic, I. *Can. J. Chem.* **1975**, *53*, 1189.

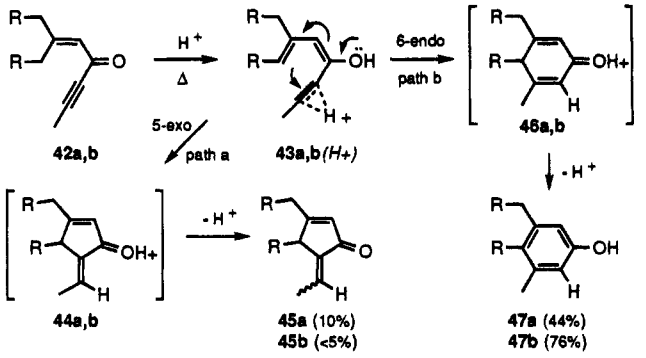
(16) Wittig reagent **37** was prepared by reaction of bromoacetyl bromide with N,O-dimethylhydroxylamine to afford the corresponding bromo amide, followed by Arbusov reaction with trimethyl phosphite: pale yellow oil, $bp_{0.06}$ 105–108 °C. **CAUTION**: On two occasions explosions occurred upon attempted distillation at a slightly higher pressure than that reported above. Compound **37** is thermally unstable above 110 °C. The diethoxy Wittig reagent corresponding to **37** is now commercially available from the Aldrich Chemical Co.: see also: Nuzillard, J.-M.; Boumendjel, A.; Massiot, G. *Tetrahedron Lett.* **1989**, *29*, 3779.

(17) Blanchette, M. A.; Choy, W.; Davis, J. T.; Essenfeld, A. P.; Masamune, S.; Rousch, W. R.; Sakai, T. *Tetrahedron Lett.* **1984**, *25*, 2183.

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

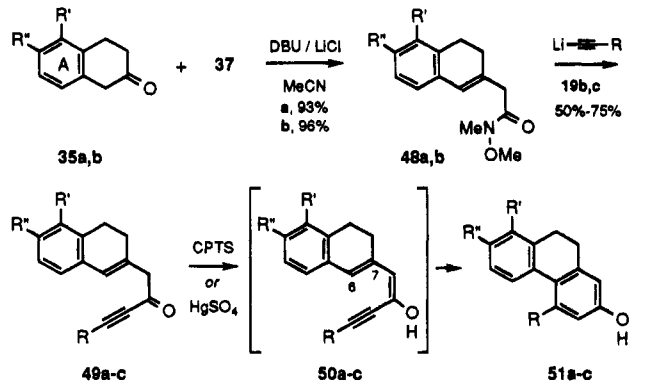
(19) We are grateful to Professor Dale Boger, of Scripps Research Institute, for providing an authentic sample of **22**.

Scheme 5



[a] **a**, R = Ph; **b**, R = H.

Scheme 6

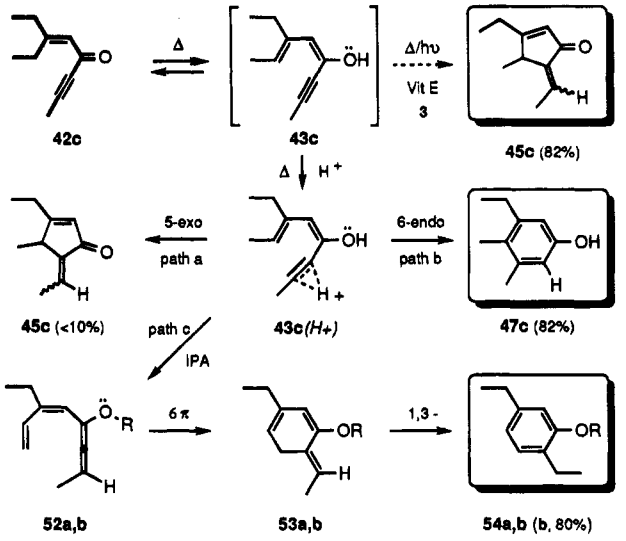


[a] **a**, R′ = Me, R″ = OMe, R = Me: 14%. **b**, R′,R″ = H; R = Me: 64%. **c**, R′ = Me, R″ = OMe, R = ethenyl: 0%.

pentenone **45a** (10%) and the new phenol derivative **47a** (44%) under acid-catalyzed conditions. In similar fashion, dimethyl enynone **42b** (R = H) afforded 76% of the phenol derivative **47b** together with trace amounts of methylenecyclopentenone **45b**.[20a] These results are consistent with a reaction pathway involving enolization and protonation to afford **43***(H+)*, which might then collapse *via* a 5*-exo* transition state to **44** (path a), or *via* a 6*-endo* transition state to **46** (path b). Simple deprotonation would then provide the observed products.

Cyclizations of type b were readily extended to ring systems related to effusol (**23**),[8] although not without some limitations (Scheme 6). Thus, β-tetralones **35a,b**[11b,14a] were cleanly converted to *endo* enynones **49a–c** by initial Wittig condensation with phosphonate **37** followed by reaction with the appropriate lithium acetylides **19b,c** (cf. also Scheme 4).[17,18] However, in contrast to the case with enynones **39** (Scheme 4), cyclizations of the type **49** → **51** are inhibited by electron-donating substituents on ring A. For example, **49b** (R″ = H) gave a 44% yield of the phenol **51b** upon heating at 200 °C with CPTS in dichlorobenzene (18 h) and a 64% yield of **51b** with $HgSO_4$ in dichlorobenzene. In contrast,

Scheme 7



[a] **a**, R = H; **b**, R = Ac.

49a (R″ = OMe) afforded only 14% of **51a** under both sets of reaction conditions. In this case, we believe, the methoxyl group tends to decrease nucleophilicity at C_6 relative to C_7 by its resonance effect, thereby working in opposition to the electron-donating effect of the enolic hydroxyl functionality. Finally, in no case were we able to observe measurable quantities of effusol precursor **51c** upon acid-catalyzed cyclization of **49c**. These last experiments were also hindered by the extreme acid and base lability of precursor **49c**.[21]

Not surprisingly, complex mixtures of products were initially obtained with substrates which could undergo cyclization by any of the three reaction pathways thus far described (paths a–c, Scheme 7). For example, diethyl enynone **42c** (bold) afforded the phenol **47c** (path b) and variable amounts of the isomeric phenol **54a** (R = H) (path c) and methylenecyclopentenone **45c** (path a) upon heating with acid catalysts. These product mixtures were solvent dependent, with significant quantities of **45c** (~10%) only observed in 1,2-dichloroalkanes or HOAc. With toluene as solvent, and CPTS as catalyst, **47c** was formed in 82% yield together with only 8% of **54a** and 0% of **45c**.[20b] However, these isomer ratios were dramatically reversed in PhBr with high concentrations of isopropenyl acetate (IPA) and TsOH as catalyst, in which case the phenol acetate **54b** (R = Ac) was formed in 80% yield with ~25:1 selectivity.[20c,d] Under these conditions, **43c***(H+)* is rapidly converted to the allenol acetate derivative **52b**,[22] which is ideally suited for cyclization via path c (vide supra). Finally, acetate **54b** was readily cleaved to the parent phenol **54a** with $NaBH_4$ in MeOH (81% yield).[13]

Nicely complementing these results is our previous finding that enynone **42c** affords an 82% yield of **45c** under neutral conditions with vitamin E (**3**) (dashed arrow in Scheme 7, photoassisted single electron transfer; see also Scheme 1).[1a] Thus, these studies provide for the highly efficient conversion of enynones of type **42** to either methylenecyclopentenones **45** or phenols of type **47** or

(20) (a) Phenol **47b** has previously been prepared by Dreiding *et al.* in 33% GC yield (22% isolated) by gas phase pyrolysis of **42b** at 700 °C: Koller, M.; Karpf, M.; Dreiding, A. S. *Tetrahedron Lett.* **1986**, *27*, 19; *Helv. Chim. Acta* **1986**, *69*, 560. (b) Phenol **47c** has previously been prepared in 30% yield from 4-ethyl-2,3,6-trimethylpyrylium perchlorate by treatment with NaOH: Rajoharison, H. G.; Soltan, H.; Arnaud, M.; Roussel, C.; Metzger, J. *Synth. Commun.* **1980**, *10*, 195. See also: Rajoharison, H. G.; Roussel, C.; Berg, U. *Tetrahedron Lett.* **1983**, *24*, 2259. (c) Phenol **54a**: Kitahonoki, K. *Chem. Pharm. Bull.* **1959**, *7*, 114. See also: Huang, Y.-Y.; Mainwaring, D. E. J. *Chem. Soc., Chem. Comm.* **1974**, 584. (d) Acetate **54b**: Fr. Pat. 2,045,926 (1971, Asahi Chemical Industry); Chem. Abstr. **1972**, *76*, 14120v.

(21) All attempts at cyclizing **49a–c** under the basic conditions reported by Corey *et al.* also led to rapid decomposition of starting materials: *cf.* Corey, E. J.; Carpino, P. *J. Am. Chem. Soc.* **1989**, *111*, 5472.

(22) House, H. O.; Thompson, W. H. *J. Org. Chem.* **1961**, *26*, 3729.

54 with virtually 100% selectivity. This methodology is clearly applicable to the synthesis of a diverse range of naturally occurring phenols and methylenecyclopentenones, and these possibilities are currently under active investigation.

Experimental Section

Melting points were determined in open capillaries and are uncorrected. ^{1}H NMR spectra were recorded at either 200 or 400 MHz and are expressed as ppm downfield from tetramethysilane.

3-(4-Methyl-3-cyclohexen-1-yl)propenal (18Z,E). A suspension of 25.9 g (60.5 mmol) of (1,3-dioxan-2-ylmethyl)-phosphonium bromide (**16**)[4] in 200 mL of dry THF was cooled to −78 °C and treated with vigorous stirring with 66.6 mmol of NaH (60% dispersion). After the solution was stirred for an additional 15 min at −78 °C, the resultant ylide was treated dropwise with a solution of 5.0 g (40.3 mmol) of 4-methyl-3-cylohexene-1-carboxaldehyde (**15**)[5] in 50 mL of dry THF while a temperature of −78 °C was maintained. After addition was complete, the reaction mixture was allowed to warm slowly to rt, and stirring was continued for an additional 16 h before the reaction was quenched by pouring the reaction mixture into 200 mL of brine. The phases were separated, and the aqueous phase was extracted with 3 × 50 mL of Et_2O. The combined organic phases were concentrated, and the residue was dissolved in petroleum ether and stirred for 1 h. The triphenylphosphine oxide which precipitated was removed by filtration through a cone of anhydrous Na_2SO_4. The filtrate was then concentrated, and the crude dioxane **17** was hydrolyzed by being dissolved in 20 mL of cold (0 °C) acetone and then treating the solution with a catalytic amount of *p*-toluenesulfonic acid (1.1 mmol) in 40 mL of water. After the solution was stirred for 2 h at 0 °C, $NaHCO_3$ (~2 g) was added, and the acetone and most of the water were removed under reduced pressure. The oil was taken up in 100 mL of Et_2O, washed twice with saturated $NaHCO_3$ and once with brine, dried over anhydrous $MgSO_4$, and concentrated. Chromatography (silica gel, 10% EtOAc/hexanes) then afforded 3.87 g (64%) of **18** as an unstable yellow oil which was used without further purification (3:1 *Z*:*E* mixture). **18Z**: R_f 0.35 (silica gel, 10% EtOAc/petroleum ether); MS *m*/*e* 150 (M^+); IR ($CHCl_3$) 2854, 2734, 1680, 1622, 1606 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38−1.61 (m, 2H), 1.62 (s, 3H), 1.76−2.15 (m, 4H), 3.10−3.36 (m, 1H), 5.34 (br s, 1H), 5.90 (dd, J = 11.2, 8.4 Hz, 1H), 6.56 (dd, J = 11.2, 11.2 Hz, 1H), 10.06 (d, J = 8.4 Hz, 1H). **18E**: R_f 0.41 (silica gel, 10% EtOAc/petroleum ether); MS *m*/*e* 150 (M^+); IR ($CHCl_3$) 2830, 2740, 1690, 1653, 1635 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.38−1.59 (m, 2H), 1.63 (s, 3H), 1.82−2.19 (m, 4H), 2.38−2.59 (m, 1H), 5.36 (br s, 1H), 6.23 (dd, J = 16.0, 8.0 Hz, 1H), 6.82 (dd, J = 16.0, 7.2 H, 1H), 9.57 (d, J = 8.0 Hz, 1H).

1-(4-Methyl-3-cyclohexen-1-yl)-1-hexen-4-yn-3-one (12Z,E). A solution consisting of 20.4 mL (53.2 mmol) of 2.6 M *n*-BuLi/hexanes and 0.6 g of triphenylmethane (indicator) in 250 mL of dry THF was cooled to −78 °C and treated with vigorous stirring with propyne gas until the pink color was discharged. The resulting orange-yellow lithiopropyne solution was stirred for an additional 15 min at -78 °C and was then treated dropwise with a solution of 6.4 g (42.6 mmol) of aldehyde **18** (*Z*:*E* mixture) in 50 mL of dry THF. The reaction mixture was stirred for a total of 1.5 h at −78 °C and allowed to warm to room temperature, and the reaction was then quenched by pouring the mixture into 300 mL of brine. The phases were separated, and the aqueous phase was extracted with 4 × 50 mL of CH_2Cl_2. The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated to afford a semicrystalline oil. Chromatography (silica gel, 25% Et_2O/hexanes) then gave 6.85 g (86%) of intermediate enynols **20** as an inseparable mixture of alcohols which were used without further purification: R_f 0.26 (silica gel, 25% Et_2O/hexanes); MS *m*/*e* 190 (M^+). A solution of 2.6 g (16.8 mmol) of enynols **20** in 150 mL of CH_2Cl_2 was cooled in an ice bath to 0 °C and treated with 9.2 g (106 mmol) of MnO_2. The reaction mixture was stirred vigorously at 0 °C for 7 h, warmed to room temperature, and filtered through fresh MnO_2 supported by a pad of Celite. The filtrate was concentrated under reduced pressure and chromatographed (silica gel, 5% EtOAc/hexanes) to afford 2.06 g (64%) of **12Z** as a yellow oil, and 1.06 g (33%) of **12E** as a yellow solid which was recrystallized from hexanes. **12Z**: R_f 0.39 (silica gel, 10% EtOAc/hexanes); MS *m*/*e* 188 (M^+); IR ($CHCl_3$) 2237, 1654, 1632, 1607 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33−2.17 (m, 6H), 1.62 (br s, 3H), 1.98 (s, 3H), 3.42−3.62 (m, 1H), 5.30−5.40 (m, 1H), 6.02−6.16 (m, 2H). **12-E**: mp 36−37 °C; R_f 0.31 (silica gel, 10% EtOAc/hexanes); MS *m*/*e* 188 (M^+); IR ($CHCl_3$) 2225, 1645, 1640, 1620 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37−1.51 (m, 2H), 1.64 (br s, 3H), 1.76−2.12 (m, 4H), 2.04 (s, 3H), 2.29−2.48 (m, 1H), 5.37 (br s, 1H), 6.11 (d, J = 15.9 Hz, 1H), 7.11 (dd, J = 15.9, 6.8 Hz, 1H). Anal. Calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 82.74; H, 8.63.

1-Ethylidene-8-methylspiro[4,5]deca-3,7-dien-2-one (13Z,E). A solution consisting of 47.0 mg (0.25 mmol) of enynone **12Z**, 1.1 equiv of vitamin E (**3**), and 5.0 equiv of 1,2-epoxyoctane (acid scavenger) in 5.0 mL of 1,2-dichlorohexane was irradiated with a 250 W sunlamp while being heated in a degassed sealed tube at 200 °C for 48 h.[1a,b] At the end of this period, most of the 1,2-dichlorohexane was removed by distillation under reduced pressure. The residue was then purified by repeated preparative TLC (silica gel, 1:1 CH_2Cl_2/hexanes, then 10% EtOAc/hexanes) to give 1.0 mg (2%) of **13Z** and 7.2 mg (15%) of **13E** as impure yellow oils which had identical spectral data as authentic samples.[3] **13Z**: R_f 0.26 (silica gel, 10% EtOAc/hexanes; MS *m*/*e* 188 (M^+); ^{1}H NMR (partial) (400 MHz, $CDCl_3$) δ 1.70 (br s, sharpens upon irradiation at 5.42, 3H), 1.91 (d, J = 7.5 Hz, collapses to an s upon irradiation at 6.60, 3H), 5.42 (br s, sharpens upon irradiation at 1.70, 1H), 6.22 (d, J = 6.1 Hz, collapses to a s upon irradiation at 7.66, 1H), 6.60 (q, J = 7.5 Hz, collapses to an s upon irradiation at 1.91, 1H), 7.66 (d, J = 6.1 Hz, collapses to a s upon irradiation at 6.22, 1H). **13E**: R_f 0.37 (silica gel, 10% EtOAc/hexanes); MS *m*/*e* 188 (M^+); ^{1}H NMR (partial) (400 MHz, $CDCl_3$) δ 1.67 (br s, sharpens upon irradiation at 5.43, 3H), 2.20 (d, J = 7.4 Hz, collapses to an s upon irradiation at 6.02, 3H), 5.43 (br s, sharpens upon irradiation at 1.67, 1H), 6.02 (q, J = 7.4 Hz, collapses to an s upon irradiation at 2.20, 1H), 6.18 (d, J = 5.9 Hz, collapses to an s upon irradiation at 7.42, 1H), 7.42 (d, J = 5.9 Hz, collapses to an s upon irradiation at 6.18, 1H).

1-Ethyl-2-hydroxy-7-methyl-5,6-dihydronaphthalene (21a). Method A. A solution consisting of 49.7 mg (0.26 mmol) of enynone **12Z**, 1.0 mg (catalyst) of collidinium *p*-toluenesulfonate (CPTS), and 1.5 mg of hydroquinone in 5 mL of freshly distilled mesitylene was degassed and heated in a sealed tube at 250 °C for 10 h.[1a,b] The reaction mixture was then cooled, concentrated under reduced pressure, and chromatographed (silica gel, 10% acetone/hexanes) to afford 35 mg (65%) of **21a** as an unstable yellow oil (analyzed as its acetate derivative **21b**). **21a:** R_f 0.31 (silica gel, 10% EtOAc/hexanes); MS *m*/*e* 188 (M^+); IR ($CHCl_3$) 1720, 1652, 1603 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16 (t, J = 7.6 H, 3H), 1.97 (s, 3H), 2.19 (t, J = 7.8 Hz, 2H), 2.69−2.75 (m, 4H), 4.52 (s, 1H), 6.45 (s, 1H), 6.53 (d, J = 7.8 Hz, 1H), 6.83 (d, J = 7.8 Hz, 1H). **Method B.** A degassed solution of 100.0 mg (0.435 mmol) of acetate **21b** in 20 mL of anhydrous MeOH was cooled to 0 °C in an ice bath and treated in a single portion, with vigorous stirring, with 99.0 mg (2.61 mmol) of $NaBH_4$. After 15 min, the ice bath was removed and stirring was continued at rt for an additional 18 h before the reaction was quenched with 30 mL of ice-cold saturated NH_4Cl. Isolation and purification as described above then gave 82.0 mg (100%) of **21a**, identical in all respects to the material prepared by method A.

2-Acetoxy-1-ethyl-7-methyl-5,6-dihydronaphthalene (21b). A solution consisting of 47.0 mg (0.25 mmol) of enynone **12Z**, 73.0 mg (0.25 mmol) of collidinium *p*-toluenesulfonate (CPTS), and 125 mg (1.25 mmol) of isopropenyl acetate (IPA) in 5 mL of freshly distilled bromobenzene was degassed and heated in a sealed tube at 200 °C for 4 h.[1a,b] The reaction mixture was then cooled, washed with saturated $NaHCO_3$ followed by brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. Chromatography (silica gel,

2.5% EtOAc/hexanes) then afforded 41.6 mg (71%) of **21b** as a yellow oil. **21b:** R_f 0.47 (silica gel, 10% EtOAc/hexanes); MS *m/e* 230 (M^+); IR ($CHCl_3$) 1751, 1686, 1650, 1198 cm^{-1}; ^1H NMR (400 MHz, CDCl3) δ 1.08 (t, J = 7.1 Hz, 3H), 1.92 (s, 3H), 2.18 (t, J = 8.0 Hz, 2H), 2.30 (s, 3H), 2.54 (q, J = 7.1 Hz, 2H), 2.74 (t, J = 8.0 Hz, 2H), 6.39 (s, 1H), 6.70 (d, J = 8.4 Hz, 1H), 6.92 (d, J = 8.4 Hz, 1H); exact mass calcd for $C_{15}H_{18}O_2$ 230.1307, found 230.1306.

3-Cyclopentylpropenal (30aZ,E). A well-stirred suspension of 6.44 g (15.0 mmol) of (1,3-dioxan-2-ylmethyl)phosphonium bromide (**16**)[4] in 50 mL of dry THF was cooled to −78 °C and treated with 16.5 mmol of NaH (60% dispersion). After the solution was stirred for an additional 15 min at −78 °C, the resultant ylide was treated dropwise with a solution of 0.88 g (10.0 mmol) of cyclopentanecarboxaldehyde (**28a**)[11a] in 10 mL of dry THF while a temperature of −78 °C was maintained. After addition was complete, the reaction mixture was allowed to warm slowly to rt, and stirring was continued for an additional 16 h before the reaction was quenched by pouring into 50 mL of brine. The phases were separated, and the aqueous phase was extracted with 3 × 25 mL of Et_2O. The combined organic phases were concentrated, and the residue was dissolved in petroleum ether and stirred for 1 h. The triphenylphosphine oxide which precipitated was removed by filtering through a cone of anhydrous Na_2SO_4. The filtrate was then concentrated, and the crude dioxane **29a** was hydrolyzed by being dissolved in 5 mL of cold (0 °C) acetone and then treated with a catalytic amount of *p*-toluenesulfonic acid (1.1 mmol) in 10 mL of water. After the solution was stirred for 2 h at 0 °C, $NaHCO_3$ (~0.5 g) was added, and the acetone and most of the water were removed under reduced pressure. The oil was taken up in 25 mL of Et_2O, washed twice with saturated $NaHCO_3$ and once with brine, dried over anhydrous $MgSO_4$, and concentrated. Chromatography (silica gel, 5% EtOAc/hexanes) then afforded 0.59 g (47%) of **30a** as an unstable yellow oil which was used without further purification (4:1 *Z:E* mixture). **30aZ:** R_f 0.48 (silica gel, 10% EtOAc/hexanes); MS *m/e* 124 (M^+); IR ($CHCl_3$) 2822, 2770, 1678 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.13−1.89 (m, 8H), 3.22−3.44 (m, 1H), 5.74 (dd, J = 10.7, 8.2 Hz, 1H), 6.41 (dd, J = 10.7, 10.7 Hz, 1H), 9.99 (d, J = 8.2 Hz, 1H). **30aE:** R_f 0.48 (silica gel, 10% EtOAc/hexanes); MS *m/e* 124 (M^+); ^1H NMR (400 MHz, $CDCl_3$) δ 1.13−1.89 (m, 8H), 2.51−2.71 (m, 1H), 5.91 (dd, J = 15.4, 7.2 Hz, 1H), 6.71 (dd, J = 15.4, 8.6 Hz, 1H), 9.43 (d, J = 7.2 Hz, 1H).

1-Cyclopentyl-1-penten-4-yn-3-one (32aZ,E). These compounds were prepared from 250 mg (2.02 mmol) of aldehydes **30aZ,E** (*Z:E* ratio = 6.5:1) and acetylene gas by an identical procedure as that used above to prepare enynones **12Z,E**, affording enynones **32a** after MnO_2 oxidation in 69% overall yield (7:1 *Z:E* mixture). Data for intermediate *(Z)*-enynol **31aZ** (unstable yellow oil): R_f 0.24 (silica gel, 10% EtOAc/hexanes); MS *m/e* 150 (M^+); IR ($CHCl_3$), 3595, 3424 br, 3307, 2115, 1653 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.16−1.34 (m, 2H), 1.49−1.84 (m, 7H), 2.47 (d, J = 2.8 Hz, 1H), 2.62−2.82 (m, 1H), 5.09−5.28 (m, 1H), 5.41 (m, 2H). Data for intermediate *(E)*-enynol **31aE** (unstable yellow oil): R_f 0.24 (silica gel, 10% EtOAc/hexanes); MS *m/e* 150 (M^+); ^1H NMR (200 MHz, $CDCl_3$) δ 1.16−1.34 (m, 2H), 1.49−1.87 (m, 7H), 2.33−2.56 (m, 1H), 2.52 (d, J = 1.6 Hz, 1H), 4.80 (m, 1H), 5.55 (dd, J = 16.4, 5.2 Hz, 1H), 5.83 (dd, J = 16.4, 8.6 Hz, 1H). Data for enynones **32a**. **32aZ**: pale yellow oil, R_f 0.44 (silica gel, 10% Et_2O/hexanes); MS *m/e* 148 (M^+); IR ($CHCl_3$) 3300, 2099, 1658, 1634, 1605 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.02−1.34 (m, 2H), 1.47−1.78 (m, 4H), 1.80−2.08 (m, 2H), 1.99 (s, 1H), 3.58−3.84 (m, 1H), 5.88−6.14 (m, 2H). **32aE:** colorless oil, R_f 0.34 (silica gel, 10% Et_2O/hexanes); MS *m/e* 148 (M^+); IR ($CHCl_3$) 3298, 2104, 1646, 1620 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.16−1.34 (m, 2H), 1.55−1.73 (m, 4H), 1.84−1.99 (m, 2H), 2.52−2.80 (m, 1H), 3.09 (s, 1H), 6.10 (dd, J = 16.0, 1.2 Hz, 1H), 7.67 (dd, J = 16.0, 8.0 Hz, 1H). Exact mass calcd for $C_{10}H_{12}O$: 148.0889. Found: 148.0881.

1-Cyclopentyl-1-hexen-4-yn-3-one (32bZ,E). These compounds were prepared from 250 mg (2.02 mmol) of aldehydes **30aZ,E** (*Z:E* ratio = 6.5:1) and propyne gas by an identical procedure as that used above to prepare enynones **12Z,E**, affording enynones **32b** after MnO_2 oxidation in 85% overall yield (7:1 *Z:E* mixture). Data for intermediate *(Z)*-enynol **31bZ** (unstable yellow oil): R_f 0.24 (silica gel, 10% EtOAc/hexanes); MS *m/e* 165 (M^+ + 1); IR ($CHCl_3$), 3600, 2228, 1654, 1003 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.19−1.28 (m, 2H), 1.49−1.82 (m, 7H), 1.83 (d, J = 2.0 Hz, 3H), 2.69−2.76 (m, 1H), 5.08−5.13 (m, 1H), 5.39−5.48 (m, 2H). Data for intermediate *(E)*-enynol **31bE** (unstable yellow oil): R_f 0.24 (silica gel, 10% EtOAc/hexanes); MS *m/e* 165 (M^+ + 1); ^1H NMR (400 MHz, $CDCl_3$) δ 1.19−1.28 (m, 2H), 1.49−1.82 (m, 7H), 1.83 (d, J = 3.0 Hz, 3H), 2.39−2.49 (m, 1H), 4.71−4.80 (m, 1H), 5.55 (dd, J = 16.0, 6.5 Hz, 1H), 5.80 (dd, J = 16.0, 8.0 Hz, 1H). Data for enynones **32b**. **32bZ**: pale yellow oil, R_f 0.35 (silica gel, 10% Et_2O/hexanes); MS *m/e* 162 (M^+); IR ($CHCl_3$) 2228, 1651, 1629, 1607 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.11−1.40 (m, 2H), 1.47−1.78 (m, 4H), 1.80−2.18 (m, 2H), 1.99 (s, 3H), 3.58−3.84 (m, 1H), 5.88−6.14 (m, 2H). **32bE**: colorless oil, R_f 0.22 (silica gel, 10% Et_2O/hexanes); MS *m/e* 162 (M^+); IR ($CHCl_3$) 2224, 1644, 1639 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.18−1.97 (m, 8H), 2.02 (s, 3H), 2.53−2.72 (m, 1H), 6.08 (d, J = 8.0 Hz, 1H), 7.09 (dd, J = 15.6, 8.0 Hz, 1H). Exact mass calcd for $C_{11}H_{14}O$: 162.1045. Found: 162.0136.

1-Cyclohexyl-1-hexen-4-yn-3-one (32cZ,E). These compounds were prepared from 6.0 g (43.0 mmol) of aldehydes **30cZ,E** (*Z:E* ratio = 1:3)[11c] and propyne gas by an identical procedure as that used above to prepare enynones **12Z,E**, affording enynones **32c** after MnO_2 oxidation in 62% overall yield (1:3 *Z:E* mixture). Data for intermediate *(Z)*-enynol **31cZ**: R_f 0.30 (silica gel, 10% EtOAc/hexanes); MS *m/e* 178 (M^+). Data for enynones **32c**. **32cZ:** R_f 0.51 (silica gel, 10% EtOAc/hexanes); MS *m/e* 177 (M^+ + 1); IR ($CHCl_3$) 2275, 1654, 1607 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.97−1.40 (m, 5H), 1.63−1.75 (m, 5H), 2.07 (s, 3H), 3.31−3.46 (m, 1H), 5.96 (d, J = 12.2 Hz, 1H), 6.02 (dd, J = 12.2, 2.0 Hz, 1H). **32cE**: bp 105−107 °C (0.65 mmHg); R_f 0.42 (silica gel, 10% EtOAc/hexanes); MS *m/e* 176 (M^+); IR ($CHCl_3$) 2221, 1640, 1619 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.05−1.40 (m, 5H), 1.58−1.87 (m, 5H), 2.01 (s, 3H), 2.25 (m, 1H), 6.07 (d, J = 15.0 Hz, 1H), 7.06 (dd, J = 15.0, 6.5 Hz, 1H). Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.67; H, 9.12.

4-Methyl-2,3-dihydro-1*H*-inden-5-ol (33a). Method A. This compound was prepared by thermolysis of 20.0 mg (0.135 mmol) of enynone **32a** (*Z:E* mixture) in 5 mL of mesitylene at 250 °C for 16 h in the presence of 0.013 equiv of CPTS and 0.05 equiv of hydroquinone, following an identical procedure as that described above for the preparation of dihydronaphthol **21a**. Preparative TLC (silica gel, 10% EtOAc/hexanes), followed by crystallization from hexanes, afforded 2.7 mg (14%) of **33a** as a yellow crystalline solid which had identical physical and spectroscopic properties as those reported by Tius et al.:[12b] mp 95.0−96.5 °C (from hexanes); R_f 0.23 (silica gel, 10% EtOAc/hexanes); MS *m/e* 148 (M^+); IR ($CHCl_3$) 3606, 1602 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.02−2.11 (m, 2H), 2.14 (s, 3H), 2.79−2.85 (m, 4H), 4.51 (s, 1H), 6.57 (d, J = 7.9 Hz, 1H), 6.90 (d, J = 7.9 Hz, 1H). **Method B.** A degassed solution of 8.0 mg (0.042 mmol) of acetate **34a** (see below) in 2.0 mL of anhydrous MeOH was cooled to 0 °C in an ice bath and treated in a single portion, with vigorous stirring, with 9.6 mg (0.25 mmol) of $NaBH_4$. After 15 min, the ice bath was removed and stirring was continued at rt for an additional 5 h before the reaction was quenched with 5 mL of ice-cold saturated NH_4Cl. Isolation and purification as described above then gave 5.7 mg (85%) of **33a**, identical in all respects to the material prepared by method A.

5-Acetoxy-4-methyl-2,3-dihydro-1*H*-indene (34a). This compound was prepared by thermolysis of 37.0 mg (0.25 mmol) of enynone **32a** (*Z:E* mixture) in 5 mL of butyronitrile at 200 °C for 16 h in the presence of 0.1 equiv of *p*-toluenesulfonic acid and 20.0 equiv of isopropenyl acetate (IPA), following an identical procedure as that described above for the preparation of dihydronaphthol acetate **21b**. The crude product, obtained by removing the reaction solvent under reduced pressure, was purified by preparative TLC (silica gel, 10% EtOAc/hexanes) to afford 14.2 mg (30%) of **34a** as a yellow oil: R_f 0.44 (silica gel, 10% EtOAc/hexanes); MS *m/e* 190 (M^+); IR ($CHCl_3$) 1751, 1193 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.20 (s, 3H), 2.20−

2.28 (m, 2H), 2.30 (s, 3H), 2.83 (t, J = 7.5 Hz, 2H), 2.88 (t, J = 7.5 Hz, 2H), 6.76 (d, J = 8.0 Hz, 1H), 7.03 (d, J = 8.0 Hz, 1H). $NaBH_4$-catalyzed cleavage of **34a** provided an 85% yield of known phenol **33a**[12b] as described above in method B.

4-Ethyl-2,3-dihydro-1*H*-inden-5-ol (33b). Method A. This compound was prepared by thermolysis of 40.0 mg (0.247 mmol) of enynone **32b** (*Z*:*E* mixture) in 5 mL of mesitylene at 250 °C for 16 h in the presence of 0.013 equiv of CPTS and 0.05 equiv of hydroquinone, following an identical procedure as that described above for the preparation of dihydronaphthol **21a**. Preparative TLC (silica gel, 10% EtOAc/hexanes) afforded 1.4 mg (4%) of **33b** as a yellow oil (analyzed as its acetate derivative **34b**): R_f 0.24 (silica gel, 10% EtOAc/hexanes); MS m/e 162 (M^+); IR ($CHCl_3$) 1600, 1491, 1273 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.14 (t, J =7.6 Hz, 3H), 2.05 (quintet, J = 7.4 Hz, 2H), 2.60 (q, J = 7.6 Hz, 2H, 2.81–2.86 (m, 4H), 4.48 (s, 1H), 6.56 (d, J = 8.0 Hz, 1H), 6.90 (d, J = 8.0 Hz, 1H). **Method B.** A degassed solution of 34.3 mg (0.168 mmol) of acetate **34b** (see below) in 8.0 mL of anhydrous MeOH was cooled to 0 °C in an ice bath and treated in a single portion, with vigorous stirring, with 37.8 mg (1.00 mmol) of $NaBH_4$. After 15 min, the ice bath was removed and stirring was continued at rt for an additional 5 h before the reaction was quenched with 5 mL of ice-cold saturated NH_4Cl. Isolation and purification as described above then gave 25.1 mg (92%) of **33b** as colorless needles, mp 89–90 °C, which had identical spectral data as the material prepared by method A.

5-Acetoxy-4-ethyl-2,3-dihydro-1*H*-indene (34b). This compound was prepared by thermolysis of 26.9 mg (0.166 mmol) of enynone **32b** (*Z*:*E* mixture) in 4.5 mL of butyronitrile at 200 °C for 16 h in the presence of 0.1 equiv of *p*-toluenesulfonic acid and 5.0 equiv of isopropenyl acetate (IPA), following an identical procedure as that described above for the preparation of dihydronaphthol acetate **21b**. The crude product, obtained by removing the reaction solvent under reduced pressure, was purified by preparative TLC (silica gel, 10% EtOAc/hexanes) to afford 15.2 mg (45%) of **34b** as a yellow oil: R_f 0.44 (silica gel, 10% EtOAc/hexanes); MS m/e 204 (M^+); IR ($CHCl_3$) 1751, 1471, 1192 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.09 (t, J = 7.5 Hz, 3H), 2.09 (quintet, J = 7.5 Hz, 2H), 2.3 (s, 3H), 2.46 (q, J = 7.5 Hz, 2H), 2.88 (m, 4H), 6.77 (d, J = 8.5 Hz, 1H), 7.17 (d, J = 8.5 Hz, 1H); exact mass calcd for $C_{13}H_{16}O_2$ 204.1151, found 204.1150. $NaBH_4$-catalyzed cleavage of **34b** provided a 92% yield of phenol **33b** as described above in method B.

1-Ethyl-2-hydroxy-5,6,7,8-tetrahydronaphthalene (33c). Method A. This compound was prepared by thermolysis of 55.0 mg (0.32 mmol) of enynone **32c** (*Z*:*E* mixture) in 5 mL of mesitylene at 250 °C for 13 h in the presence of 0.013 equiv of CPTS and 0.05 equiv of hydroquinone, following an identical procedure as that described above for the preparation of dihydronaphthol **21a**. Preparative TLC (silica gel, 10% EtOAc/hexanes) afforded 10.5 mg (19%) of **33c** as a yellow oil which crystallized from low-boiling petroleum ether: mp 93–94 °C; R_f 0.43 (silica gel, 10% EtOAc/hexanes); MS m/e 176 (M^+); IR ($CHCl_3$) 3618, 3388 br, 1690, 1641 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.11 (t, J = 7.6 Hz, 3H), 1.71–1.80 (m, 4H), 2.61 (q, J = 7.6 Hz, 2H), 2.62–2.72 (m, 4H), 4.45 (s, 1H), 6.56 (d, J = 8.2 Hz, 1H), 6.79 (d, J = 8.2 Hz, 1H); exact mass calcd for $C_{12}H_{16}O$ 176.1202, found 176.1188. **method B.** A degassed solution of 29.0 mg (0.133 mmol) of acetate **34c** (see below) in 4.0 mL of anhydrous MeOH was cooled to 0 °C in an ice bath and treated in a single portion, with vigorous stirring, with 30.2 mg (0.79 mmol) of $NaBH_4$. After 15 min, the ice bath was removed and stirring was continued at rt for an additional 5 h before the reaction was quenched with 5 mL of ice-cold saturated NH_4Cl. Isolation and purification as described above then gave 22.7 mg (97%) of **33c** as a colorless solid which was identical in all respects to the material prepared by method A.

2-Acetoxy-1-ethyl-5,6,7,8-tetrahydronaphthalene (34c). A solution consisting of 44.0 mg (0.25 mmol) of enynone **32c** (*Z*:*E* mixture), 4.8 mg (0.10 equiv) of *p*-toluenesulfonic acid monohydrate, and 500 mg (20.0 equiv) of isopropenyl acetate in 5.0 mL of butyronitrile was degassed by bubbling nitrogen through it for 5 min. The reaction mixture was then heated at reflux under nitrogen for 26 h, the butyronitrile was removed under reduced pressure, and the crude product was purified by preparative TLC (silica gel, 5% EtOAc/hexanes) to afford 48.5 mg (89%) of **34c** as a yellow oil: R_f 0.44 (silica gel, 10% EtOAc/hexanes); MS m/e 218 (M^+); IR ($CHCl_3$) 1756, 1474, 1198 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.06 (t, 3H, J = 7.6 Hz), 1.71–1.82 (m, 4H), 2.30 (s, 3H), 2.49 (q, J = 7.6 Hz, 2H), 2.69–2.79 (m, 4H), 6.75 (d, J = 8.1 Hz, 1H), 6.92 (d, J = 8.1 Hz, 1H). $NaBH_4$-catalyzed cleavage of **34c** provided a 97% yield of phenol **33c** as described above in method B.

3,4-Dihydro-6-methoxy-5-methyl-1-(2-propenyl)-2(1*H*)-naphthalenone (36a). A solution of 1.06 g (5.57 mmol) of 6-methoxy-5-methyl-2-tetralone (**35a**)[14a] in 8 mL of benzene was treated with a solution of 0.76 g (1.9 eq) of pyrrolidine in 1.5 mL of benzene at rt under a nitrogen atmosphere, and the resulting mixture was heated at reflux for 2.5 h. The water produced during the reaction was absorbed with molecular sieves in a Soxhlet extractor. After distillation of the benzene, a solution of 2.60 g (3.8 eq) of allyl bromide in 8 mL of dioxane was introduced to the residue at rt and the resulting mixture was heated at reflux for 19 h. After the solution was cooled to rt, 5 mL of a dilute aqueous HCl solution (0.23%) was added and the resulting mixture was heated at reflux for 1 h. After about two thirds of the total solvent was distilled, 15 mL of H_2O and 15 mL of Et_2O were added and the separated aqueous layer was extracted with 3 × 15 mL of Et_2O. The combined organic extracts were washed with 12 mL of saturated sodium bisulfite solution and 12 mL of brine, dried ($MgSO_4$), concentrated, and chromatographed (silica gel, 7% EtOAc/hexanes) to afford 1.03 g (81%) of **36a** as a light yellow oil: R_f 0.40 (silica gel, 20% EtOAc/hexanes); MS m/e 230 (M^+); IR (CH_2Cl_2) 3011, 2940, 1714, 1588 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.20 (s, 3H), 2.46–2.70 (m, 4H), 3.04 (m, 2H), 3.45 (t, J = 6.5 Hz, 1H), 3.81 (s, 3H), 5.00 (m, 2H), 5.71 (m, 1H), 6.75 (d, J = 9.0 Hz, 1H), 6.94 (d, J = 9.0 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 11.4, 24.3, 36.2, 37.4, 52.8, 55.5, 108.5, 117.0, 123.5, 125.7, 128.6, 135.2, 136.0, 156.2, 212.2; exact mass calcd for $C_{15}H_{18}O_2$+H^+ 231.1385, found 231.1386.

3,4-Dihydro-1-(2-propenyl)-2(1*H*)-naphthalenone (36b).[15c] This material was prepared from 2.64 mL (20.0 mmol) of β-tetralone (**35b**),[11b] 3.19 mL (1.9 equiv) of pyrrolidine, and 6.70 mL (3.8 equiv) of allyl bromide following an identical procedure as that described above for the preparation of **36a**. Chromatography (silica gel, 5% EtOAc/hexanes) afforded 2.73 g (74%) of **36b** as a light yellow oil, which had spectral data in agreement with the published values:[15c] R_f 0.67 (silica gel, 20% EtOAc/hexanes); IR (CH_2Cl_2) 3065, 3050, 1716 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.59 (m, 2H), 2.69 (m, 2H), 3.05 (m, 1H), 3.15 (m, 1H), 3.53 (t, J = 6.5 Hz, 1H), 5.02 (m, 2H), 5.74 (m, 1H), 7.22 (m, 4H).

3,4-Dihydro-*N*,6-dimethoxy-*N*,5-dimethyl-1-(2-propenyl)-2-naphthaleneacetamide [38a*(endo)*] and *(E)*-2-[3,4-Dihydro-6-methoxy-5-methyl-1-(2-propenyl)-2(1*H*)-naphthalenylidene]-*N*-methoxy-*N*-methylacetamide [38a*(E-exo)*]. A well-stirred suspension of 184 mg (1.2 equiv) of LiCl in 30 mL of dry acetonitrile was treated sequentially at rt, under an atmosphere of nitrogen, with 916 mg (1.0 equiv) of dimethyl ((*N*-methoxy-*N*-methylcarbamoyl)methyl)phosphonate (**37**),[16] 0.54 mL (1.1 equiv) of DBU, and finally a solution of 729 mg (1.0 equiv) of ketone **36a** in 4 mL of dry acetonitrile. The resulting mixture was stirred under nitrogen at rt for 7 days. The solvent was then removed under reduced pressure, and the residue was diluted with 50 mL of CH_2Cl_2, 40 mL of brine, and 20 mL of water. The separated aqueous layer was extracted with 4 × 50 mL of CH_2Cl_2, and the combined organic extracts were dried ($MgSO_4$), filtered, concentrated, and chromatographed (silica gel, 20% EtOAc/hexanes) to afford 749 mg (75%) of amide **38a***(endo)* and 174 mg (17%) of amide **38a***(E-exo)*. **38a*(endo)*:** colorless flake crystals, mp 87.0–89.0 °C (from Et_2O); R_f 0.17 (silica gel, 20% EtOAc/hexanes); IR (CH_2Cl_2) 3002, 2938, 1650, 1597 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.18 (s, 3H) 2.32 (t, J = 8.0 Hz, 2H), 2.76 (t, J = 8.0 Hz, 2H), 3.22 (s, 3H), 3.29 (d, J = 5.0 Hz, 2H), 3.43 (s, 2H), 3.72 (s, 3H), 3.83 (s, 3H), 5.05 (m, 2H), 5.95 (m, 1H), 6.70 (d, J = 10.0 Hz, 1H), 7.14 (d, J = 10.0 Hz, 1H). Anal. Calcd for $C_{19}H_{25}O_3N$: C, 72.35; H, 7.99; N, 4.44. Found: C, 72.38; H,

8.06; N, 4.42. **38a(*E-exo*):** off white crystals, mp 65.5–67.0 °C (from hexanes); R_f 0.10 (silica gel, 20% EtOAc/hexanes); IR (CH_2Cl_2) 3002, 2938, 1650, 1597 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.12 (s, 3H), 2.43–2.81 (m, 6H), 3.01 (m, 1H), 3.21 (s, 3H), 3.69 (s, 3H), 3.82 (s, 3H), 4.98 (m, 2H), 5.91 (m, 1H), 6.29 (s, 1H), 6.76 (d, J = 9.0 Hz, 1H), 7.02 (d, J = 9.0 Hz, 1H). Anal. Calcd for $C_{19}H_{25}O_3N$: C, 72.35; H, 7.99; N, 4.44. Found: C, 72.28; H, 8.11; N, 4.33.

3,4-Dihydro-1-(2-propenyl)-2-naphthaleneacetamide [38b*(endo)*] and 2-[3,4-Dihydro-1-(2-propenyl)-2(1*H*)-naphthalenylidene]-*N*-methoxy-*N*-methylacetamide [38b-*(E-exo)*]. A well-stirred suspension of 538 mg (1.2 equiv) of LiCl in 120 mL of dry acetonitrile was treated sequentially at rt, under an atmosphere of nitrogen, with 2.88 g (1.2 equiv) of dimethyl ((*N*-methoxy-*N*-methylcarbamoyl)methyl)phosphonate (**37**),[16] 1.70 mL (1.0 equiv) of DBU, and finally a solution of 2.12 g (1.0 equiv) of ketone **36b** in 10 mL of dry acetonitrile. The resulting mixture was stirred under nitrogen at rt for 8 days. Isolation and purification as described above for **38a** then gave 1.35 g (43%) of amide **38b***(endo)* and 1.22 g (40%) of amide **38b***(E-exo)* as yellow oils. **38b*(endo)*:** R_f 0.17 (silica gel, 30% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 2.33 (t, J = 8.0 Hz, 2H), 2.79 (t, J = 8.0 Hz, 2H), 3.20 (s, 3H), 3.30 (d, J = 5.5 Hz, 2H), 3.42 (s, 2H), 3.71 (s, 3H), 5.05 (m, 2H), 5.94 (m, 1H), 7.07–7.28 (m, 4H). **38b*(E-exo)*:** R_f 0.31 (silica gel, 30% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 2.43 (m, 1H), 2.57 (m, 2H), 2.76 (m, 1H), 2.87 (m, 1H), 3.02 (m, 1H), 3.22 (s, 3H), 3.69 (s, 3H), 4.94 (m, 2H), 5.05 (t, J = 7.5 Hz, 1H), 5.87 (m, 1H), 6.30 (br s, 1H), 7.05–7.18 (m, 4H).

1-[3,4-Dihydro-6-methoxy-5-methyl-1-(2-propenyl)-2-naphthalenyl]-3-butyn-3-one [39a*(endo)*]. A solution of 5.3 mg (0.02 mmol) of Ph_3CH in 6.6 mL of dry THF was cooled to −78 °C under nitrogen and was treated with vigorous stirring with 0.28 mL (1.5 equiv) of 2.5 M *n*-butyllithium/hexanes to afford a pink-colored solution. After the solution was stirred for 10 min, acetylene gas was bubbled through a drying tube into the reaction mixture until the pink color was discharged. After stirring for an additional 10 min at −78 °C, the reaction mixture was treated dropwise with a solution of 135 mg (0.43 mmol) of amide **38a***(endo)* in 2.5 mL of THF, and after addition was complete the reaction mixture was allowed to warm to 0 °C (ice-water bath). After an additional 1 h of stirring at 0 °C, the reaction was quenched with 7 mL of saturated aqueous NH_4Cl solution and 1.5 mL of H_2O, and the separated aqueous layer was extracted with 4 × 10 mL of ether. The combined extracts were dried ($MgSO_4$), filtered, concentrated, and chromatographed (silica gel, 5% EtOAc/hexanes) to afford 108 mg (89%) of the *endo* enynone **39a***(endo)* as yellow flake crystals: mp 53.5–54.5 °C (from MeOH); R_f 0.51 (silica gel, 5% EtOAc/hexanes); IR (CH_2Cl_2) 3281, 3012, 2942 1678, 1594 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.19 (s, 3H), 2.34 (t, J = 8.0 Hz, 2H), 2.78 (t, J = 8.0 Hz, 2H), 3.24 (s, 1H), 3.29 (d, J = 5.5 Hz, 2H), 3.51 (s, 2H), 3.74 (s, 3H), 5.04 (m, 2H), 5.93 (m, 1H), 6.71 (d, J = 9.0 Hz, 1H), 7.16 (d, J = 9.0 Hz, 1H). Anal. Calcd for $C_{19}H_{20}O_2$: C, 81.40; H, 7.19. Found: C, 81.24; H, 7.14.

1-[3,4-Dihydro-1-(2-propenyl)-2-naphthalenyl]-3-butyn-3-one [39b*(endo)*]. A solution of 32.0 mg (0.07 mmol) of Ph_3CH in 35 mL of dry THF was cooled to −78 °C under nitrogen and was treated with vigorous stirring with 1.17 mL (1.5 equiv) of 2.5 M *n*-butyllithium/hexanes to afford a pink-colored solution. After the solution was stirred for 10 min, acetylene gas was bubbled through a drying tube into the reaction mixture until the pink color was discharged. After stirring for an additional 10 min at −78 °C, the reaction mixture was treated dropwise with a solution of 517 mg (1.0 equiv) of amide **38b***(endo)* in 6.0 mL of THF, and after addition was complete the reaction mixture was allowed to warm to 0 °C (ice-water bath) and stirred for an additional 1 h. Isolation and purification as described for **39a** then afforded 311 mg (69%) of *endo* enynone **39b***(endo)* as a yellow oil: R_f 0.54 (silica gel, 20% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 2.33 (t, J = 8.0 Hz, 2H), 2.77 (t, J = 8.0 Hz, 2H), 3.22 (s, 1H), 3.28 (d, J = 5.5 Hz, 2H), 3.50 (s, 2H), 5.05 (m, 2H), 5.92 (m, 1H), 7.03–7.30 (m, 4H).

9,10-Dihydro-7-methoxy-3,8-dimethyl-4-(2-propenyl)-2-phenanthrenol Acetate (41a). A solution consisting of 59.9 mg (0.21 mmol, 1.0 equiv) of enynone **39a***(endo)*, 62.9 mg (1.0 equiv) of collidinium *p*-toluenesulfonate (CPTS), and 3.56 mg (0.1 equiv) of *tert*-butylcatechol (TBC) in 5.3 mL of Ac_2O was degassed and heated in a sealed tube at 160 °C for 3 h.[1a,b] The reaction mixture was then cooled, and the Ac_2O was removed under reduced pressure. Chromatography (silica gel, CH_2Cl_2) then afforded 32 mg (47%) of **41a** as pale yellow granular crystals: mp 119.0–120.0 °C (from Et_2O); R_f 0.72 (silica gel, CH_2Cl_2); IR (CH_2Cl_2) 3002, 2941, 2838, 1757, 1591, 1483, 1439, 1370, 1214, 1104, 1092, 1053, 924 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.16 (s, 3H), 2.21 (s, 3H), 2.33 (s, 3H), 2.62 (m, 4H), 3.83 (s, 3H), 5.24 (dd, J = 18.0, 2.5 Hz, 1H), 5.51 (dd, J = 10.0, 2.5 Hz, 1H), 6.70 (d, J = 9.0 Hz, 1H), 6.73 (m, 1H), 6.85 (s, 1H), 7.64 (d, J = 9.0 Hz, 1H). Anal. Calcd for $C_{21}H_{22}O_3$: C, 78.23; H, 6.88. Found: C, 78.70; H, 6.89.

9,10-Dihydro-3-methyl-4-(2-propenyl)-2-phenanthrenol Acetate (41b). A solution consisting of 116 mg (0.49 mmol, 1.0 equiv) of enynone **39b***(endo)*, 144 mg (1.0 equiv) of collidinium *p*-toluenesulfonate (CPTS), and 8.20 mg (0.1 equiv) of *tert*-butylcatechol (TBC) in 12 mL of Ac_2O was degassed and heated in a sealed tube at 160 °C for 3 h.[1a,b] The reaction mixture was then cooled, and the Ac_2O was removed under reduced pressure. Chromatography (silica gel, 20% EtOAc/hexanes) then afforded 40 mg (29%) of **41b** as a yellow oil: R_f 0.50 (silica gel, 20% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 2.20 (s, 3H), 2.36 (s, 3H), 2.75 (m, 4H), 5.28 (dd, J = 18.5, 2.5 Hz, 1H), 5.50 (dd, J = 11.5, 2.5 Hz, 1H), 6.85 (dd, J = 18.5, 11.5 Hz, 1H), 6.90 (s, 1H), 7.10–7.30 (m, 3H), 7.83 (d, J = 7.5 Hz, 1H).

5-Ethenyl-9,10-dihydro-1,6-dimethyl-2,7-phenanthrenediol (Juncusol) (22). A solution consisting of 52.3 mg (0.16 mmol) of **41a** and 109 mg (12.5 equiv) of $LiSCH_3$ in 7 mL of HMPA was heated at 200 °C for 2.5 h under an atmosphere of nitrogen.[7f] After being cooled to rt, the reaction mixture was poured into 20 mL of cold H_2O and extracted with 4 × 25 mL of Et_2O. The combined extracts were washed with 20 mL of H_2O and 20 mL of brine, dried over $MgSO_4$, filtered, and concentrated to give an oily residue. Preparative TLC (silica gel, CH_2Cl_2) then afforded 31.4 mg (73%) of juncusol (**22**) as a yellow crystalline compound, identical in all respects with an authentic sample:[19] mp 172.7–173.7 °C (needles from benzene); R_f 0.17 (silica gel, CH_2Cl_2); IR (CH_2Cl_2) 3585, 3050, 2977, 1593, 1111 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.22 (s, 3H), 2.26 (s, 3H), 2.65 (m, 4H), 4.71 (s, 1H), 4.74 (s, 1H), 5.21 (dd, J = 18.0, 1.8 Hz, 1H), 5.49 (dd, J = 11.5, 1.8 Hz, 1H), 6.58 (d, J = 8.5 Hz, 1H), 6.64 (s, 1H), 6.75 (dd, J = 18.0, 11.5 Hz, 1H), 7.50 (d, J = 8.5 Hz, 1H); Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.04; H, 6.85.

3-Benzyl-5-methyl-4-phenylphenol (47a). This compound was prepared by thermolysis of 20.4 mg (0.075 mmol) of enynone **42a**[1a] in 1.5 mL of degassed bromobenzene at 200 °C for 15 h in the presence of 0.1 equiv of CPTS, following an identical procedure as that described above for the preparation of dihydronaphthol **21a**. The crude product, obtained by removing the reaction solvent under reduced pressure, was purified by preparative TLC (silica gel, 5% EtOAc/low-boiling petroleum ether) to afford 2 mg (10%) of methylenecyclopentenone **45a**[1a] and 9.0 mg (44%) of **47a** as a colorless solid: mp 82–83 °C (from low-boiling petroleum ether); R_f 0.21 (silica gel, 10% EtOAc/hexanes); MS m/e 274 (M^+); IR ($CHCl_3$) 3598, 3086, 1609, 1593, 1148 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.96 (s, 3H), 3.63 (s, 2H), 4.61 (s, 1H), 6.46 (d, J = 2.5 Hz, 1H), 6.61 (d, J = 2.5 Hz, 1H), 6.94 (m, 2H), 7.04 (m, 2H), 7.11–7.19 (m, 3H), 7.28–7.35 (m, 3H).

3,5-Dimethylphenol (47b).[20a] This compound was prepared by thermolysis of 61.0 mg (0.50 mmol) of enynone **42b**[1a] in 10 mL of degassed toluene at 250 °C for 11 h in the presence of 0.1 equiv of CPTS, following an identical procedure as that described above for the preparation of dihydronaphthol **21a**. The crude product, obtained by removing the reaction solvent under reduced pressure, was purified by preparative TLC (silica gel, 10% EtOAc/hexanes) to afford 46.1 mg (76%) of **47b** as a colorless solid which had spectral data in agreement with the published values:[20a] mp 62–63 °C (from low-boiling

petroleum ether, lit.[20a] mp 60.7.−62.5 °C); R_f 0.20 (silica gel, 10% EtOAc/hexanes); mass spectrum, *m/e* (rel intensity) 122 (M^+, 97), 121 (35), 107 (100), 91 (16), 79 (13), 77 (24); IR ($CHCl_3$) 3699, 3336 br, 1621, 1596, 1474, 1153 cm^{-1}; NMR ($CDCl_3$) δ 2.23 (s, 6H), 4.52 (s, 1H), 6.42 (s br, 2H), 6.54 (s br, 1H); exact mass calcd for $C_8H_{10}O$ 122.0729, found: 122.0728.

3-Ethyl-4,5-dimethylphenol (47c).[20b] This compound was prepared by thermolysis of 38.0 mg (0.25 mmol) of enynone **42c**[1a] in 5 mL of degassed toluene at 250 °C for 16 h in the presence of 0.1 equiv of CPTS and 0.05 equiv hydroquinone, following an identical procedure as that described above for the preparation of dihydronaphthol **21a**. The crude product, obtained by removing the reaction solvent under reduced pressure, was purified by flash chromatography (silica gel, 10% EtOAc/low-boiling petroleum ether) to afford 31.1 mg (82%) of **47c** as a colorless solid which had spectral data in agreement to the published values:[20b] mp 76−77 °C (from low-boiling petroleum ether); R_f 0.24 (silica gel, 10% EtOAc/hexanes); MS *m/e* 150 (M^+), 135, 121, 107, 91; IR ($CHCl_3$) 3600, 3400 br, 1615, 1603 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.15 (t, J = 7.6 Hz, 3H), 2.09 (s, 3H), 2.21 (s, 3H), 2.57 (q, J = 7.6 Hz, 2H), 4.43 (s, 1H), 6.74 (s, 2H). Anal. Calcd for $C_{10}H_{14}O$: C, 79.96; H, 9.40. Found: C, 79.89; H, 9.45.

3,4-Dihydro-*N*,6-dimethoxy-*N*,5-dimethyl-2-naphthaleneacetamide (48a). A well-stirred suspension of 298 mg (1.2 equiv) of LiCl in 60 mL of dry acetonitrile was treated sequentially at rt, under an atmosphere of nitrogen, with 1.44 g (1.2 equiv) of dimethyl ((*N*-methoxy-*N*-methylcarbamoyl)-methyl)phosphonate (**37**),[16] 0.84 mL (1.0 equiv) of DBU, and finally a solution of 1.07 g (5.64 mmol, 1.0 equiv) of β-tetralone **35a**[14a] in 10 mL of dry acetonitrile. The resulting mixture was stirred under nitrogen at rt for 3 days. Isolation and purification as described above for **38a** then afforded 1.44 g (93%) of pure *endo* amide **48a** as a yellow oil: R_f 0.27 (30% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 2.12 (s, 3H), 2.32 (t, J = 8.0 Hz, 2H), 2.79 (t , J = 8.0 Hz, 2H), 3.19 (s, 3H), 3.32 (s, 2H), 3.68 (s, 3H), 3.78 (s, 3H), 6.24 (s, 1H), 6.63 (d, J = 8.5 Hz, 1H), 6.82 (d, J = 8.5 Hz, 1H).

3,4-Dihydro-*N*-methoxy-*N*-methyl-2-naphthaleneacetamide (48b). A well-stirred suspension of 1.66 g (1.2 equiv) of LiCl in 360 mL of dry acetonitrile was treated sequentially at rt, under an atmosphere of nitrogen, with 8.22 g (1.2 equiv) of dimethyl ((*N*-methoxy-*N*-methylcarbamoyl)-methyl)phosphonate (**37**),[16] 4.84 mL (1.0 equiv) of DBU, and finally 4.29 mL (32.4 mmol, 1.0 equiv) of β-tetralone **35b**.[11b] The resulting mixture was stirred under nitrogen at rt for 4.5 days. Isolation and purification as described above for **38a** then afforded 7.23 g (96%) of pure *endo* amide **48b** as a yellow oil: R_f 0.16 (30% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 2.35 (t, J = 8.2 Hz, 2H), 2.83 (t, J = 8.2 Hz, 2H), 3.20 (s, 3H), 3.34 (s, 2H), 3.70 (s, 3H), 6.31 (s, 1H), 6.97 (d, J = 6.5 Hz, 1H), 7.08 (m, 3H).

1-(3,4-Dihydro-6-methoxy-5-methyl-2-naphthalenyl)-3-pentyn-2-one (49a). A solution of 10.0 mg (0.05 equiv) of Ph_3CH in 14 mL of dry THF was cooled to −78 °C under nitrogen and was treated with vigorous stirring with 0.43 mL (1.2 equiv) of 2.5 M *n*-butyllithium/hexanes to afford a pink-colored solution. After the solution was stirred for 10 min, propyne gas was bubbled through a drying tube into the reaction mixture until the pink color was discharged. After stirring for an additional 10 min at −78 °C, the reaction mixture was treated dropwise with a solution of 224 mg (0.81 mmol, 1.0 equiv) of amide **48a** in 3.0 mL of THF, and after addition was complete the reaction mixture was allowed to warm to 0 °C (ice-water bath) and stirred for an additional 1 h. Isolation and purification as described above for **39a** then afforded 151 mg (73%) of enynone **49a** as a yellow oil: R_f 0.52 (silica gel, 20% EtOAc/hexanes); MS *m/e* 254 (M^+); IR (CH_2Cl_2) 3070, 3040, 2225, 1670, 1650 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.98 (s, 3H), 2.13 (s, 3H), 2.28 (t, J = 8.0 Hz, 2H), 2.79 (t, J = 8.0 Hz, 2H), 3.33 (s, 2H), 3.80 (s, 3H), 6.29 (s, 1H), 6.64 (d, J = 8.0 Hz, 1H), 6.85 (d, J = 8.0 Hz, 1H).

1-(3,4-Dihydro-2-naphthalenyl)-3-pentyn-2-one (49b). A solution of 17.0 mg (0.05 equiv) of Ph_3CH in 25 mL of dry THF was cooled to −78 °C under nitrogen and was treated with vigorous stirring with 0.71 mL (1.2 equiv) of 2.5 M *n*-butyllithium/hexanes to afford a pink-colored solution. After the solution was stirred for 10 min, propyne gas was bubbled through a drying tube into the reaction mixture until the pink color was discharged. After stirring for an additional 10 min at −78 °C, the reaction mixture was treated dropwise with a solution of 311 mg (1.35 mmol, 1.0 equiv) of amide **48b** in 4.0 mL of THF, and after addition was complete the reaction mixture was allowed to warm to 0 °C (ice-water bath) and stirred for an additional 1 h. Isolation and purification as described above for **39a** then afforded 141 mg (50%) of enynone **49b** as a yellow oil: R_f 0.70 (silica gel, 20% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 1.99 (s, 3H), 2.30 (t, J = 8.2 Hz, 2H), 2.83 (t, d, J = 8.2 Hz, 2H), 3.37 (s, 2H), 6.36 (s, 1H), 7.00 (d, J = 7.0 Hz, 1H), 7.10 (m, 3H).

1-(3,4-Dihydro-6-methoxy-5-methyl-2-naphthalenyl)-5-hexen-3-yn-2-one (49c). A solution of 29.5 mg (0.05 eq) of Ph_3CH in 40 mL of dry THF was cooled to −78 °C under nitrogen and was treated with vigorous stirring with 1.4 mL (1.5 equiv) of 2.5 M *n*-butyllithium/hexanes to afford a pink-colored solution. After being stirred for 10 min, the reaction mixture was treated with 0.7 mL (1.5 equiv) of 50% 1-buten-3-yne/hexanes and stirring was continued for an additional 10 min at −78 °C. The reaction mixture was then treated dropwise with a solution of 642 mg (2.33 mmol, 1.0 equiv) of amide **48a** in 8.0 mL of THF, and after addition was complete the reaction mixture was allowed to warm to 0 °C (ice-water bath) and stirred for an additional 1 h. Isolation and purification as described above for **39a** then afforded 357 mg (58%) of enynone **49c** as a yellow oil: R_f 0.48 (silica gel, 20% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 2.15 (s, 3H), 2.30 (t, J = 8.2 Hz, 2H), 2.81 (t, J = 8.2 Hz, 2H), 3.41 (s, 2H), 3.81 (s, 3H), 5.78 (m, 1H), 5.81 (m, 2H), 6.33 (s, 1H), 6.65 (d, J = 8.5 Hz, 1H), 6.86 (d, J = 8.5 Hz, 1H).

9,10-Dihydro-7-methoxy-4,8-dimethyl-2-phenanthrenol (51a). A solution consisting of 29.0 mg (0.12 mmol, 1.0 equiv) of enynone **49a**, 17.0 mg (0.5 equiv) of collidinium *p*-toluenesulfonate (CPTS), and 2.0 mg (0.1 equiv) of *tert*-butylcatechol (TBC) in 2.8 mL of bromobenzene was heated at 200 °C in a degassed sealed tube for 17 h. The reaction mixture was then cooled, concentrated under reduced pressure, and chromatographed (silica gel, 20% EtOAc/hexanes) to afford 4.1 mg (14%) of phenanthrenol **51a** as a yellow oil: R_f 0.40 (silica gel, 20% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 2.22 (s, 3H), 2.52 (s, 3H), 2.66 (m, 4H), 3.85 (s, 3H), 6.58 (d, J = 3.0 Hz, 1H), 6.62 (d, J = 3.0 Hz, 1H), 6.77 (d, J = 8.5 Hz, 1H), 7.39 (d, J = 8.5 Hz, 1H).

9,10-Dihydro-4-methyl-2-phenanthrenol (51b). Method A. A solution consisting of 32.9 mg (0.16 mmol, 1.0 equiv) of enynone **49b**, 4.6 mg (0.1 equiv) of collidinium *p*-toluenesulfonate (CPTS), and 2.7 mg (0.1 equiv) of *tert*-butylcatechol (TBC) in 4.0 mL of 1,2-dichlorobenzene was heated at 200 °C in a degassed sealed tube for 17 h. The reaction mixture was then cooled, concentrated under reduced pressure, and chromatographed (silica gel, 20% EtOAc/hexanes) to afford 6.9 mg (44%) of phenanthrenol **51b** as a yellow oil: R_f 0.35 (silica gel, 20% EtOAc/hexanes); MS *m/e* 210 (M^+); ^1H NMR (400 MHz, $CDCl_3$) δ 2.54 (s, 3H), 2.68 (br s, 4H), 4.75 (s, 1H), 6.59 (d, J = 2.5 Hz, 1H), 6.62 (d, J = 2.5 Hz, 1H), 7.14 (t, J = 7.5 Hz, 1H), 7.23 (m, 2H), 7.56 (d, J = 8.0 Hz, 1H). **Method B.** A solution consisting of 56.9 mg (0.27 mmol, 1.0 equiv) of enynone **49b** and 8.0 mg (0.1 equiv) of $HgSO_4$ in 6.4 mL of 1,2-dichlorobenzene was heated in a degassed sealed tube at 200 °C for 18 h. The reaction mixture was then cooled, concentrated under reduced pressure, and chromatographed (silica gel, 20% EtOAc/hexanes) to afford 36.4 mg (64%) of **51b**, identical with the material prepared by method A above.

2-Acetoxy-1,4-diethylbenzene (54b).[20d] A solution consisting of 45.0 mg (0.30 mmol, 1.0 equiv) of enynone **42c**, 0.10 equiv of *p*-toluenesulfonic acid, and 5.0 equiv of isopropenyl acetate (IPA) in 0.9 mL of freshly distilled bromobenzene was degassed and heated in a sealed tube at 200 °C for 0.5 h.[1a,b] The reaction mixture was then cooled, concentrated under reduced pressure, and chromatographed (silica gel, 1% EtOAc/hexanes) to afford 46.1 mg (80%) of **54b** as a yellow oil:[20d] R_f 0.34 (silica gel, 10% EtOAc/hexanes); MS *m/e* (rel intensity) 192 (M^+, 13), 150 (71), 135 (100), 121 (24); IR ($CHCl_3$) 1749,

1461, 1453, 1421, 1372, 1233, 1204 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.20 (t, J = 8.0 Hz, 3H), 1.23 (t, J = 8.0 Hz, 3H), 2.30 (s, 3H), 2.48 (q, J = 8.0 Hz, 2H, 2.60 (q, J = 8.0 Hz, 2H, 6.82 (s, 1H), 7.01 (d, J = 7.0 Hz, 1H, 7.15 (d, J = 7.0 Hz, 1H).

2,5-Diethylphenol (54a).[20c] A degassed solution of 192 mg (1.00 mmol) of acetate **54b** in 25 mL of anhydrous MeOH was cooled to 0 °C in an ice bath and treated in a single portion, with vigorous stirring, with 227 mg (6.00 mmol) of $NaBH_4$. After 15 min, the ice bath was removed and stirring was continued at rt for an additional 4 h before the reaction was quenched with 30 mL of ice-cold saturated NH_4Cl. Isolation and purification as described above for **21a** then gave 121 mg (81%) of **54a** as a yellow oil which had physical properties in agreement with the published values.[20c] **54a:** bp 50–54 °C (0.125 mm); R_f 0.28 (silica gel, 10% EtOAc/hexanes); MS m/e (rel intensity) 150 (M^+, 29), 135 (100), 121 (23); IR ($CHCl_3$) 3605, 3371 br, 1626, 1588, 1217 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.19 (t, J = 7.5 Hz, 3H), 1.20 (t, J = 7.6 Hz, 3H), 2.52 (q, J = 7.6 Hz. 2H), 2.56 (q, J = 7.5 Hz, 2H), 4.61 (s, 1H), 6.58 (s, 1H), 6.71 (d, J = 7.8 H, 1H), 7.03 (d, J = 7.8 Hz, 1H); exact mass calcd for $C_{10}H_{14}O$ 150.1045, found 150.1056.

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Supplementary Material Available: Copies of ^1H NMR spectra for compounds **12Z, 12E, 18Z, 18E, 21a, 21b, 22**(synthetic), **22**(authentic), **30aZ/E, 32aZ, 32aE, 32bZ, 32bE, 32cZ, 32cE, 33a, 33b, 33c, 34a, 34b, 34c, 36a, 36b, 38a**(*endo*), **38a**(*E-exo*), **38b**(*endo*), **38b**(*E-exo*), **39a**(*endo*), **39b**(*endo*), **41a, 41b, 47a, 47b, 47c, 48a, 48b, 49a, 49b, 49c, 51a, 51b, 54a,** and **54b** (42 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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