# Enynones in Organic Synthesis. 6. Synthesis of Spirocyclic Methylenecyclopentenones and Analogs of the Methylenomycin Class of Antibiotics. Mechanism of Phenol Catalysis

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Spirocyclic methylenecyclopentenones of general structure **18** were prepared in a single step from bis-acetylenic alcohols **29** by a process involving initial oxy-Cope rearrangement to afford (*Z*)-enynones **30-Z** followed by electrocyclic ring closure. Mechanistic studies indicate that the initial step leading from **30-Z** to **18** is a thermal 1,5-prototropic shift to afford dienols which can cyclize by a symmetry-allowed ($\pi^4$s + $\sigma^2$s + $\pi^2$a) process. This last step is catalyzed by certain phenols having low oxidation potentials, most likely by a mechanism involving single electron transfer. Dramatic rate enhancements were also observed for the cyclization of simple enynones **37** to methylenecyclopentenones **39** upon catalysis with either α-tocopherol (vitamin E, **40**) or *tert*-butylcatechol (**41**). Further enhancements in both rate and yield were obtained under conditions of photoassisted single electron transfer (PET), which afforded **39** in yields of 80–98%.

## Introduction

Several years ago we described an unequivocal synthesis of gnididione (**4**),[1] a sesquiterpene of the guaiane class which was among the first members of this skeletal type isolated which contained a furan ring.[2] A key intermediate in our synthesis of **4** was the tertiary alcohol **1**, which was converted in a single step to gnididione ketal **3**, from which the natural product was liberated by mild acid hydrolysis (Figure 1). The sequence leading from **1** to **3** made use of a chemo- and stereospecific oxy-Cope rearrangement,[3] which yielded acetylenic ketone **2** with unambiguous control over stereochemistry at C-1 and C-10. Acetylenic ketone **2**, in turn, underwent a rapid (Diels–Alder)–(retro-Diels–Alder) reaction,[4] which generated both the perhydroazulene and furan rings of **3** with complete regiochemical control.

During the course of these studies, we also explored the possibility that dehydrognididione ketal **7** might be derived from the acetylenic enone **6-Z** by a straightforward extension of the methodology employed for the synthesis of **3** (Scheme 1). This approach was attractive because it offered the possibility that **6-Z** might be conveniently prepared by an oxy-Cope rearrangement of the tertiary alcohol **5**,[3] itself available in multigram quantities from the corresponding ester. In fact, thermolysis of **5** provided an excellent yield of the expected mixture of **6-Z** and **6-E** at temperatures between 80 and 90 °C. At higher temperatures, however, we were surprised to find that **6-Z** gave none of the desired furan **7** but rather was cleanly converted to the spirocyclic methylenecyclopentenone **8**, which was isolated as an equilibrium mixture of (*E*)- and (*Z*)-isomers (*E*:*Z* ≈1:1,

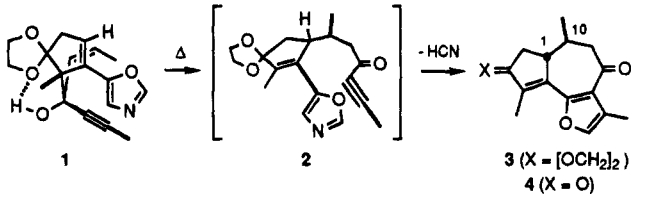
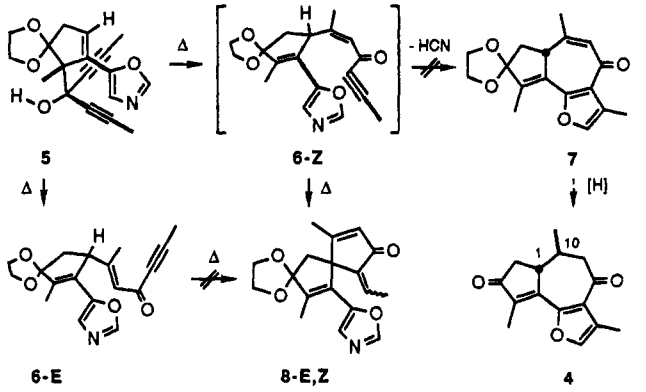



**Figure 1.**

**Scheme 1**




80–90% yield, 110 °C, toluene). Acetylenic enone **6-E**, in contrast, was totally unreactive at temperatures up to 160 °C and slowly decomposed at temperatures above 200°. At the time, transformations of the type **6-Z** → **8** were unprecedented, although Dreiding et al. have since reported on similar conversions occurring in low yield in the vapor phase at 600–800 °C[5] and Agosta et al. have described a related photochemical reaction of mesityl ketones.[6] The potential utility of transformations of the type **6-Z** → **8** is considerable in view of the large number of spirocyclic compounds found in nature, and the difficulties frequently encountered in the synthesis of

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(1) (a) Jacobi, P. A.; Selnick, H. G. *J. Org. Chem.* **1990**, *55*, 202. (b) Jacobi, P. A.; Selnick, H. G. *J. Am. Chem. Soc.* **1984**, *106*, 3041.

(2) Kupchan, S. M.; Shizuri, Y.; Baxter, R. L.; Haynes, H. R. *J. Org. Chem.* **1977**, *42*, 348.

(3) (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.

(4) Jacobi, P. A. In *Advances in Heterocyclic Natural Product Synthesis*, Volume II; Pearson, W. H., Ed.; Jai Press Inc.: Greenwich, CT, 1992.

(5) Koller, M.; Karpf, M.; Dreiding, A. S. *Tetrahedron Lett.* **1986**, *27*, 19; *Helv. Chim. Acta.* **1986**, *69*, 560.

(6) (a) Rao, V. B.; Wolff, S.; Agosta, W. C. *J. Am. Chem. Soc.* **1985**, *107*, 521. (b) Agosta, W. C.; Caldwell, R. A.; Jay, J.; Johnston, L. J.; Venepalli, B. R.; Scaiano, J. C.; Singh, M.; Wolff, S. *J. Am. Chem. Soc.* **1987**, *109*, 3050.

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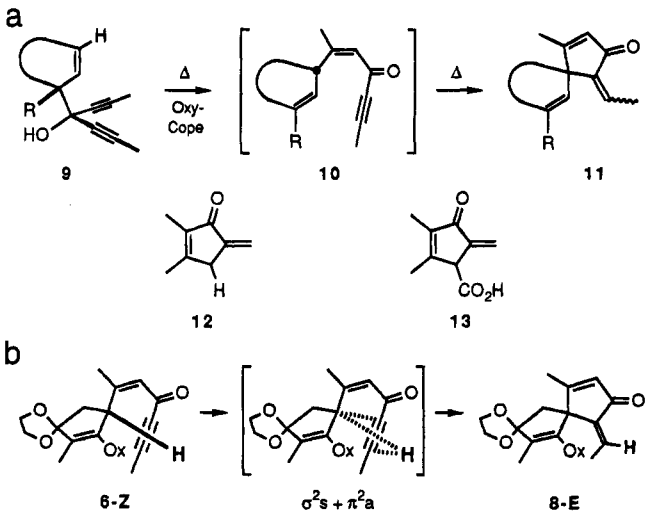



Figure 2.

quaternary carbon centers.[7] In addition, the methylenecyclopentenone functionality found in **8** is an important component of various antibiotics[8] and cytotoxic agents.[9] In this paper we describe our mechanistic studies of this unusual cyclization reaction, which led to the development of a general protocol for effecting tandem (oxy-Cope)–(spirocyclization) reactions of the type represented by **9** → **11** (Figure 2a).[10a] In addition, we have expanded upon this methodology for the synthesis of several analogs of the important methylenecyclopentenone antibiotics methylenomycin B (**12**) and desepoxy-4,5-didehydromethylenomycin A (**13**).[10b,d]

## Discussion and Results

**A. Spirocyclic Methylenecyclopentenones.** A number of observations pointed toward a concerted process (or processes) for the conversion of **6-Z** to **8**. For example, cyclization was not inhibited by radical scavengers, and all attempts at acid or base catalysis caused extensive decomposition. In addition, reaction was most efficient in relatively nonpolar solvents such as toluene and showed no rate acceleration with increasing solvent polarity. Finally, as noted above (Scheme 1), (*E*)-enynone **6-E** was completely unreactive toward thermal cyclization, suggesting a geometrical requirement for orbital overlap. On the basis of this last result, we considered the possibility that **8-E** might be formed directly from **6-Z** via a $\sigma^2s + \pi^2a$ addition of the $\gamma$-(C–H) bond across the acetylenic $\pi$-system, as suggested by Dreiding et al. for related vapor-phase transformations at 600–800 °C (Figure 2b).[3a,5] However, this possibility seemed remote in view of the mildness of the conditions employed in the present case (110 °C).

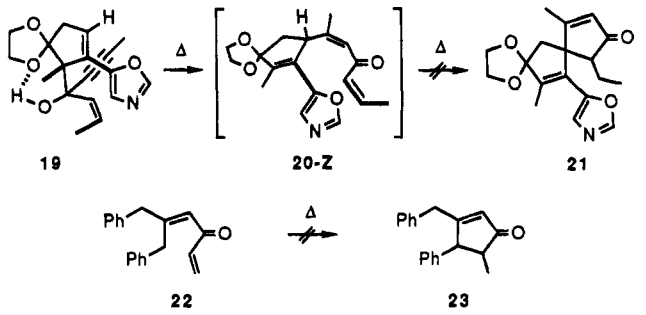
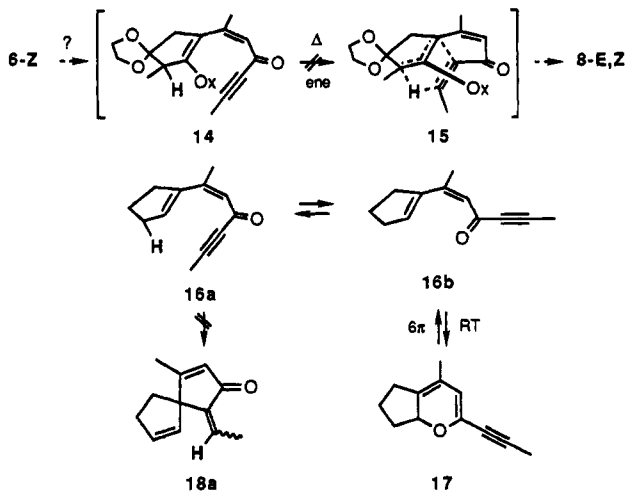



Figure 3.

**Scheme 2**

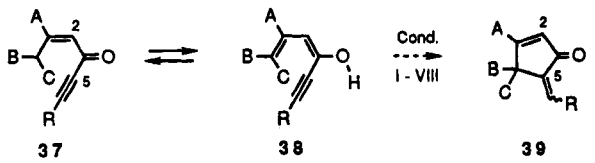



We also explored the possibility that **6-Z** might be converted to **8** via a mechanism involving initial isomerization to the fully conjugated dienone **14**, followed by an intramolecular ene reaction (Scheme 2, Ox = 5-oxazolo). This pathway could afford either **8-E** or **8-Z** as the product of kinetic control, depending upon whether chair- or boat-like transition state **15** were operative. However, the ene mechanism was excluded on the basis of model studies with the closely related dienone **16** and other experiments to be described later. Thus, **16** reacted exclusively through conformation **16b** to afford an equilibrium mixture of **16** and dihydropyran **17**,[10e] the product of 6$\pi$-electrocyclization.[11,12] No trace of the methylenecyclopentenone **18a** could be detected.

Of particular interest, we found that the in-plane orbitals of the acetylene are required for spiroannulation. Thus, cross-conjugated ketone **20-Z**, derived by chemoselective oxy-Cope rearrangement of tertiary alcohol **19**,[1a] was completely unreactive toward cyclization to ethylcyclopentenone **21** (Figure 3), in contrast to the case with the closely related enynone **6-Z** (cf. Scheme 1). Similar results were obtained with the model system **22**, which afforded mainly decomposition products upon attempted cyclization to **23** (the unreactive nature of **22** is in marked contrast to that of the closely related acetylenes **37a,b**, described below, which are among the most reactive substrates toward cyclization [Table 1]).[10f]

(7) Martin, S. F. *Tetrahedron* **1980**, *36*, 419.
(8) For a list of references for this class of compound, see: Smith, A. B., III; Boschelli, D. *J. Org. Chem.* **1983**, *48*, 1217.
(9) (a) Noyori, R.; Suzuki, M. *Science* **1993**, *259*, 44 and references cited therein. (b) *Advances in Prostaglandin, Thromboxane, and Leukotriene Research*, Volumes 11–21; Ravin: New York, 1983–1991.
(10) Preliminary communications: (a) Jacobi, P. A.; Armacost, L. M.; Kravitz, J. I.; Martinelli, M. J.; Selnick, H. G. *Tetrahedron Lett.* **1988**, *29*, 6865. (b) Jacobi, P. A.; Armacost, L. M.; Kravitz, J. I.; Martinelli, M. J. *Tetrahedron Lett.* **1988**, *29*, 6869. (c) Jacobi, P. A.; Kravitz, J. I. *Tetrahedron Lett.* **1988**, *29*, 6873. (d) Jacobi, P. A.; Cann, R. O.; Skibbie, D. F. *Tetrahedron Lett.* **1992**, *33*, 2265. (e) Kravitz, J. I Ph.D. Thesis, Wesleyan University, Middletown, CT, 1988. (f) Martinelli, M. J. Ph.D. Thesis, Wesleyan University, Middletown, CT, 1984.
(11) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Verlag Chemie/Academic Press Inc.: New York, 1970.
(12) For a closely related example, see: (a) Okamura, W. H.; Peter, R.; Reischl, W. *J. Am. Chem. Soc.* **1985**, *107*, 1034. See also: (b) Marvell, E. N. *Thermal Electrocyclic Reactions*; Academic Press: New York, 1980, p 305–319. Enynone **16** was generated *in situ* by addition of propynylmagnesium bromide to the corresponding Weinreb amide (cf. ref 4).

**Table 1**



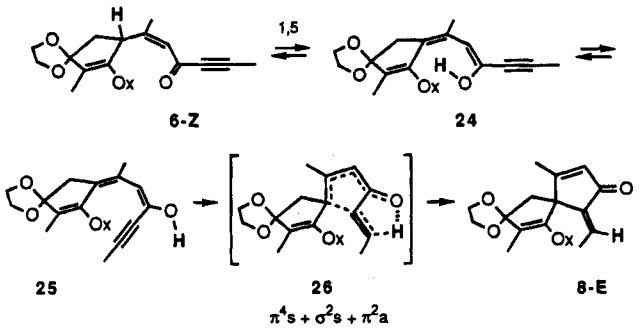

37 38 39

| # | Cmpd. | A | B | C | R | Cond. | hr | %39 | (Z/E) |
|---|---|---|---|---|---|---|---|---|---|
| 1. | 37a | Bn | Ph | H | Me | I | 10 | 38 | (1/1) |
| 2. | | | | | | II | 127 | 10 | (E)[a] |
| 3. | | | | | | III | 5 | 92 | (3/5) |
| 4. | | | | | | IV | 1 | 98 | (1/3) |
| 5. | 37b | Bn | Ph | H | H | I | 16 | 20 | - |
| 6. | | | | | | III | 21 | 48 | - |
| 7. | 37c | Me | H | H | Me | V | 48 | 0 | - |
| 8. | | | | | | VI | 48 | 13 | (E)[a] |
| 9. | | | | | | VII | 48 | 0 | - |
| 10. | | | | | | VIII | 17 | 16 | (1/2) |
| 11. | 37d | Et | Me | H | Me | V | 72 | 5 | (E)[a] |
| 12. | | | | | | VI | 10 | 56 | (1/2) |
| 13. | | | | | | VII | 4 | 8 | (2/1) |
| 14. | | | | | | VIII | 4 | 82[b] | (2/1) |
| 15. | 37e | Et | Me | H | H | V | 5 | 0 | - |
| 16. | | | | | | VI | 4 | 30[b] | - |
| 17. | | | | | | VII | 5 | 11 | - |
| 18. | | | | | | VIII | 4 | 98[b] | - |
| 19. | 37f | Pr | Et | H | Me | V | 5 | 0 | - |
| 20. | | | | | | VI | 12 | 36 | (1/1) |
| 21. | | | | | | VII | 5 | 9 | (1/3) |
| 22. | | | | | | VIII | 12 | 92 | (1/1) |
| 23. | 37g | Bu | Pr | H | Me | V | 5 | tr | (E)[a] |
| 24. | | | | | | VI | 5 | 16 | (1/3) |
| 25. | | | | | | VII | 5 | 8 | (1/3) |
| 26. | | | | | | VIII | 7 | 80 | (2/1) |
| 27. | 37h | *i*-Pr | Me | Me | Me | V | 5 | tr | (E)[a] |
| 28. | | | | | | VI | 4 | 61[b] | (1/1) |
| 29. | | | | | | VII | 5 | 15 | (E)[a] |
| 30. | | | | | | VIII | 4 | 96[b] | (1/1) |

(a) Only isomer observed. (b) GC yield. Isolated yield 5-10% lower.

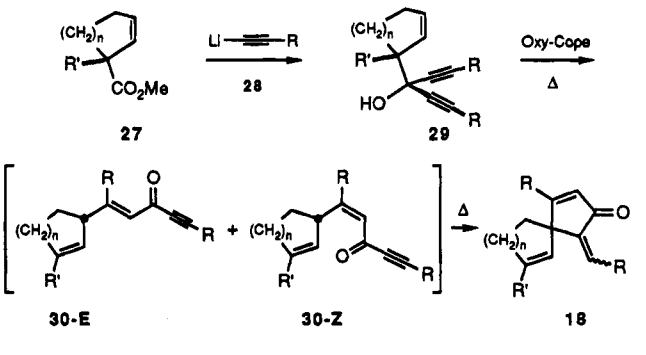
(I) Toluene, 250 °C. (II) Dichloroethane, 5 eq $NaHCO_3$, 83 °C. (III) Dichloroethane, 5 eq $NaHCO_3$, 83 °C, 1.1 eq TBC. (IV)1,2-Dichlorobutane, 5 eq $NaHCO_3$, 125 °C, 1.1 eq TBC. (V) 1,2-dichlorohexane, 5 eq 1,2-epoxyoctane, 200 °C. (VI) 1,2-di-chlorohexane, 5 eq 1,2-epoxyoctane, 200 °C, 1.1 eq Vitamin E. (VII) 1,2-dichlorohexane, 5 eq 1,2-epoxyoctane, 200 °C, hν. (VIII) 1,2-dichlorohexane, 5 eq 1,2-epoxyoctane, 200 °C, 1.1 eq Vitamin E, hν.

**Scheme 3**




Taken together, these observations are consistent with a mechanism involving an initial 1,5-prototropic shift to afford enol **24**,[11] which would be favored by the bis-allylic nature of the migrating hydrogen H-1 (bold) (Scheme 3, Ox = 5-oxazolo). Once formed, **24** could undergo equilibration to the more stable enol **25**,[6b] which has the proper geometry for cyclization to **8-E** via a ($\pi^4$s + $\sigma^2$s + $\pi^2$a) electrocyclic reaction (cf. transition state **26**).[11] This last step would be facilitated by the nucleophilicity of the terminus of the dienol and the electrophilicity of the acetylene.[13] In support of a concerted cyclization leading from **25** to **8-E**, model studies indicate that *(E)*-methylenecyclopentenones are the products of kinetic control,

**Scheme 4**




| | 29 | 30-E | 30-Z | 18 |
|---|---|---|---|---|
| a : n = 1, R' = H, R = Me | (25%)[I] | (0%)[II] | 0% | (43%)[I] (81%)[II] |
| b : n = 1, R' = Me, R = Me | (14%)[I] | (0%)[II] | 0% | (37%)[I] (79%)[II] |
| c : n = 2, R' = H, R = Me | (10%)[I] | (0%)[II] | 0% | (18%)[I] (55%)[II] |
| d : n = 2, R' = Me, R = Me | (17%)[I] | (0%)[II] | 0% | (29%)[I] (66%)[II] |
| e : n = 1, R' = H, R = Ph | (00%)[I] | (0%)[II] | 0% | (09%)[I] (70%)[II] |
| f : n = 1, R' = H, R = H | (00%)[I] | (0%)[II] | 0% | (<1%)[I] (<1%)[II] |

(I) toluene or mesitylene, Δ. (II) toluene, Δ, 4-*t*-butylcatechol

while the *(Z)*-isomers arise by equilibration (vide infra). This outcome is in accord with a direct transfer of the enolic hydrogen in **25** (bold) to the syn face of the acetylene (cf. **26**, Scheme 3).

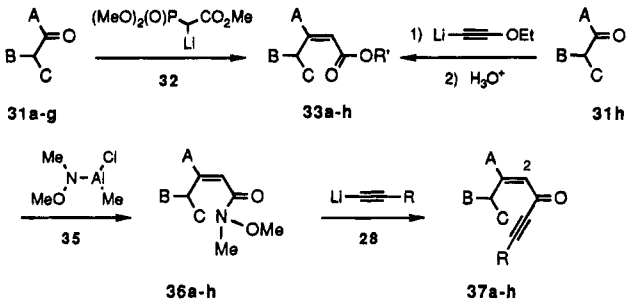
The generality of conversions of the type **6-Z** → **8** was tested with a number of less complicated analogs, which were readily prepared from the corresponding methyl 2-cycloalkenyl carboxylates **27a–d**[14] by reaction with lithium acetylides **28a,e,f** (Scheme 4). As indicated, cyclopentene derivatives **29a** and **29b** gave mixtures of the corresponding enynones **30-Ea,b** (15–25%) and spirocyclic methylenecyclopentenones **18a,b** (35–45%) upon heating in toluene or mesitylene at 250 °C for 12–16 h (conditions I). Under these conditions, little if any of the isomeric enynones **30-Za,b** could be isolated, presumably because they underwent facile cyclization to **18a,b**. In identical fashion, cyclohexene derivatives **29c** and **29d** afforded the methylenecyclopentenones **18c** (18%) and **26d** (29%), together with the enynones **30-Ec** (10%) and **30-Ed** (17%). Some degree of latitude was also possible in the nature of the acetylenic substituent R. For example, **29e** (R = Ph) gave a 9% yield of **18e** after 6 h at 230 °C, in addition to 18% of recovered starting material. However, the terminal acetylenic derivative **29f** gave only trace amounts of the spiroannulation product **18f**, apparently due to decomposition during the oxy-Cope process.

In an effort to minimize decomposition, these same transformations were repeated in the presence of various polymerization inhibitors. Of these, 4-*tert*-butylcatechol (TBC) proved to be the most effective, affording much cleaner reaction mixtures when present in catalytic amounts (~0.1 equiv). *Of greater interest, however, both the yield and rate for the conversions of* ***29*** *to* ***18*** *were substantially increased in the presence of excess TBC.* For example, **29a** gave an 81% yield of **18a** after 6 h at 250 °C with 1.1 equiv of TBC (0.05 N) (conditions II, Scheme

(13) We are grateful to Professor Kendall Houk, of the University of California, Los Angeles, for helpful discussions regarding the mechanism of this reaction.

(14) (a) Rhoads, S. J.; Chattopadhyay, J. K.; Waali, E. E. *J. Org. Chem.* **1970**, *35*, 3355. (b) Davies, S. G.; Whithan, G. H. *J. Chem. Soc., Perkin Trans. I* **1976**, 2279.

**Scheme 5**




4), while the same reaction required 12 h to give a 43% yield of **18a** in the absence of TBC (conditions I). Also, utilizing conditions II, even (*E*)-enynone **30-Ea** was completely consumed. Similar results were obtained with acetylenic alcohols **29b–29e**, with **29e** providing a particularly striking contrast between conditions I and II (9% vs 70%). These rate enhancements might be partly due to TBC functioning as a mild acid catalyst in the enolization of both **30-E** and **30-Z**, which is required for spirocyclization (cf. Scheme 2). However, as described below, more substantive effects are involved as well.

**B. Phenol-Catalyzed Cyclizations of Enynones to Methylenecyclopentenones.** In order to study the catalytic effect of TBC, we prepared a number of 2-unsubstituted enynone derivatives **37** following the general route outlined in Scheme 5 (*note*: for consistency, enynone numbering corresponds to that of the derived 2-cyclopenten-1-ones; cf. Table 1, below). For **37a-g**, the key intermediates **33a–g** (R′ = Me) were prepared in 78–99% yield via Horner–Wadsworth–Emmons reaction of lithium trimethyl phosphonoacetate (**32**) with the commercially available ketones **31a–g** (A,B,C = Me, *n*-alkyl, benzyl).[15] However, for **33h** (A = *i*-Pr; B,C = Me; R′ = Et), which is very sterically hindered, it was necessary to employ a two-step procedure involving initial condensation of **31h** with the less bulky reagent lithium ethoxyacetylide (**34**), followed by acid-catalyzed Rupe rearrangement (43% overall yield).[16] Once in hand, acrylic esters **33** were readily converted to the Weinreb amides **36** by reaction with aluminum amide **35** (60–75%),[17] and finally, **36** reacted smoothly with lithium acetylides **28** to afford the desired enyones **37** (62–99%; substituents are given in Table 1).[18]

Our initial cyclization studies were carried out with dibenzyl enynone **37a** (R = Me), which gave a 38% yield of methylenecyclopentenone **39a** upon heating in toluene for 10 h at 250 °C (Table 1, entry 1, *E*:*Z* ~ 1:1) and a 10% yield of **39a** after 127 h at 83 °C in 1,2-dichloroethane (entry 2, (*E*)-isomer only). In similar fashion, **37b** (R = H) afforded 20% of **39b** after 16 h at 250 °C (entry 5). Not surprisingly, substrates which are not activated by extended conjugation were much less reactive toward thermal conversion to enolic species of type **38** and subsequent cyclization. Thus, under similar conditions, aliphatic enynones **37c–h** were either recovered unchanged (entries 7, 15, 19) or gave only trace amounts of **39** (entries 11, 23, 27).

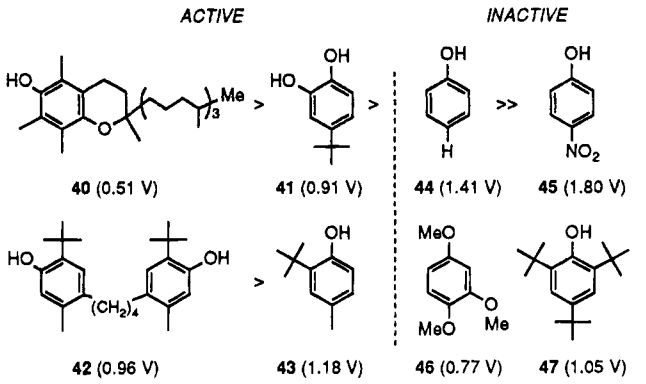



**Figure 4.**

As in the case with the spirocyclic methylenecyclopentenones **18** (cf. Scheme 4), we observed a dramatic increase in rate when the cyclization of **37a** to **39a** was carried out in the presence of excess TBC. Thus, while **37a** gave a 10% yield of **39a** after 127 h at 83 °C in the uncatalyzed reaction (entry 2), *the identical product was obtained in 92% yield after 5 h at 83 °C in the presence of 1.1 equiv of TBC (0.02 N) (entry 3) and in 98% yield after 1 h at 125 °C with TBC (entry 4)*. In analogous fashion, the yield of **39b** increased from 20% at 250 °C (entry 5) to 48% at 83 °C (entry 6).

Interestingly, substantial rate enhancements were also observed with excess α-tocopherol (vitamin E, **40**) and to a lesser extent with certain other phenols whose relative catalytic activity is summarized in Figure 4. With unactivated enynones **37c–h**, vitamin E (**40**) was the catalyst of choice since it showed much less tendency to undergo competing Michael addition to the triple bond. Thus, considerable increases in both rate and yield were observed for enynones **37c–** in the presence of excess **40** (conditions V vs VI), with the smallest effect being observed with the simplest member of the series, **37c**. Even in this last case, however, the yield of **39c** increased from 0% (entry 7) to 13% (entry 8) with added vitamin E (**40**).[19] All reactions were carried out in the presence of acid scavengers ($NaHCO_3$ or 1,2-epoxyoctane) to assure against catalysis by adventitious acid impurities.

The nature of the catalytic effect of phenols **40–43** was a matter of considerable interest. In principle, **40–43** could function as weakly acidic catalysts for enolization of **37** to **38**,[20a] the initial step required for cyclization (vide supra). However, no rate acceleration was observed with other weak acids, and catalytic activity did not correlate with phenol acidity.[20b] For example, *p*-nitrophenol (**45**), the most acidic member of the series, had no rate accelerating effect, and phenol (**44**) was only marginally active. In addition, catalytic activity generally increased with increasing substitution by electron-donating groups, a trend which is opposite to that expected for relative acidities (the exception of phenol **47** will be discussed below).[20b] Finally, with stronger acids, such as collidine·TsOH, the reaction of enynones **37** followed a completely different pathway, providing a novel synthesis of highly substituted phenols.[21]

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(16) Sharma, V. K.; Hooshang, S.-Z.; Garnett, P. J. *J. Org. Chem.* **1983**, *48*, 2379.
(17) Levin, J. I.; Turos, E.; Weinreb, S. M. *Synth. Commun.* **1982**, *12*, 989.
(18) Nahm, S.; Weinreb, S. M. *Tetrahedron Lett.* **1981**, *22*, 3815.
(19) In related studies, Dreiding et al. obtained 0% of methylenecyclopentenone **39c** upon gas-phase pyrolysis of **37c** at 700 °C (cf. ref 5).
(20) (a) Lienhard, G. E.; Wang, T.-C. *J. Am. Chem. Soc.* **1969**, *91*, 1146. (b) Rochester, C. H. In *The Chemistry of the Hydroxyl Group*, Part 1; Patai, S., Ed.; John Wiley and Sons: New York, 1981.
(21) Jacobi, P. A.; Zheng, W. *Tetrahedron Lett.* **1991**, *32*, 1279. See also ref 10c, and following papers in this series.

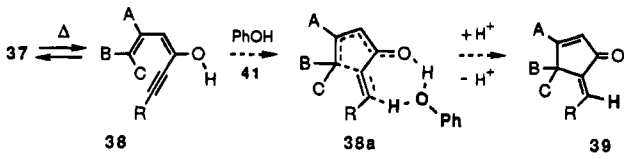



Figure 5.

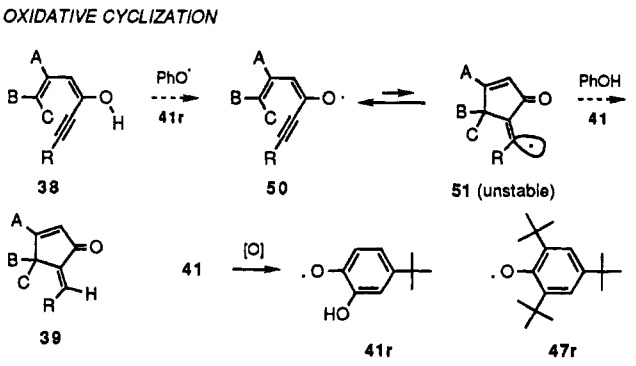



Figure 6.

We also considered the possibility that phenols **40**–**43** might act as "polyfunctional catalysts",[22] by facilitating proton transfer from oxygen in dienols **38** to the terminal sp carbon of the acetylenic bond (cf. **38a**, Figure 5). If this were the case, ring closure to methylenecyclopentenones **39** could take place concurrently with proton transfer. This idea had appeal because many such catalysts are known which can donate and accept a proton in a concerted fashion[22] and models indicate that transition-state structures of type **38a** should be geometrically favorable. However, although the existence of species such as **38a** cannot be ruled out, we were dissuaded by the fact that no catalytic activity was observed with other known catalysts of this class, such as 2-pyridinone (**48**) and 2-pyrrolidinone (**49**). These last two materials function by repeatedly cycling between two tautomeric states, and they are especially active in certain proton-transfer processes.[22]

Finally, we have excluded a mechanism in which *tert*-butylcatechol (**41**) functions as a source of phenoxy radical **41r**, which in principle could initiate an oxidative free radical cyclization via a "site-specific" abstraction of a hydrogen atom from enol **38** (Figure 6).[23] Once formed, enoxy radical **50** could undergo cyclization to the vinyl radical **51**, which upon hydrogen atom abstraction from **41** would give methylenecyclopentenone **39** [a chain propagating step involving **38** and **51** can be ruled out on the basis of the rate dependence of cyclization on the concentration of *tert*-butylcatechol (**41**)[10a,b]]. As precedent for this cyclization, it is well known that enoxy radicals, derived by enol oxidation, can undergo intramolecular additions across carbon–carbon double bonds if the derived carbon radicals are sufficiently stable (2° or 3°).[24]

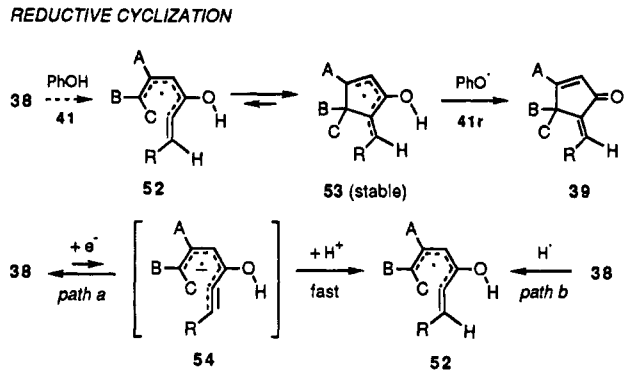



Figure 7.

In the present case, however, one would expect that the equilibrium between enoxy radical **50** and vinyl radical **51** would lie far in the direction of **50**. In any event, no cyclization was ever observed under conditions known to convert **41** to **41r**,[25] including, for example, exposure to a variety of oxidizing reagents[24,25] and also equilibration of **41** with the stable phenoxy radical **47r**.[25a] Interestingly, traces of cyclized product **39d** were obtained upon heating **37d** with excess **47r** under conditions where **47** itself has no catalytic activity. However, the major products in these experiments were those involving decomposition and coupling.[24e]

In comparison to the case of oxidative free radical cyclization described above (Figure 6), radicals of type **52**, derived by *reduction* of enol **38**, should undergo an energetically favorable cyclization to highly stabilized radicals of type **53** (Figure 7). Abstraction of the hydroxyl hydrogen atom by *tert*-butylcatechol radical **41r** would then afford methylenecyclopentenone **39**. Although both the oxidative and reductive mechanisms leading from **38** to **39** invoke the intermediacy of radical species, the difference between these two processes is striking. In particular, cyclization of **50** to **51** involves the cyclization of a relatively stable oxypentadienyl radical to an unstable vinyl radical (cf. Figure 6). As noted above, this transformation is likely to be energetically unfavorable. In contrast, however, cyclization of **52** to **53** transforms a relatively unstable vinylpentadienyl radical to a very stable ketylpentadienyl radical (note that **52** has no ketyl character). This difference in radical stability could provide both a thermodynamic driving force for ring closure and an attractive rationale for the observed rate accelerations.

Radical **52** might be derived from **38** by either of two thermodynamically equivalent processes: electron transfer followed by proton transfer (path a),[26c] or transfer of a hydrogen atom (path b) (Figure 7). Since phenols are well known to function as single electron transfer agents,[26a,b] it was of interest to see if a correlation could be drawn between catalytic activity and oxidation potential. This turned out to be the case for most of the phenols shown in Figure 4, whose oxidation potentials ($E_{1/2}$) were measured under identical conditions of solvent (3 mM $CH_2Cl_2$) and supporting electrolyte (0.125 M $Et_4$-

(22) (a) Rony, P. R. *J. Am. Chem. Soc.* **1969**, *91*, 6090 and references cited therein. (b) Swain, C. G.; Brown, J. F., Jr. *J. Am. Chem. Soc.* **1952**, *74*, 2538.

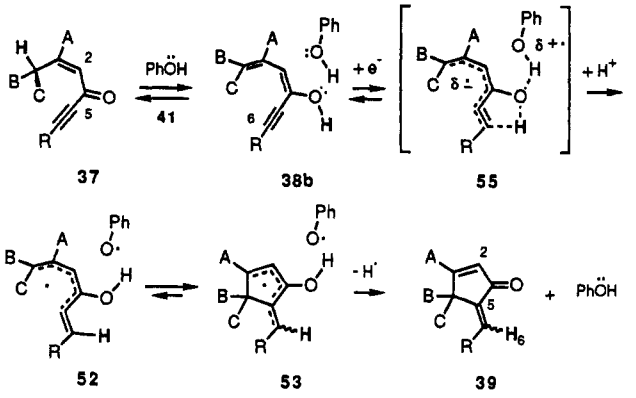
(23) (a) Denisov, E. T.; Khudyakov, I. V. *Chem. Rev.* **1987**, *87*, 1313. (b) Mahoney, L. R.; DaRooge, M. A. *J. Am. Chem. Soc.* **1975**, *97*, 4722

(24) For examples of enoxy radicals adding across carbon–carbon double bonds, see: (a) Snider, B. B.; Mohan, R.; Kates, S. A. *Tetrahedron Lett.* **1987**, *28*, 841. (b) Mohan, R.; Kates, S. A.; Dombroski, M. A.; Snider, B. B. *Ibid.* **1987**, *28*, 845 and references cited therein. (c) Corey, E. J.; Kang, M.-C. *J. Am. Chem. Soc.* **1984**, *106*, 5384. (d) Ernst, A. B.; Fristad, W. E. *Tetrahedron Lett.* **1985**, *26*, 3761. For an example of a phenoxy–enoxy radical coupling, see: (e) Kende, A. S.; Ebetino, F. H; Ohta, T. *Tetrahedron Lett.* **1985**, *26*, 3063.

(25). (a) Mihailovic, M. L.; Cekovic, Z. In *The Chemistry of the Hydroxyl Group*, Part 1; Patai, S., Ed.; John Wiley and Sons: New York, 1981. (b) Musso, H. In *Oxidative Coupling of Phenols*; Battersby, A. R., Taylor, W. I., Eds.; Marcel Dekker: New York, 1967.

(26) (a) Ingold, K. U. *Chem. Rev.* **1961**, *61*, 563. (b) Weinberg, N. L.; Weinberg, H. R. *Chem. Rev.* **1968**, *68*, 449. (c) Lewis, F. D. *Acc. Chem. Res.* **1986**, *19*, 401.

**Scheme 6**




$PF_6$).[27,28] In agreement with an electron-transfer mechanism, the rate of conversion of **37** to **39** varied inversely with the oxidation potential of phenols **40**–**45**, with *p*-nitrophenol (**45**, $E_{1/2}$ = 1.80 V) being totally ineffective and catalytic activity generally increasing with increasing substitution by electron-donating groups.[25] Not surprisingly, phenol **47** and aromatic ether **46** had no effect on reaction rate, even though both of these species are strong electron donors ($E_{1/2}$ = 1.05 and 0.77 V, respectively). With **47**, steric hindrance would undoubtedly hinder electron transfer (vide infra), and **46** lacks the phenolic hydrogen necessary to give radical intermediates of type **52**. Finally, in all cases catalytic activity was either eliminated, or markedly reduced, in the presence of strong electron acceptors such as TCNE.

We believe that these data are best accommodated by the mechanism outlined in Scheme 6, in which enolization of **37** to **38** is followed by single electron reduction. In principle, reduction of **38** via path a should be feasible even if electron transfer is highly endothermic, as long as it is followed by a rapid, and irreversible, proton transfer (cf. Figure 7).[26c] However, we favor a reacting geometry in which electron transfer and proton transfer occur in a synchronous fashion, thereby avoiding the intermediacy of high energy radical-anions of type **54**. One such geometry is the hydrogen-bonded species **38b**, in which electron transfer can take place concurrently with intramolecular proton transfer from the enolic hydroxyl group to C-6. In addition to having obvious entropic advantages, the hydrogen-bonding interaction in **38b** should lower both the LUMO energy of **38** and the oxidation potential of **41**. Decreases in $E_{1/2}$ for **41** on the order of 0.3–0.4 V appear reasonable.[29]

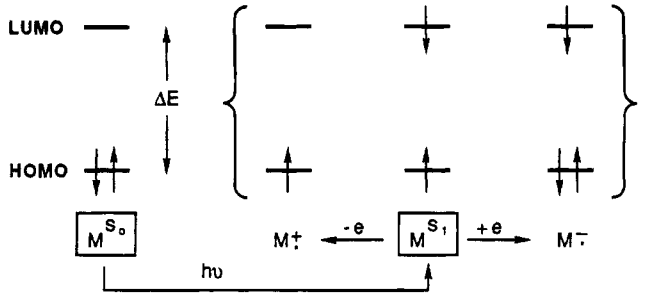



**Figure 8.**

It is important to emphasize that electron/proton transfer in **38b** leads directly to the neutral radical **52**, via transition state **55** which has a minimum of dipolar character. This transition state is in accord with the observation that catalyzed cyclizations are favored in moderately polar, non-hydrogen bonding solvents (reaction is particularly fast in 1,2-dichloroalkanes). Not surprisingly, catalytic activity falls dramatically in polar solvents which disrupt hydrogen bonding. To complete the sequence, cyclization of **52** to **53** is followed by hydrogen atom abstraction, which regenerates **41** and affords mixtures of (*E*)- and (*Z*)-methylenecyclopentenones **39** (in contrast to the concerted process [cf. Scheme 3], bond rotation in **52** will compete with cyclization). It is interesting to note that no molecular reorganization is required throughout the entire cyclization process, since **41** remains properly positioned for both initial electron/proton transfer (**38b** → **55**) and subsequent hydrogen atom abstraction (**53** → **39**).

The electron-transfer pathway finds both theoretical and experimental support in the work of Fox et al.,[30a] who demonstrated that cyclization of certain trienes is dramatically accelerated by reversible single electron reduction. In part this is due to a flattening of the conjugated $\pi$-system, which facilitates orbital overlap of the terminal atoms. Other examples of acceleration of pericyclic reactivity by electroreduction are also known, although the rearranged products are usually obtained in a reduced oxidation level.[30b]

Finally, as supporting evidence, it was of interest to see if the cyclization of **38** to **39** might be further accelerated under conditions of photoassisted electron transfer (PET, Figure 8).[31] This phenomenon takes advantage of the fact that electronic excited-state species of type $M^{S1}$ are both better single electron donors *and* single electron acceptors than the corresponding ground-state species $M^{S0}$ (the excitation energy $\Delta E$ provided by irradiation supplies the thermodynamic driving force for electron transfer.)[31] In particular, $M^{S1}$ is a superior donor to $M^{S0}$ because loss of an electron can occur from a high energy orbital ($M^{S1} \rightarrow M^{+\cdot}$). Conversely, $M^{S1}$ is also a superior acceptor to $M^{S0}$ because it can accept an electron into a ground-state orbital ($M^{S1} \rightarrow M^{-\cdot}$). In principle, it is of little consequence whether vitamin E (**40**) or enols **38** are the photoactive species (both absorb in the region of 300 nm).

In any event, dramatic increases in both rate and yield for cyclization to **39** were in fact observed under PET conditions (Table 1). *Thus, **37d–h** afforded 80–98%*

(27) Although considerable data exists concerning the oxidation potential of phenols,[25,26a,b] most of these potentials have not been measured under standardized conditions of solvent, electrode couple, and supporting electrolyte. In addition, the 1,2-dichlorinated alkane solvents employed for these cyclizations are not common solvents for organic electrochemistry, making the comparison between cyclization rate and reported oxidation potentials even more difficult. Therefore, the oxidation potentials ($E_{1/2}$) for the phenols **40**–**47** which were evaluated as catalysts were measured under identical conditions of solvent (3 mM $CH_2Cl_2$) and supporting electrolyte (0.125 M $Et_4PF_6$), using a Pt working electrode vs an $Ag/AgNO_3$ reference electrode.[28]

(28) We are grateful to Professor Albert J. Fry of this department for assistance with the electrochemical experiments and for many helpful discussions.

(29) Multiphoton ionization photoelectron spectroscopy on hydrogen-bonded phenol in the gas phase has shown that the ionization potential of the donor phenol is lowered by 0.40 eV.[29a,b] This corresponds to a 0.36-V reduction in oxidation potential using the empirically derived relation of Miller et al.[29c] (a) Gonohe, N.; Haruo, A.; Naohiko, M.; Ito, M. *J. Phys. Chem.* **1985**, *89*, 364. (b) Fuke, K.; Yoshiuchi, H.; Kaya, K. *Chem. Phys. Lett.* **1984**, *108*, 179. (c) Miller, L. L.; Nordblom, G. D.; Mayeda, E. A. *J. Org. Chem.* **1972**, *37*, 916.

(30) (a) Fox, M. A.; Hurst, J. R. *J. Am. Chem. Soc.* **1984**, *106*, 7626. (b) See footnote 11 in ref 30a.

(31) For leading references, see: (a) Mariano, P. S. *Acc. Chem. Res.* **1983**, *16*, 130. (b) Gassman, P. G.; Bottorff, K. J. *J. Am. Chem. Soc.* **1987**, *109*, 7547; *J. Org. Chem.* **1988**, *53*, 1097. See also ref 26c.

*yields of the corresponding methylenecyclopentenones* ***39d–h*** *upon photolysis at 300 nm/200 °C in the presence of vitamin E (**40**) (conditions VIII).* Control experiments, involving photolysis at 200 °C in the absence of **40**, gave only trace amounts of **39** under otherwise identical conditions (conditions VII). Also, no reaction was observed upon photolysis of **37d–h** at ambient temperature in the presence of **40**. This last observation lends further support to the intermediacy of enols **38d–h**, which are only generated at elevated temperatures (cf. Scheme 3).

We believe that the work described in this paper opens important new opportunities for the synthesis of methylenecyclopentenones and related materials. In the paper which follows,[32] we describe some additional studies of substituent effects on reaction rate and also the application of this methodology to the synthesis of four of the most important members of the methylenomycin class of antibiotics.

## 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.

**6-Methyl-7-(5-oxazolyl)-α,α-di-1-propynyl-1,4-dioxaspiro[4.4]non-7-ene-6-methanol (5).** A stream of propyne gas was bubbled through a solution consisting of 1.50 mL (3.00 mmol, 1.84 equiv) of 2.00 N ethylmagnesium bromide/ether in 40.0 mL of THF at rt for 15 min. At the end of this period, stirring was continued for 1 min and the resulting solution of 1-propynylmagnesium bromide was then treated with a solution of 432 mg (1.63 mmol, 1.00 equiv) of 6-carbomethoxy-6-methyl-7-(5-oxazolyl)-1,4-dioxaspiro[4.4]non-7-ene[1a] in 7 mL of THF in a dropwise fashion with efficient stirring. The resulting pale yellow solution was allowed to stir at rt for 4 h and was then poured into a mixture of 100 mL of pH 7 buffer solution and 40 mL of $CH_2Cl_2$. The layers were separated and the aqueous layer was extracted with 3 × 40 mL of $CH_2Cl_2$. The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure, and the crude product was triturated with ether. The residue was recrystallized from ether to give 410 mg (80%) of **5** as a pale yellow crystalline solid, mp 156–7 °C ($R_f$ 0.43, silica gel, $Et_2O$): MS *m/e* 313 ($M^+$); IR (KBr) 3420 (br), 2910, 2235 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) δ 1.53 (s, 3H), 1.72 (s, 3H), 1.75 (s, 3H), 2.29 (dd, *J* = 4.0, 17.5 Hz, 1H), 3.08 (dd, *J* = 2.5, 17.5 Hz, 1H), 4.03 (m, 4H), 6.36 (dd, *J* = 2.50, 4.0 Hz, 1H), 7.10 (s, 1H), 7.75 (s, 1H). Anal. Calcd for $C_{18}H_{19}O_4N$: C, 68.99; H, 6.11; N, 4.47. Found: C, 68.79; H, 5.86; N, 4.30.

**6-[9-Methyl-8-(5-oxazolyl)-1,4-dioxaspiro[4.4]non-8-en-7-yl]-2-hepten-5-yn-4-one (6).** A mixture of 101 mg (0.32 mmol) of **5** and 3.00 mg of hydroquinone in 15 mL of dry, degassed toluene was heated at reflux for 14 h under an inert atmosphere. At the end of this period, the reaction mixture was cooled to rt and concentrated under reduced pressure and the crude product purified by preparative TLC (silica gel, $Et_2O$) to afford 28.0 mg (28%) of **6-Z** (pale yellow oil) and 61.0 mg (61%) of **6-E** (amorphous solid). **6-Z**: MS *m/e* 313 ($M^+$); IR ($CHCl_3$) 2222, 1645, 1601 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) δ 1.64 (s, 3H), 1.78 (dd, *J* = 3.0, 14.0 Hz, 1H), 1.94 (s, 3H), 1.99 (s, 3H), 2.52 (dd, *J* = 9.0, 14.0 Hz, 1H), 4.01 (m, 4H), 5.25 (m, 1H), 6.17 (br, 1H), 7.04 (s, 1H), 7.84 (s, 1H). **6-E**: MS *m/e* 313 ($M^+$); IR ($CHCl_3$) 2222, 1650, 1603, 1493 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) δ 1.88 (dd, *J* = 3.0, 14.0 Hz, 1H), 1.94 (s, 3H), 1.96 (s, 3H), 1.99 (s, 3H), 2.38 (dd, *J* = 9.0, 14.0 Hz, 1H), 3.63 (m, 4H), 3.99 (m, 4H), 6.21 (s, 1H), 7.03 (s, 1H), 8.03 (s, 1H).

**8-Ethylidene-11,13-dimethyl-12-(5-oxazolyl)-1,4-dioxadispiro[4.1.4.2]trideca-10,12-dien-9-one (8).** A solution of 101 mg (0.32 mmol) of **5** and 6.50 mg of hydroquinone in 10.0 mL of dry degassed mesitylene was heated at reflux for 3 h. At the end of this period, the reaction mixture was cooled to rt and was concentrated under reduced pressure and the crude product was purified by preparative TLC to afford 21.0 mg (21%) of **8-Z** ($R_f$ 0.44, silica gel, $Et_2O$), 20.0 mg (20%) of **8-E** ($R_f$ 0.39, silica gel, $Et_2O$), and 55.0 mg (55%) of **6-E** (alternatively, **8-E,Z** were formed in 80–90% yield upon thermolysis of **6-Z** in refluxing toluene). **8-Z**: MS *m/e* 313 ($M^+$); IR ($CHCl_3$) 1690, 1649, 1616 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) δ 1.84 (d, *J* = 1.1 Hz, 3H), 1.98 (s, 3H), 2.12 (d, *J* = 8.0 Hz, 3H), 2.14 (d, *J* = 14.0 Hz, 1H), 2.29 (d, *J* = 14.0 Hz, 1H), 4.01 (m, 4H), 6.04 (q, *J* = 8.0 Hz, 1H), 6.11 (q, *J* = 1.0 Hz, 1H), 6.84 (s, 1H), 7.78 (s, 1H). **8-E**: mp 130–1 °C; MS *m/e* 313 ($M^+$); IR ($CHCl_3$) 1696, 1654, 1616 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) δ 1.68 (d, *J* = 8.0 Hz, 3H), 1.90 (d, *J* = 1.0 Hz, 3H), 2.00 (s, 3H), 2.27 (d, *J* = 15.0 Hz, 1H), 2.47 (d, *J* = 15.0 Hz, 1H), 4.09 (m, 4H), 6.13 (br s, 1H), 6.56 (q, *J* = 8.0 Hz, 1H), 6.85 (s, 1H), 7.78 (s, 1H). The peaks at δ 1.68, 1.90, and 6.13 collapsed to singlets upon irradiation at δ 6.56, 6.13, and 1.68, respectively. Anal. Calcd for $C_{18}H_{19}O_4N$: C, 68.99; H, 6.11; N, 4.46. Found: C, 68.25; H, 6.07; N, 4.20.

**Preparation of Cycloalkenylalkadiynyl Carbinols 29a–d,f: General Procedure.** A solution of 1.43 mmol of triphenylmethane in 100 mL of THF at −78 °C was treated with 2.5 M *n*-butyllithium in hexanes (60.0 mmol, 3.00 equiv) to afford a pink solution. An appropriate alkyne gas was bubbled through the resulting pink solution until the pink color was discharged. Stirring was continued for an additional 5 min at −78 °C, and then a solution of the known 2-cycloalkenyl 1-carboxylates **27a–d**[14] (60.0 mmol, 3.00 equiv) in 50 mL of THF was added to the stirring colorless solution in a dropwise fashion. After addition was complete, the reaction mixture was allowed to warm to rt and was then stirred for an additional 1 h. At the end of this period, the reaction mixture was diluted with 200 mL of brine. The layers were separated and the aqueous layer was extracted with 3 × 100 mL of $CH_2Cl_2$. The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure, and the crude product was chromatographed (silica gel) to afford the carbinols **29a–d,f**.

**α,α-Di-1-propynyl-2-cyclopentene-1-methanol (29a).** This material was prepared in 61% yield from 2.52 g (20.0 mmol) of carboxylate **27a** and propyne gas following the general procedure described above. Purification by chromatography (silica gel, 20% EtOAc/hexanes, $R_f$ 0.49), followed by recrystallization from petroleum ether, gave 2.13 g of **29a** as colorless crystals, mp 46 °C: IR ($CHCl_3$) 3594, 2924, 2263, 2246 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 1.9 (s, 6H), 1.80–2.50 (m, 5H), 3.19 (br m, 1H), 5.79 (m, 1H), 5.99 (m, 1H); $^{13}$C NMR (400 MHz, $CDCl_3$) 3.20, 3.50, 24.9, 32.4, 58.5, 79.4, 79.5, 79.7, 129.6, 134.1. Anal. Calcd for $C_{12}H_{14}O$: C, 82.70; H, 8.11. Found: C, 82.47; H, 8.15.

(32) Jacobi, P. A.; Brielmann, H. L.; Cann, R. O. *J. Org. Chem.*, following paper in this issue.

**α,α-Di-1-propynyl-1-methyl-2-cyclopentene-1-methanol (29b).** This material was prepared in 58% yield from 3.38 g (24.0 mmol) of carboxylate **27b** and propyne gas following the general procedure described above. Purification by chromatography (silica gel, 20% EtOAc/hexanes, $R_f$ 0.6) gave 2.66 g of **29b** as a pale yellow oil: MS *m/e* 173 ($M^+$ − 15 [$CH_3$]); IR ($CHCl_3$) 3500, 3050, 2975, 2225 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 1.30 (s, 3H), 1.55 (m, 2H), 1.85 (s, 6H), 2.35 (m, 3H), 5.65 (m, 1H), 5.88 (m, 1H). Anal. Calcd for $C_{13}H_{16}O$: C, 82.92; H, 8.58. Found: C, 82.82; H, 8.61.

**α,α-Di-1-propynyl-2-cyclohexene-1-methanol (29c).** This material was prepared in 28% yield from 2.30 g (16.0 mmol) of carboxylate **27c** and propyne gas following the general procedure described above. Purification by chromatography (silica gel, 100% hexanes to 10% EtOAc/hexanes, $R_f$ 0.57) gave **29b** as a pale yellow oil: MS *m/e* 173 ($M^+$ − 15 [$CH_3$]); IR ($CHCl_3$) 3600, 2920, 2850, 2225 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 1.85 (s, 6H), 1.50–2.00 (m, 6H), 2.50 (m, 1H), 5.90 (m, 2H); exact mass calcd for ($C_{13}H_{16}O$) 188.1202, found 189.1280 ($M^+$ + 1).

**α,α-Di-1-propynyl-1-methyl-2-cyclohexene-1-methanol (29d).** This material was prepared in 84% yield from 6.29 g (41.0 mmol) of carboxylate **27d** and propyne gas following the general procedure described above. Purification by chromatography (silica gel, 20% EtOAc/hexanes, $R_f$ 0.62) gave 6.91 g of **29d** as colorless crystals, mp 64–5 °C: MS *m/e* 187 ($M^+$ − 15 [$CH_3$]); IR ($CHCl_3$) 3597, 3020, 2939, 2260 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 1.20 (s, 3H), 1.60–2.00 (m, 6H), 1.90 (s, 6H), 2.27 (br, 1H), 5.77 (d, 1H), 5.90 (m, 1H). Anal. Calcd for $C_{14}H_{18}O$: C, 83.10; H, 8.98. Found: C, 83.17; H, 9.06.

**α,α-Di-1-ethynyl-2-cyclopentene-1-methanol (29f).** This material was prepared in 56% yield from 6.3 g (50.0 mmol) of carboxylate **27a** and acetylene gas following the general procedure described above. Purification by chromatography (silica gel, 20% EtOAc/hexanes, $R_f$ 0.45), followed by recrystallization from hexanes gave 4.07 g of **29f** as a white amorphous powder: MS *m/e* 146 ($M^+$); IR ($CHCl_3$) 3588, 3307, 2950, 2255, 2120 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 2.05 (m, 2H), 2.35 (m, 1H), 2.50 (m, 1H), 2.55 (s, 2H), 3.30 (m, 1H), 5.80 (m, 1H), 6.00 (m, 1H). Anal. Calcd for $C_{10}H_{10}O$: C, 82.15; H, 6.91. Found: C, 82.06; H, 6.90.

**α,α-Bis(phenylethynyl)-2-cyclohexene-1-methanol (29e).** A stirring solution of 3.30 mL (30.0 mmol, 3.00 equiv) of phenylacetylene in 80.0 mL of THF was cooled to −78 °C and slowly treated with 12.0 mL (30.0 mmol, 3.00 equiv) of 2.50 M *n*-butyllithium in hexanes. The resulting solution of 1-lithio-2-phenylacetylide was stirred at −78 °C for 15 min and was then treated dropwise with a solution of 1.26 g (10.0 mmol, 1.00 equiv) of carboxylate **27a** in 20 mL of THF. After addition was complete, stirring was continued at −78 °C for 1.5 h and the reaction mixture was then poured into 100 mL of brine. The layers were separated and the aqueous layer was extracted with 3 × 100 mL of $CH_2Cl_2$. The combined organic extracts were dried ($Na_2SO_4$) and concentrated under reduced pressure, and the crude product was chromatographed (silica gel, 20% EtOAc/hexanes, $R_f$ 0.56) to afford 2.77 g (93%) of carbinol **29e** as a yellow oil: MS *m/e* 298 ($M^+$); IR ($CHCl_3$) 3588, 3040, 2949, 2229, 1600 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 2.10–2.40 (m, 4H), 3.40 (br m, 1H), 5.85 (m, 1H), 6.00 (m, 1H), 7.70 (m, 6H); 7.45 (m, 4H); exact mass calcd for $C_{22}H_{18}O$ 298.1358, found 298.1359.

**Preparation of Spirocyclic Methylenecyclopentenones 18a–e: General Procedure. Method A.** A solution of 0.58 mmol of carbinol **29** in 10 mL of dry toluene was transferred by syringe to a Pyrex tube which had previously been washed, rinsed with saturated $NaHCO_3$ solution, followed by distilled water, and dried at 150 °C overnight. The reaction mixture was degassed by freezing the tube under reduced pressure (0.25 mmHg) in a liquid nitrogen bath for 5 min, closing the stopcock, and then allowing the reaction mixture to warm to rt. The freeze–thaw process was repeated five times. The tube was then cooled under vacuum as before and sealed with an oxygen/propane gas torch. The sealed tube was allowed to warm to rt and was then heated in a preheated oven at 250 °C for 12–15 h. At the end of this period, the tube was carefully removed from the oven, allowed to cool to rt, frozen in a liquid nitrogen bath, and opened by touching a white-hot glass rod to an etched area of the tube. After the reaction mixture had warmed to rt, the contents were transferred to a flask and the solution was concentrated to dryness under reduced pressure. The residue was chromatographed to afford the methylenecyclopentenones **18a–e** and the enynones **30-E**.

**Method B (Catalysis by TBC).** A mixture of 0.13 mmol (1.00 equiv) of carbinol **29** and 24.0 mg (0.14 mmol, 1.10 equiv) of *tert*-butylcatechol (TBC) in 6 mL of dry toluene was transferred by syringe to a Pyrex tube which had previously been washed and dried as described in method A above. The reaction mixture was degassed and sealed as in method A and heated at 225 °C for 4–12 h. The reaction mixture was then transferred to a separatory funnel and washed with 2 × 5 mL of 1 M NaOH solution to remove TBC. The organic layer was dried ($MgSO_4$), concentrated to dryness, and purified by preparative TLC (1000 μm) to afford the methylenecyclopentenones **18a–e**.

**1-Ethylidene-4-methylspiro[4.4]nona-3,6-dien-2-one (18a).** This material was prepared in 43% yield from 100 mg (0.58 mmol) of carbinol **29a** by method A described above and in 81% yield following method B. Purification by preparative TLC (silica gel, 20% EtOAc/hexanes) gave **18a** as a 1:1 (*E:Z*) isomeric mixture. **18a-E**: pale yellow crystals (from hexanes), mp 30–1 °C; $R_f$ 0.32; MS *m/e* 174 ($M^+$); IR ($CHCl_3$) 1691, 1650 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) δ 1.75 (d, $J$ = 7.6 Hz, 3H), 1.91 (d, $J$ = 1.6 Hz, 3H), 2.06 (m, 2H), 2.60 (m, 2H), 5.27 (dt, $J$ = 6.0, 14.0 Hz, 1H), 5.97 (m, 2H), 6.55 (q, $J$ = 7.6 Hz, 1H). **18a-Z**: yellow oil; $R_f$ 0.53; MS *m/e* 174 ($M^+$); IR ($CHCl_3$) 1688, 1645 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) δ 1.91 (s, 3H), 2.08 (m, 2H), 2.17 (d, $J$ = 7.2 Hz, 3H), 2.51 (m, 2H), 5.25 (m, 1H), 5.89 (q, $J$ = 7.2 Hz, 1H), 5.99 (m, 2H). Anal. Calcd for $C_{12}H_{14}O$: C, 82.70; H, 8.11. Found: C, 82.72; H, 8.15.

**1-Ethylidene-4,7-dimethylspiro[4.4]nona-3,6-dien-2-one (18b).** This material was prepared in 79% yield from 39.0 mg (0.21 mmol) of carbinol **29b** by method B described above and in 37% yield following method A. Purification by preparative TLC (silica gel, 20% EtOAc/hexanes) gave **18b** as a 1:2 (*E:Z*) isomeric mixture. **18b-E**: yellow oil; $R_f$ 0.39; MS *m/e* 188 ($M^+$); IR ($CHCl_3$) 1684, 1641, 1612 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) δ 1.74 (d, $J$ = 7.60 Hz, 3H), 1.88 (d, $J$ = 1.20 Hz, 3H), 1.92 (br, 3H), 1.98–2.31 (m, 2H), 2.50 (m, 2H), 4.89 (br, 1H), 5.95 (br, 1H), 6.52 (q, $J$ = 7.60 Hz, 1H). Anal. Calcd for $C_{13}H_{16}O$: C, 82.92; H, 8.58. Found: C, 83.00; H, 8.58. **18b-Z**: yellow oil; $R_f$ 0.57. MS *m/e* 188 ($M^+$); IR ($CHCl_3$) 1688, 1648, 1608 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) δ 1.78

(d, $J$ = 1.50 Hz, 3H), 1.87 (d, $J$ = 1.60 Hz, 3H), 1.94–2.12 (m, 2H), 2.15 (d, $J$ = 7.20 Hz, 3H), 2.39 (m, 2H), 4.86 (q, $J$ = 1.50 Hz, 1H), 5.87 (q, $J$ = 7.20 Hz, 1H), 5.91 (br, 1H).

**1-Ethylidene-4-methylspiro[4.5]deca-3,6-dien-2-one (18c).** This material was prepared in 55% yield from 20 mg (0.11 mmol) of carbinol **29c** by method B described above and in 18% yield following method A. Purification by preparative TLC (silica gel, 20% EtOAc/hexanes) gave **18c** as a 1:1 (*E*:*Z*) isomeric mixture. **18c-E**: yellow oil; $R_f$ 0.41; MS $m/e$ 188 ($M^+$); IR ($CHCl_3$) 1688, 1683, 1645 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$ 1.76 (m, 2H), 1.83 (d, $J$ = 8.00 Hz, 3H), 1.88–2.24 (m, 4H), 2.03 (s, 3H), 5.20 (d, 1H), 6.02 (s, 1H), 6.05 (m, 1H), 6.53 (q, $J$ = 8.00 Hz, 1H); exact mass calcd for $C_{13}H_{16}O$ 188.1202, found 189.1281 (M + 1). **18c-Z**: yellow oil; $R_f$ 0.61; MS $m/e$ 188 ($M^+$); IR ($CHCl_3$) 1685, 1641 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$ 1.74 (m, 2H), 1.96 (s, 3H), 2.14 (m, 4H), 2.18 (d, $J$ = 8.00 Hz, 3H), 5.20 (d, 1H), 5.97 (q, $J$ = 8.00 Hz, 1H), 6.02 (m, 2H).

**1-Ethylidene-4,7-dimethylspiro[4.5]deca-3,6-dien-2-one (18d).** This material was prepared in 29% yield from 145 mg (0.72 mmol) of carbinol **29d** by method A described above and in 66% yield following method B. Purification by preparative TLC (silica gel, 20% EtOAc/hexanes) gave **18d** as a 1:1 (*E*:*Z*) isomeric mixture. **18d-E**: yellow oil; $R_f$ 0.40; MS $m/e$ 202 ($M^+$); IR ($CHCl_3$) 1696, 1651, 1611 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$ 1.70 (s, 3H), 1.65–1.86 (m, 6H), 1.74 (d, $J$ = 8.00 Hz, 3H), 2.00 (s, 3H), 4.91 (s, 1H), 5.96 (s, 1H), 6.48 (q, $J$ = 8.00 Hz, 1H); exact mass calcd for $C_{14}H_{18}O$ 202.1358, found 202.1347). **18d-Z**: yellow oil; $R_f$ 0.60; MS $m/e$ 202 ($M^+$); IR ($CHCl_3$) 1690, 1644, 1613 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$ 1.30–2.01 (m, 6H), 1.69 (s, 3H), 1.91 (s, 3H), 2.14 (d, $J$ = 8.0 Hz, 3H), 4.88 (br s, 1H), 5.90 (q, $J$ = 8.0 Hz, 1H), 5.97 (s, 1H).

**4-Phenyl-1-(phenylmethylene)spiro[4.4]nona-3,6-dien-2-one (18e).** This material was prepared in 70% yield from 39.0 mg (0.13 mmol) of carbinol **29e** by method B described above and in 9% yield following method A. Purification by preparative TLC (silica gel, 20% EtOAc/hexanes) gave **18e** as a 4:3 (*E*:*Z*) isomeric mixture. **18e-E**: colorless solid, mp 121–23 °C; $R_f$ 0.49; MS $m/e$ 298 ($M^+$); IR ($CHCl_3$) 3061, 2912, 1675, 1625 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 2.10 (m, 1H), 2.25 (m, 1H), 2.30 (m, 2H), 5.75 (m, 1H), 6.00 (m, 1H), 6.50 (s, 1H), 7.35 (m, 6H), 7.50 (m, 4H), 7.55 (s, 1H); exact mass calcd for $C_{22}H_{18}O$ 298.1358, found 298.1359. **18e-Z**: yellow oil; $R_f$ 0.60; MS $m/e$ 298 ($M^+$); IR ($CHCl_3$) 3020, 1678, 1620 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 2.20 (m, 1H), 2.40 (m, 1H), 2.70 (m, 2H), 5.80 (m, 1H), 6.20 (m, 1H), 6.60 (s, 1H), 6.70 (s, 1H), 7.40 (m, 6H), 7.70 (m, 2H), 8.05 (m, 2H).

**2-(2-Cyclopenten-1-yl)-2-hepten-4-yn-3-one (30a-E).** This material was obtained in 25% yield as a byproduct from the cyclization of 100 mg (0.58 mmol) of carbinol **29a** following method A described above: yellow oil; $R_f$ 0.65 (silica gel, 20% EtOAc/hexanes); MS $m/e$ 174 ($M^+$); IR ($CHCl_3$) 2221, 1667, 1599 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$ 1.98 (s, 3H), 2.14 (d, $J$ = 1.2 Hz, 3H), 2.20 (m, 2H), 2.36 (m, 2H), 3.35 (m, 1H), 5.55 (m, 1H), 5.89 (m, 1H), 6.09 (br m, 1H); exact mass calcd for $C_{12}H_{14}O$ 174.1045, found 174.1049.

**2-(3-Methyl-2-cyclopenten-1-yl)-2-hepten-5-yn-4-one (30b-E).** This material was obtained in 14% yield as a byproduct from the cyclization of 100 mg (0.53 mmol) of carbinol **29b** following method A described above: yellow oil; $R_f$ 0.60 (silica gel, 20% EtOAc/hexanes); MS $m/e$ 188 ($M^+$); IR ($CHCl_3$) 2220, 1669, 1651, 1605 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$ 1.57–1.70 (m, 2H), 1.75 (br s, 3H), 1.98 (s, 3H), 2.10 (br s, 3H), 2.24 (m, 2H), 3.34 (m, 1H), 5.15 (br s, 1H), 6.09 (br s, 1H); exact mass calcd for $C_{13}H_{16}O$ 188.1202, found 188.1202.

**2-(2-Cyclohexen-1-yl)-2-hepten-5-yn-4-one (30c-E).** This material was obtained in 10% yield as a byproduct from the cyclization of 100 mg (0.53 mmol) of carbinol **29c** following method A described above: yellow oil; $R_f$ 0.63 (silica gel, 20% EtOAc/hexanes); MS $m/e$ 188 ($M^+$); IR ($CHCl_3$) 2215, 1687, 1650 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$ 1.42–1.97 (m, 6H), 1.96 (s, 3H), 2.16 (br s, 3H), 2.83 (br s, 1H), 5.49 (m, 1H), 5.87 (m, 1H), 6.12 (br s, 1H); exact mass calcd for $C_{13}H_{16}O$ 188.1202, found 189.1278 (M + 1).

**2-(3-Methyl-2-cyclohexen-1-yl)-2-hepten-5-yn-4-one (30d-E).** This material was obtained in 17% yield as a byproduct from the cyclization of 145 mg (0.72 mmol) of carbinol **29d** following method A described above: yellow oil; $R_f$ 0.67 (silica gel, 20% EtOAc/hexanes); MS $m/e$ 202 ($M^+$); IR ($CHCl_3$) 2219, 1669, 1650, 1605 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$ 1.42–1.99 (m, 6H), 1.70 (s, 3H), 2.00 (s, 3H), 2.18 (s, 3H), 2.82 (m, 1H), 5.22 (br s, 1H), 6.12 (br s, 1H); exact mass calcd for $C_{14}H_{18}O$ 202.1358, found 203.1437 (M + 1).

**Preparation of Acrylic Esters 33: General Procedure.** A solution consisting of 0.57 mol (1.10 equiv) of 10.0 M *n*-butyllithium/hexanes in 400 mL of dry $Et_2O$ was cooled to −20 °C under nitrogen and treated with 0.57 mol (1.10 equiv) of trimethyl phosphonoacetate in 50 mL of dry $Et_2O$. After 20 min of stirring, the resulting mixture was treated with 1.0 mol (1.90 equiv) of HMPA, followed by dropwise addition of 0.52 mol (1.00 equiv) of freshly distilled disubstituted ketone **31a–g** in 50 mL of dry $Et_2O$. The cooling bath was allowed to evaporate and the reaction mixture was stirred at room temperature until no change in the ratio of product to starting material was detected by GC (~40–50 h). The reaction mixture was then poured into 500 mL of water, the phases were separated, and the aqueous phase was extracted with 3 × 100 mL of $Et_2O$. The combined organic phases were washed with 500 mL of 1 N HCl, followed by 500 mL of brine, and then dried over anhydrous $MgSO_4$. The crude oil obtained by carefully concentrating the extracts under reduced pressure at room temperature was flash chromatographed (silica gel) to afford **33a–g**.

**4-Phenyl-3-(phenylmethyl)-2-butenoic Acid, Methyl Ester (33a).** This material was prepared in 100% yield from 25.0 g (120 mmol) of diphenylacetone (**31a**) by the procedure described above. Purification by chromatography (silica gel, 100% hexanes to 5% $Et_2O$/hexanes) gave 32.0 g of **33a** as a colorless oil, bp 175 −8 °C (0.33 mm), $R_f$ 0.54 (10% EtOAc/hexanes) (note that **33a** = **33b**): IR ($CHCl_3$) 1714, 1648 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 3.36 (s, 2H), 3.74 (s, 3H), 4.03 (s, 2H), 5.77 (br s, 1H), 7.10–7.20 (m, 10H).

**3-Ethyl-2-pentenoic Acid, Methyl Ester (33d).** This material was prepared in 91% yield from 44.9 g of 3-pentanone (**31d**) by the procedure described above. Purification by chromatography (silica gel, 2.5% $Et_2O$/hexanes) gave 67.2 g of **33d** as a pale yellow oil, bp 29 °C (0.85 mm), $R_f$ 0.36 (5% $Et_2O$/pentanes) (note that **33d** = **33e**): MS $m/e$ 142 ($M^+$); IR ($CHCl_3$) 3015, 1708, 1647 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.01 (t, $J$ = 7.3 Hz, 3H), 1.02 (t, $J$ = 7.6 Hz, 3H), 2.15 (q, $J$ = 7.3 Hz, 2H),

2.57 (q, $J$ = 7.6 Hz, 2H), 3.64 (s, 3H), 5.57 (s, 1H). Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.33; H, 9.89.

**3-Propyl-2-hexenoic Acid, Methyl Ester (33f).** This material was prepared in 93% yield from 25.9 g of 4-heptanone (**31f**) by the procedure described above. Purification by chromatography (silica gel, 2.5% $Et_2O$/hexanes) afforded 35.9 g of **33f** as a pale yellow oil, bp 108–9 °C (37 mm), $R_f$ 0.51 (10% $Et_2O$/hexanes): MS $m/e$ 170 ($M^+$); IR ($CHCl_3$) 1715, 1632 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 0.90 (t, $J$ = 7.30 Hz, 3H), 0.93 (t, $J$ = 7.30 Hz, 3H), 1.45–1.48 (m, 4H), 2.10 (t, $J$ = 7.50 Hz, 2H), 2.55 (t, $J$ = 7.90 Hz, 2H), 3.66 (s, 3H), 5.61 (s, 1H). Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.65. Found: C, 70.60; H, 10.67.

**3-Butyl-2-heptenoic Acid, Methyl Ester (33g).** This material was prepared in 78% yield from 25.9 g of dibutyl ketone **31g** by the procedure described above. Purification by distillation under reduced pressure gave 35.1 g of **33g** as a pale yellow oil, bp 140 °C (37 mm), $R_f$ 0.58 (5% EtOAc/hexanes): MS $m/e$ 198 ($M^+$); IR ($CHCl_3$) 1710, 1641 $cm^{-1}$; $^1H$ NMR (400 Hz, $CDCl_3$) $\delta$ 0.87–0.92 (m, 6H), 1.26–1.48 (m, 8H), 2.12 (t, $J$ = 7.60 Hz, 2H), 2.58 (t, $J$ = 7.60 Hz, 2H), 3.66 (s, 3H), 5.60 (s, 1H). Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.71; H, 11.16.

**4-Methyl-3-(1-methylethyl)-2-pentenoic Acid, Ethyl Ester (33h).** A solution of 10.0 g (121 mmol, 1.30 equiv) of ethoxyacetylene in 100 mL of dry THF at −78 °C under a nitrogen atmosphere was treated with 37.2 mL (93.1 mmol, 1.0 equiv) of 2.50 M $n$-butyllithium in hexanes over a 10-min period. The solution was stirred for an additional 2 h at −78 °C, during which the color of the solution changed from orange to brown. At the end of this period, a solution of 10.6 g (93.1 mmol, 1.0 equiv) of freshly distilled 2,4-dimethyl-3-pentanone (**31h**) in 20 mL of dry THF was added to the mixture in a dropwise fashion. After addition was complete, the reaction mixture was allowed to warm to rt. After being stirred at rt for 3.5 h, the reaction mixture was poured into 300 mL of a 10% aqueous $H_2SO_4$ solution and stirred at rt for an additional 12 h. At the end of this period, the phases were separated and the aqueous phase was extracted with 3 × 100 mL of $Et_2O$. The combined organic extracts were washed sequentially with 2 × 250 mL of water, 250 mL of saturated $NaHCO_3$ solution, and 250 mL brine and then dried over anhydrous $MgSO_4$. The crude product obtained after carefully concentrating the dried extracts under reduced pressure at rt was chromatographed (silica gel, 1–5% $Et_2O$/hexanes) to afford 7.21 g (43%) of **33h** as a yellow oil, bp 120–2 °C, $R_f$ 0.48 (10% EtOAc/hexanes): MS $m/e$ 184 ($M^+$); IR ($CHCl_3$), 1706, 1639, 1148 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.04 (d, $J$ = 6.7 Hz, 6H), 1.05 (d, $J$ = 7.0 Hz, 6H), 1.26 (t, $J$ = 7.3 Hz, 3H), 2.52 (septet, $J$ = 6.7 Hz, 1H), 4.03 (septet, $J$ = 7.0 Hz, 1H), 4.11 (q, $J$ = 7.3 Hz, 2H), 5.62 (s, 1H). Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.10; H, 10.94. Found: C, 71.76; H, 11.01.

**Preparation of Weinreb Amides 36a–h: General Procedure.** A suspension of 200 mmol (2.5 equiv) of *N,O*-dimethylhydroxylamine hydrochloride in 100 mL of dry benzene was cooled to 0 °C under nitrogen and was treated in a dropwise fashion with 200 mmol (2.5 equiv) of 2.0 M trimethylaluminum in toluene over a period of 15 min. After addition was complete, the cooling bath was removed, the solution was allowed to warm to rt, and stirring was continued at rt for 1 h. At the end of this period, the resulting chloroaluminum amide reagent **35** was diluted with 40 mL of dry benzene and then treated dropwise with a solution of 80.3 mmol (1.0 equiv) of ester **33a–h** in 400 mL of dry benzene. The reaction mixture was stirred at rt for 24–44 h and was then carefully poured into 1 L of an ice-cold 0.50 M aqueous HCl solution. The phases were separated and the aqueous phase was extracted with 3 × 100 mL of $Et_2O$. The combined organic phases were washed with brine and dried over anhydrous $Na_2SO_4$. The crude yellow oil obtained after removing the solvent under reduced pressure was flash chromatographed (silica gel) to afford **36a–h**.

***N*-Methoxy-*N*-methyl-4-phenyl-3-(phenylmethyl)-2-butenamide (36a).** This material was prepared in 59% yield from 24.0 g of ester **33a** by the procedure described above. Purification by chromatography (silica gel, 4% EtOAc/hexanes) gave 15.7 g of **36a** as a pale yellow oil, $R_f$ 0.10 (15% EtOAc/hexanes) (note that **36a** = **36b**): $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$ 3.24 (s, 3H), 3,37 (s, 2H), 3.62 (s, 3H), 3.98 (s, 2H), 6.20 (br s, 1H), 7.12–7.18 (m, 10H).

***N*-Methoxy-*N*,3-dimethyl-2-butenamide (36c).** This material was prepared in 83% yield from 7.65 g of 3-methyl-2-butenoyl chloride and 6.8 g (1.1 equiv) of *N,O*-dimethylhydroxylamine hydrochloride by a modification of the procedure described above. Purification by distillation under reduced pressure (108 °C, 28 mm) gave 7.66 g of **36c** as a pale yellow oil, $R_f$ 0.54 (50% EtOAc/hexanes): $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$ 1.83 (s, 3H), 2.06 (s, 3H), 3.12 (s, 3H), 3.60 (s, 3H), 6.05 (s, 1H).

**3-Ethyl-*N*-methoxy-*N*-methyl-2-pentenamide (36d).** This material was prepared in 68% yield from 11.4 g of ester **33d** by the procedure described above. Purification by chromatography (silica gel, 25% $Et_2O$/hexanes) gave 9.3 g of **36d** as a pale yellow oil, bp 47 °C (0.025 mm), $R_f$ 0.21 (note that **36d** = **36e**): MS $m/e$ 171 ($M^+$); IR ($CHCl_3$) 3023, 1651, 1625 $cm^{-1}$; $^1H$ NMR (400 Hz, $CDCl_3$) $\delta$ 1.07 (t, $J$ = 7.4 Hz, 3H), 1.08 (t, $J$ = 7.6 Hz, 3H), 2.17 (q, $J$ = 7.4 Hz, 2H), 2.55 (q, $J$ = 7.6 Hz, 2H), 3.18 (s, 3H), 3.64 (s, 3H), 6.02 (br s, 1H). Anal. Calcd for $C_9H_{17}NO_2$: C, 63.13; H, 10.01; N, 8.08. Found: C, 62.98; H, 9.97; N, 8.08.

***N*-Methoxy-*N*-methyl-3-propyl-2-hexenamide (36f).** This material was prepared in 70% yield from 17.0 g of of ester **33f** by the procedure described above. Purification by chromatography (silica gel, 10% $Et_2O$/hexanes) gave 13.9 g of **36f** as a pale yellow oil, bp 89–91 °C (0.50 mm), $R_f$ 0.18 (10% EtOAc/hexanes): MS $m/e$ 199 ($M^+$); IR ($CHCl_3$) 3026, 1659, 1630 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 0.91 (t, $J$ = 7.20 Hz, 3H), 0.93 (t, $J$ = 7.2 Hz, 3H), 1.44–1.52 (m, 4H), 2.11 (t, $J$ = 7.6 Hz, 2H), 2.51 (t, $J$ = 7.9 Hz, 2H), 3.18 (s, 3H), 3.65 (s, 3H), 6.05 (br s, 1H).

**3-Butyl-*N*-methoxy-*N*-methyl-2-heptenamide (36g).** This material was prepared in 72% yield from 19.8 g of ester **33g** by the procedure described above. Purification by chromatography (silica gel, 15% EtOAc/hexanes) gave 16.4 g of **36g** as a pale yellow oil, bp 95–6 °C (0.35 mm), $R_f$ 0.23 (10% EtOAc/hexanes): MS $m/e$ 227 ($M^+$); IR ($CHCl_3$) 3025, 1646, 1623 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 0.89 (t, $J$ = 7.1 Hz, 3H), 0.90 (t, $J$ = 7.3 Hz, 3H), 1.28–1.47 (m, 8H), 2.13 (t, $J$ = 7.6 Hz, 2H), 2.53 (t, $J$ = 7.7 Hz, 2H), 3.18 (s, 3H), 3.65 (s, 3H), 6.05 (br s, 1H).

***N*-Methoxy-*N*,4-dimethyl-3-(1-methylethyl)-2-pentenamide (36h).** This material was prepared in 28%

yield from 8.5 g of of ester **33h** by the procedure described above. Purification by chromatography (silica gel, 10% $Et_2O$/hexanes) gave 2.0 g of **36h** as a pale yellow oil, $R_f$ 0.12 (10% EtOAc/hexanes): MS *m/e* 199 ($M^+$); IR ($CHCl_3$) 3011, 1646, 1620 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.03 (d, $J$ = 6.8 Hz, 6H), 1.08 (d, $J$ = 6.8 Hz, 6H), 2.50 (septet, $J$ = 6.8 Hz, 1H), 3.18 (s, 3H), 3.62 (s, 3H), 3.66–3.80 (m, 1H), 6.04 (br s, 1H).

**Preparation of Enynones 37a–h: General Procedure.** A solution of 1.5 g of triphenylmethane (indicator) in 800 mL of dry THF was cooled under a nitrogen atmosphere to −78 °C and treated with 57.7 mmol (1.37 equiv) of 2.5 M *n*-butyllithium in hexanes. The appropriate alkyne gas, dried by being passed through a $CaCl_2$ drying tube, was bubbled through the pink solution via a dispersion tube until the pink color was discharged. The resulting colorless solution was stirred for an additional 15 min at −78 °C and was then treated with 41.9 mmol (1.00 equiv) of amide **36a–h**. The reaction mixture was allowed to warm to rt, was stirred for 3 h at rt, and was then poured into 1 L of a 2% aqueous HCl solution saturated with NaCl. The phases were separated and the aqueous phase was extracted with 3 × 100 mL of $Et_2O$. The combined organic phases were dried over anhydrous $Na_2SO_4$ and carefully concentrated under reduced pressure at rt. The crude product was flash chromatographed (silica gel) to afford **37a–h**.

**1-Phenyl-2-(phenylmethyl)-2-hepten-5-yn-4-one (37a).** This material was prepared in 62% yield from 2.56 g of amide **36a** and propyne gas by the procedure described above. Purification by chromatography (silica gel, 10% EtOAc/hexanes) gave 1.50 g of **37a** as colorless crystals, mp 41 °C (from hexanes), $R_f$ 0.59 (20% EtOAc/hexanes): MS *m/e* 274 ($M^+$); IR ($CHCl_3$), 3030, 2227, 1712 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.90 (s, 3H), 3.25 (s, 2H), 3.90 (s, 2H), 6.07 (s, 1H), 6.90–7.30 (m, 10H); exact mass calcd for $C_{20}H_{18}O$ 274.1358, found 274.1356.

**6-Phenyl-5-(phenylmethyl)-4-hexen-1-yn-3-one (37b).** This material was prepared from 3.00 g of amide **36a** and acetylene gas by the procedure described above. Purification by chromatography (silica gel, 2% EtOAc/hexanes) gave **37a** as a pale yellow oil, $R_f$ 0.57 (20% EtOAc/hexanes): MS *m/e* 260 ($M^+$); IR ($CHCl_3$), 3018, 2099, 1656, 1605 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 3.33 (s, 1H), 3.55 (s, 2H), 4.20 (s, 2H), 6.40 (s, 1H), 7.20–7.50 (m, 10H); exact mass calcd for $C_{19}H_{16}O$ 260.1202, found 260.1204.

**2-Methyl-2-hepten-5-yn-4-one (37c).** This material was prepared in 100% yield from 7.66 g of amide **36c** and propyne gas by the procedure described above. Purification by distillation under reduced pressure (49–50 °C, 4 mm) gave 6.94 g of **37c** as a pale yellow oil, $R_f$ 0.64 (20% EtOAc/hexanes): IR ($CHCl_3$), 2214, 1646, 1605 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.80 (s, 3H), 1.90 (s, 3H), 2.10 (s, 3H), 6.05 (s, 1H). Anal. Calcd for $C_8H_{10}O$: C, 78.64; H, 8.27. Found: C, 78.37; H, 8.29.

**6-Ethyl-5-octen-2-yn-4-one (37d).** This material was prepared in 89% yield from 7.17 g of amide **36d** and propyne gas by the procedure described above. Purification by chromatography (silica gel, 5–10% $Et_2O$/hexanes) gave 5.60 g of **37d** as a pale yellow oil, bp 50–3 °C (0.02 mm), $R_f$ 0.61 (10% EtOAc/hexanes): MS *m/e* 150 ($M^+$); IR ($CHCl_3$), 2223, 1650, 1605 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.05 (t, $J$ = 7.6 Hz, 6H), 1.99 (s, 3H), 2.19 (q, $J$ = 7.6 Hz, 2H), 2.61 (q, $J$ = 7.6 Hz, 2H), 6.03 (s, 1H). Anal. Calcd for $C_{10}H_{14}O$: C, 79.96; H, 9.40. Found: C, 79.83; H, 9.38.

**5-Ethyl-4-hepten-1-yn-3-one (37e).** This material was prepared in 67% yield from 3.00 g of amide **36d** and acetylene gas by the procedure described above. Purification by chromatography (silica gel, 5% $Et_2O$/hexanes) gave 1.76 g of **37e** as a pale yellow oil, bp 53–4 °C (4.8 mm), $R_f$ 0.49 (10% EtOAc/hexanes): MS *m/e* 136 ($M^+$); IR ($CHCl_3$) 3302, 2102, 1650, 1608 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.06 (t, $J$ = 7.5 Hz, 3H), 1.07 (t, $J$ = 7.4 Hz, 3H), 2.21 (q, $J$ = 7.4 Hz, 2H), 2.60 (q, $J$ = 7.5 Hz, 2H), 3.10 (s, 1H), 6.10 (s, 1H); exact mass calcd for $C_9H_{12}O$ 136.0888, found 136.0889.

**6-Propyl-5-nonen-2-yn-4-one (37f).** This material was prepared in 99% yield from 8.31 g of amide **36f** and propyne gas by the procedure described above. Purification by chromatography (silica gel, 2.5% $Et_2O$/hexanes) gave 7.39 g of **37f** as a yellow oil, bp 95–6 °C (0.6 mm), $R_f$ 0.57 (10% EtOAc/pentanes): MS *m/e* 178 ($M^+$); IR ($CHCl_3$), 2228, 1642, 1600 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 0.91 (t, $J$ = 8.5 Hz, 3H), 0.93 (t, $J$ = 8.5 Hz, 3H), 1.45–1.52 (m, 4H), 1.99 (s, 3H), 2.11 (dt, $J$ = 1.2, 7.6 Hz, 2H), 2.58 (t, $J$ = 7.0 Hz, 2H), 6.05 (s, 1H). Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.84; H, 10.23.

**6-Butyl-5-decen-2-yn-4-one (37g).** This material was prepared in 98% yield from 9.51 g of amide **36g** and propyne gas by the procedure described above. Purification by chromatography (silica gel, 2% $Et_2O$/hexanes) gave 8.51 g of **37g** as a yellow oil, bp 106–9 °C (0.25 mm), $R_f$ 0.56 (10% EtOAc/hexanes). MS (CI), *m/e* 207 ($M^+$ + 1 [H]); IR ($CHCl_3$), 2228, 1648, 1597 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 0.90 (t, $J$ = 7.2 Hz, 6H), 1.29–1.47 (m, 8H), 1.99 (s, 3H), 2.13 (t, $J$ = 7.60 Hz, 2H), 2.61 (t, $J$ = 7.80 Hz, 2H), 6.04 (s, 1H). Anal. Calcd for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.56; H, 10.77.

**7-Methyl-6-(1-methylethyl)-5-octen-2-yne-4-one (37h).** This material was prepared in 89% yield from 1.90 g of amide **36h** and propyne gas by the procedure described above. Purification by chromatography (silica gel, 2.5% $Et_2O$/hexanes) gave 1.51 g of **37h** as a yellow oil, bp 62–5 °C (0.10 mm), $R_f$ 0.51 (10% EtOAc/hexanes): MS (CI) *m/e* 179 ($M^+$ + 1 [H]); IR ($CHCl_3$), 2225, 1644, 1603 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.03 (d, $J$ = 6.9 Hz, 6H), 1.06 (d, $J$ = 6.8 Hz, 6H), 2.00 (s, 3H), 2.56 (septet, $J$ = 6.8 Hz, 1H), 4.04 (septet, $J$ = 6.9 Hz, 1H), 6.06 (s, 1H). Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.78; H, 10.23.

**Preparation of Alkylidenecyclopentenones 39a–h: General Procedures. Method I.** A solution of 0.21 mmol of enynones **37** in 5.00 mL of dry toluene was transferred by syringe to a Pyrex tube which had previously been washed, rinsed, and dried as described above (cf. **18a–e**). The reaction mixture was degassed and sealed as previously described. The sealed tube was allowed to warm to rt and was then heated in a preheated oven at 250 °C for 10–16 h. At the end of this period, the tube was carefully removed from the oven, allowed to cool to rt, frozen in a bath of liquid nitrogen, and cracked opened by touching a white-hot glass rod to an etched area of the tube. After the reaction mixture warmed to rt, it was transferred to a flask and the solution was concentrated under reduced pressure to dryness. The residue was purified by preparative TLC (silica gel, 500–1000 $\mu$m) to afford the cyclopentenones **39**. **Method II.** A mixture of 0.37 mmol (1.00 equiv) of enynones **37** and 1.85 mmol (5.0 equiv) of $NaHCO_3$ in 9.30 mL of 1,2-dichloroethane was degassed by five freeze–thaw cycles as described above. The reaction

mixture was then heated at reflux (83 °C) for >100 h. At the end of this period, the mixture was allowed to cool to rt, the solvent was removed under reduced pressure, and the crude product was chromatographed (silica gel) to afford the cyclopentenones **39**. **Method III.** A mixture of 0.09 mmol (1.00 equiv) of enynones **37**, 0.10 mmol (1.10 equiv) of TBC, and 0.45 mmol (5.00 equiv) of $NaHCO_3$ in 6.00 mL of 1,2-dichloroethane was degassed as described above for method II. The reaction mixture was then heated at reflux (83 °C) for 5–21 h. At the end of this period, the reaction mixture was cooled to rt and washed with 3 × 5 mL of 1 N NaOH (to remove TBC), and the solvent was removed under reduced pressure. The crude product was chromatographed (silica gel) to afford the cyclopentenones **39**. **Method IV.** A mixture of 0.09 mmol (1.00 equiv) of enynones **37**, 0.10 mmol (1.10 equiv) of TBC, and 0.45 mmol (5.00 equiv) of $NaHCO_3$ in 6 mL of 1,2-dichlorobutane was degassed as in method III above, and the reaction mixture was heated at reflux (124 °C) for 0.5–1 h. At the end of this period, the reaction mixture was cooled to rt, the solvent was removed under reduced pressure, and the crude product was chromatographed (silica gel) to afford the cyclopentenones **39**. **Method V.** A mixture of 0.21 mmol (1.00 equiv) of enynones **37** and 1.05 mmol (5.00 equiv) of 1,2-epoxyoctane in 5 mL of 1,2-dichlorohexane was transferred by syringe to a Pyrex tube which had previously been washed, rinsed, and dried as described above (cf. **18a–e**). The reaction mixture was degassed and sealed as described previously and heated at 200 °C for 5–72 h. Following the usual workup, the crude product was purified by preparative TLC (500–1000 μm) to afford the cyclopentenones **39**. **Method VI.** A mixture of 0.21 mmol (1.00 equiv) of enynones **37**, 0.23 mmol (1.10 equiv.) of vitamin E, and 1.05 mmol (5.00 equiv) of 1,2-epoxyoctane in 5 mL of 1,2-dichlorohexane was transferred by syringe to a Pyrex tube which had previously been washed, rinsed, and dried as described above (cf. **18a–e**). The reaction mixture was degassed and sealed as described previously and heated at 200 °C as in method V for 5–48 h. Following the usual workup, the crude product was purified by preparative TLC (500–1000 μm) to afford the cyclopentenones **39**. **Method VII.** A mixture of 0.21 mmol (1.00 equiv) of enynones **37** and 1.05 mmol (5.00 equiv) of 1,2-epoxyoctane in 5 mL of 1,2-dichlorohexane was transferred by syringe to a Pyrex tube which had previously been washed, rinsed, and dried as described above (cf. **18a–e**). The reaction mixture was degassed and sealed as described previously and was irradiated with an ultraviolet sunlamp while being heated in an oil bath at 200 °C for 4–48 h. Following the usual workup, the crude product was purified by preparative TLC (500–1000 μm) to afford the cyclopentenones **39**. **Method VIII.** A mixture of 0.25 mmol (1.00 equiv) of enynones **37**, 0.28 mmol (1.10 equiv) of vitamin E, and 1.25 mmol (5.00 equiv) of 1,2-epoxyoctane in 5 mL of 1,2-dichlorohexane was transferred by syringe to a Pyrex tube which had previously been washed, rinsed, and dried as described above (cf. **18a–e**). The reaction mixture was degassed and sealed as described previously and was irradiated with an ultraviolet sunlamp while being heated in an oil bath at 200 °C for 4–48 h. Following the usual workup, the crude product was purified by preparative TLC (500–1000 μm) to afford the cyclopentenones **39**.

**5-Ethylidene-4-phenyl-3-(phenylmethyl)-2-cyclopenten-1-one (39a)**. This material was prepared as a 3:1 *E:Z* isomer mixture in 98% yield from 25.0 mg of enynone **37a** by method IV described above. **39a-E**: colorless crystals (from hexane), mp 82–3 °C; $R_f$ 0.43 (20% EtOAc/hexanes): MS *m/e* 274 ($M^+$); IR ($CHCl_3$) 1700, 1655, 1605 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) δ 1.47 (d, *J* = 7.6 Hz, 3H), 3.27 (d, *J* = 16.8 Hz, 1H), 3.52 (d, *J* = 16.8 Hz, 1H), 4.32 (s, 1H), 6.09 (s, 1H), 6.64 (dq, *J* = 2.0, 7.6 Hz, 1H), 7.00–7.42 (m, 10H); exact mass calcd for $C_{20}H_{18}O$ 274.1358, found 274.1358. **39a-Z**: yellow oil, $R_f$ 0.53 (20% EtOAc/hexanes): MS *m/e* 274 ($M^+$); IR ($CHCl_3$) 1707, 1692, 1610 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) δ 2.10 (d, *J* = 6.8 Hz, 3H), 3.23 (d, *J* = 12.8 Hz, 1H), 3.49 (d, *J* = 12.8 Hz, 1H), 4.16 (s, 1H), 5.80 (q, *J* = 6.8 Hz, 1H), 6.10 (s, 1H), 7.00–7.40 (m, 10H).

**5-Methylene-4-phenyl-3-(phenylmethyl)-2-cyclopenten-1-one (39b).** This material was prepared in 48% yield from 26.0 mg of enynone **37b** by method III described above: yellow oil, $R_f$ 0.21 (20% EtOAc/hexanes): MS *m/e* 260 ($M^+$); $^1H$ NMR (400 MHz, $CDCl_3$) δ 3.30–3.60 (dd, 2H), 4.30 (s, 1H), 5.10 (s, 1H), 6.10 (s, 1H), 6.20 (s, 1H), 7.00–7.40 (m, 10H); exact mass calcd for $C_{19}H_{16}O$ 260.1202, found 260.1209.

**5-Ethylidene-3-methyl-2-cyclopenten-1-one (39c).** This material was prepared in 13% yield from 50.0 mg of enynone **37c** by method VI described above (*E*-isomer only). **39c-E**: colorless crystals, mp 270 −72 °C; $R_f$ 0.45 (20% EtOAc/pentanes): MS *m/e* 122 ($M^+$); IR ($CHCl_3$) 1699, 1655, 1620 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 1.81 (d, *J* = 7.1 Hz, 3H), 2.16 (s, 3H), 3.06 (br s, 2H), 6.08 (s, 1H), 6.55 (dq, *J* = 7.1, 0.3 Hz, 1H); exact mass calcd for $C_8H_{10}O$ 122.0729, found 122.0737.

**3-Ethyl-5-ethylidene-4-methyl-2-cyclopenten-1-one (39d)**. This material was prepared as a 1:2 *E:Z* mixture in 82% yield (GC, 79% isolated) from 38.0 mg of enynone **37d** by method VIII described above. **39d-E**: yellow oil, $R_f$ 0.38 (20% EtOAc/pentanes): MS *m/e* 150 ($M^+$); IR ($CHCl_3$) 3029, 1698, 1653, 1609 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 1.24 (dd, *J* = 8.2, 7.8 Hz, 3H), 1.60 (d, *J* = 7.30Hz, 3H), 1.87 (d, *J* = 7.2 Hz, 3H), 2.29 (dq, *J* = 17.5, 7.8 Hz, 1H), 2.52 (dq, *J* = 17.5, 8.2 Hz, 1H), 3.31 (q, *J* = 7.3 Hz, 1H), 6.04 (s, 1H), 6.53 (q, *J* = 7.2 Hz, 1H); exact mass calcd for $C_{10}H_{14}O$ 150.1045, found 150.1050. **39d-Z**: yellow oil, $R_f$ 0.53 (20% EtOAc/pentanes): MS *m/e* 150 ($M^+$); IR ($CHCl_3$) 3035, 3031, 1688, 1643, 1608 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 1.12 (t, *J* = 7.3 Hz, 3H), 1.15 (d, *J* = 7.0 Hz, 3H), 2.13–2.29 (m, 1H), 2.11 (d, *J* = 7.3 Hz, 3H), 2.44 (dq, *J* = 16.0, 7.3 Hz, 1H), 3.12 (q, *J* = 7.0 Hz, 1H), 6.02 (m, 2H).

**3-Ethyl-4-methyl-5-methylene-2-cyclopenten-1-one (39e).** This material was prepared in 98% yield (GC, 39% isolated) from 40.8 mg of enynone **37e** by method VIII described above: yellow oil, $R_f$ 0.28 (10% acetone/hexanes); MS *m/e* 136 ($M^+$); IR ($CHCl_3$) 1697, 1647, 1605 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 1.18 (dd, *J* = 8.0, 7.30 Hz, 3H), 1.24 (d, *J* = 7.4 Hz, 3H), 2.30 (dq, *J* = 17.9, 8.0 Hz, 1H), 2.50 (dq, *J* = 17.9, 7.3 Hz, 1H), 3.26 (q, *J* = 7.4 Hz, 1H), 5.28 (s, 1H), 6.00 (s, 1H), 6.09 (s, 1H); exact mass calcd for $C_9H_{12}O$ 136.0888, found 136.0891.

**4-Ethyl-5-ethylidene-3-propyl-2-cyclopenten-1-one (39f).** This material was prepared as a 1:1 *E:Z* mixture in 92% yield from 44.5 mg of enynone **37f** by method VIII described above: **39f-E**: yellow oil, $R_f$ 0.26 (10% EtOAc/pentanes); MS *m/e* 178 ($M^+$); IR ($CHCl_3$) 1698, 1654, 1610 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 0.59 (t, *J* = 7.5 Hz, 3H), 0.97 (t, *J* = 7.4 Hz, 3H), 1.54–1.68 (m, 2H), 1.71–1.82 (m, 1H), 1.85 (d, *J* = 7.3 Hz, 3H), 1.87–1.96 (m, 1H), 2.23 (ddd, *J* = 15., 6.3, 6.3 Hz, 1H),

2.37 (ddd, $J$ = 15.2, 6.2, 6.2 Hz, 1H), 3.44 (br s, 1H), 6.12 (s, 1H), 6.57 (dq, $J$ = 7.3, 1.60 Hz, 1H); exact mass calcd for $C_{12}H_{18}O$ 178.1358, found 178.1370. **39f-Z**: yellow oil, $R_f$ 0.36 (10% EtOAc/pentanes); MS $m/e$ 178 ($M^+$); IR ($CHCl_3$) 1690, 1652, 1608 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 0.61 (t, $J$ = 7.5 Hz, 3H), 0.95 (t, $J$ = 7.5 Hz, 3H), 1.39–1.65 (m, 4H), 2.09–2.34 (m, 2H), 2.19 (d, $J$ = 7.3 Hz, 3H), 3.15 (br, 1H), 5.98 (q, $J$ = 7.3 Hz, 1H), 6.06 (s, 1H).

**3-Butyl-5-ethylidene-4-propyl-2-cyclopenten-1-one (39g).** This material was prepared as a 1:2 *E*:*Z* mixture in 80% yield from 51.5 mg of enynone **37g** by method VIII described above: **39g-E**: yellow oil, $R_f$ 0.23 (10% EtOAc/pentanes); MS $m/e$ 206 ($M^+$); IR ($CHCl_3$) 1694, 1654, 1606 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 0.81 (t, $J$ = 7.5 Hz, 3H), 0.90 (t, $J$ = 7.3 Hz, 3H), 1.29–1.42 (m, 4H), 1.46–1.60 (m, 4H), 1.86 (d, $J$ = 7.3 Hz, 3H), 2.20–2.28 (m, 1H), 2.36–2.44 (m, 1H), 3.41 (br s, 1H), 6.06 (br s, 1H), 6.53 (q, $J$ = 7.3 Hz, 1H). **39g-Z**: yellow oil, $R_f$ 0.41 (10% EtOAc/pentanes); MS $m/e$ 206 ($M^+$); IR ($CHCl_3$) 1688, 1645, 1608 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 0.84 (t, $J$ = 7.2 Hz, 3H), 0.91 (t, $J$ = 7.3 Hz, 3H), 1.31–1.66 (m, 8H), 2.21 (d, $J$ = 7.3 Hz, 3H), 2.15–2.44 (m, 2H), 3.17 (br s, 1H), 6.00 (q, $J$ = 7.3 Hz, 1H), 6.04 (s, 1H); exact mass calcd for $C_{14}H_{22}O$ 206.1672, found 206.1671.

**5-Ethylidene-4,4-dimethyl-3-(1-methylethyl)-2-cyclopenten-1-one (39h).** This material was prepared as a 1:1 *E*:*Z* mixture in 96% yield (GC, 81% isolated) from 44.5 mg of enynone **37h** by method VIII described above. **39h-E**: yellow oil, $R_f$ 0.23 (10% EtOAc/pentanes); MS $m/e$ 178 ($M^+$); IR ($CHCl_3$) 1695, 1651, 1605 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.26 (d, $J$ = 6.8 Hz, 6H), 1.41 (s, 6H), 2.02 (d, $J$ = 7.6 Hz, 3H), 2.69 (septet, $J$ = 6.8 Hz, 1H), 6.17 (s, 1H), 6.61 (q, $J$ = 7.6 Hz, 1H). **39h-Z**: yellow oil, $R_f$ 0.63 (10% EtOAc/pentanes); MS $m/e$ 178 ($M^+$); IR ($CHCl_3$) 1687, 1645, 1606 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.23 (d, $J$ = 6.8 Hz, 6H), 1.28 (s, 6H), 2.29 (d, $J$ = 7.4 Hz, 3H), 2.61 (septet, $J$ = 6.8 Hz, 1H), 6.07 (q, $J$ = 7.4 Hz, 1H), 6.12 (s, 1H); exact mass calcd for $C_{12}H_{18}O$ 178.1358, found 178.1357.

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**Supplementary Material Available:** Copies of NMR spectra for compounds **5**, **6-Z**, **6-E**, **8-Z**, **8-E**, **18a–e** (**Z** and **E**), **29a–f**, **30a–e** (**E**), **33a–h**, **36a–h**, **37a–h**, and **39a–h** (**Z** and **E**) (56 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.