Pergamon

Tetrahedron 55 (1999) 29–62

TETRAHEDRON

Synthesis and Cycloaromatization Kinetics of Aromatic Allene Enynes

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Received 11 April 1997; accepted 23 October 1998

Abstract: Aryl- and cyclopropyl-substituted allene enynes were prepared by a double olefination procedure from various aldehydes, and their cycloaromatization reactions were subjected to kinetics measurements in methanol and 1,4-cyclohexadiene solvents. The results support previous proposals of a polar diradical transition state for the cycloaromatization process. © 1998 Elsevier Science Ltd. All rights reserved.

The intriguing structure and reactivity of the enediyne antitumor antibiotics has captured the intense attention of chemists and biochemists for the past several years.[1] The most significant aspect of the chemistry of these compounds is their ability to generate highly reactive intermediates under mild, controlled conditions. The longest-studied member of this class, the neocarzinostatin chromophore (NCSC), contains a diene-diyne core that undergoes a triggered rearrangement to an yne-ene-cumulene moiety that is the immediate progenitor of a reactive species responsible for DNA damage *in vitro*.[2] The simplest fragment to undergo a similar rearrangement is an allene enyne unit.[3] Studies of such systems are of significance not only for the mechanistic insights they provide relative to the natural system, but also toward the design and construction of simple NCSC analogues that may be directed toward cellular targets in novel ways. Although many kinetic analyses of the Bergman enediyne cycloaromatization reaction have appeared,[4] only three such studies of the allene enyne variant have been published.[3a,b;5a]

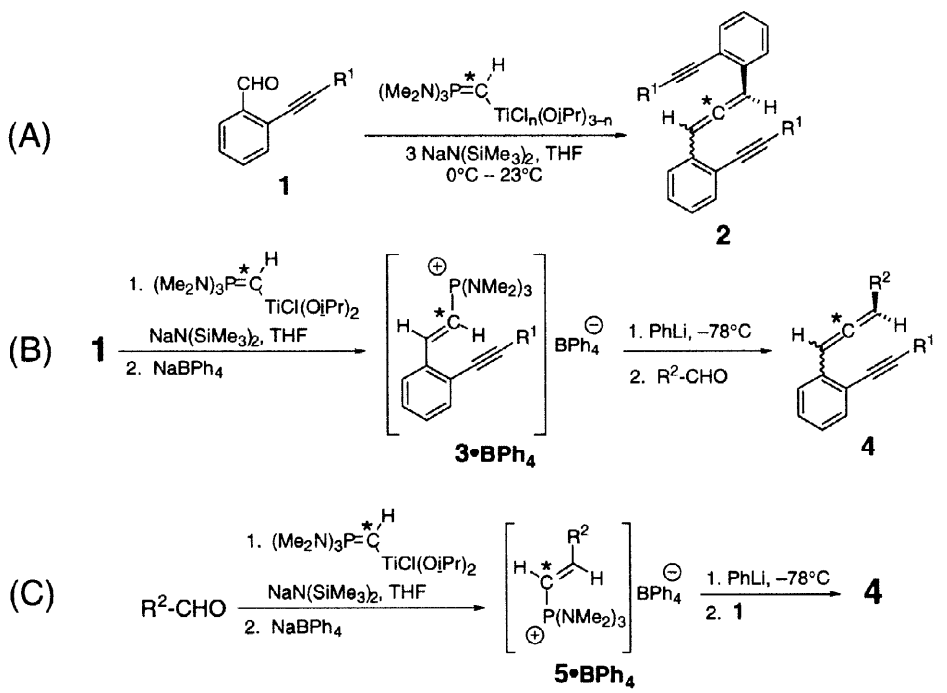
We have developed a convenient methodology for the assembly of allene compounds from two aldehyde units and a doubly oxophilic "carbon atom" synthon.[6] Here we report the results of our exploration of the allene enyne cycloaromatization process, taking advantage of the ability of the double olefination technique to generate candidate compounds from convenient starting materials. We have investigated the cycloaromatization rate and product selectivity in response to changes in the steric and electronic properties of substituents on the allene enyne framework, building on the pioneering studies of the Myers group.[3a] The results provide an expanded set of data that supports the Myers proposal of a common transition state in both polar and nonpolar solvents, after which the reaction pathways diverge in response to the nature of the solvent. The reaction rate is shown to be sensitive to the steric bulk of the alkyne substituent, and consistent correlations between calculated minimum-energy conformations and observed rates and activation enthalpies have been identified. Variations in the electronic nature of the allene substituent for a series of *para*-substituted phenyl groups have a relatively small effect on rate, supporting previous proposals of an early transition state, and suggesting that the transition state has substantial diradical character. Cyclopropyl-substituted allenes are readily synthesized and undergo cycloaromatization with cyclopropyl ring opening under both dipolar and diradical conditions. The implications of these results for the use of simple allene enyne structures as functional mimics of naturally-occurring enediynes are discussed.

PII: S0040-4020(98)01022-9

RESULTS

Allene Enyne Synthesis

Allene enynes were prepared by one of three related procedures, employing the doubly oxophilic ylide reagent prepared *in situ* from $TiCl_2(OiPr)_2$, $(Me_2N)_3P{=}CH_2$, and $NaN(SiMe_3)_2$,[6] as shown in Scheme 1: (A) the one-pot coupling of acetylenic aldehydes **1** to provide diynes **2**; (B) the conversion of acetylenic aldehydes **1** to vinylphosphonium salts **3**,[6c,d] followed by coupling with simple aromatic aldehydes to give allenes **4**; and (C) the conversion of simple aldehydes to vinylphosphonium salts **5**,[6c,d] followed by coupling with acetylenic aldehydes. The aldehyde components employed are shown in Fig. 1; acetylenic aldehydes **1** were constructed in high yield by Pd-catalyzed coupling of aromatic iodides or bromides and terminal alkynes.[7] Vinylphosphonium salts **3** and **5** were produced in 22-70% yield, and allenes were obtained as shown in Table 1. While the yields were not high (and were not optimized), the methodology allows for the preparation of useful quantities of material in rapid fashion. The allenes are usually the least polar component of the product mixture and are easy to purify by chromatography. The methodology is thus well suited to providing material for a structure-activity study of this type.



Scheme 1

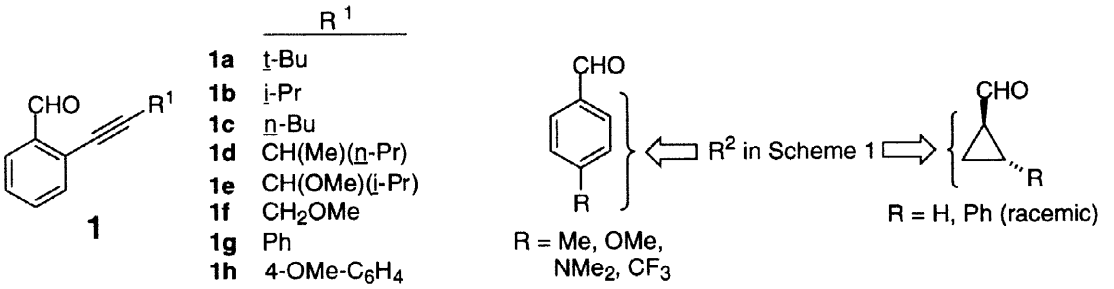


Fig. 1. Aldehyde components used in allene synthesis.

Table 1. Yields of Allenes **2** and **4** (Scheme 1).

Compound	R^1	R^2	Yield[a]	Method
2a	t-Bu	n/a	**50**	**A**
2b	i-Pr	n/a	**30**	**A**
2c	n-Bu	n/a	**6**	**A**
4a	t-Bu	(4-Me)-C_6H_4	**64, 44**	B, C
4b	t-Bu	(4-OMe)-C_6H_4	53	B
4c	t-Bu	(4-NMe_2)-C_6H_4	13	B
4d	t-Bu	(4-CF_3)-C_6H_4	30	B
4e	t-Bu	*trans*-2-Ph-cyclopropyl	62	B
4f	t-Bu	cyclopropyl	60	B
4g	i-Pr	(4-Me)-C_6H_4	30	C
4h	i-Pr	(4-OMe)-C_6H_4	42	C
4i	i-Pr	*trans*-2-Ph-cyclopropyl	33	C
4j	n-Bu	*trans*-2-Ph-cyclopropyl	14	C
4k	CH(Me)(n-Pr)	(4-Me)-C_6H_4	25	B
4l	CH(OMe)(iPr)	(4-Me)-C_6H_4	28	C
4m	CH_2OMe	(4-Me)-C_6H_4	7	C
4n	C_6H_5	(4-Me)-C_6H_4	n/a[b]	C
4o	(4-OMe)-C_6H_4	(4-Me)-C_6H_4	n/a[b]	C

(a) For Method A, % isolated yield with respect to phosphorus methylide; for Methods B and C, % isolated yield with respect to vinylphosphonium salt. Excess aldehyde is recovered in 80-90% of theoretical amount. (b) Not isolated in pure form (see text).

Notable aspects of the allene condensation chemistry are as follows.

(1) ^{13}C enrichment is provided by the use of $(Me_2N)_3P{=}^{13}CH_2$, prepared in high yield on large scale[6a,c] or generated *in situ* from $^{13}CH_3I$. The convenient incorporation of this label at the central allene carbon is crucial to the kinetic investigations described below.

(2) The one-pot double olefination process is shown for the first time to be somewhat tolerant of substitution *ortho* to the aldehyde function.

(3) Yields of allene diynes **2a-c** by the one-pot procedure (method A) diminish with decreasing size of the terminal alkyne substituent, and are sensitive to the temperature of the reaction and workup. When prepared at room temperature, **2b** is obtained in 7% yield, whereas the yield is 30% when the reaction and chromatography are performed at 0–4°C. Allene **2c** is only isolable at low temperature. As discussed below, these observations are the result of increased rates of cycloaromatization with smaller substituents. The yields of allene enynes from the stepwise procedures follow the same trend (compare **4e** and **4f** vs. **4i** vs. **4j** in Table 1). Thus, acetylenic vinylphosphonium salts with alkyne substituents smaller than *tert*-butyl are poor substrates for conversion to allenes. For example, isopropyl aldehyde **1b** affords vinylphosphonium salt **3b** in satisfactory yield, but we were unable to convert this compound to an allene by deprotonation and trapping with 4-methylbenzaldehyde. Interestingly, the closely-related compound **3d**, differing only in the length of an alkyl chain at the propargylic position, is successfully converted to allene **4k** under identical conditions. We

believe that allenic phosphoranes are generated from salts such as **3b**, but decompose before they can be trapped by an added aldehyde.[8]

(4) Cyclopropyl and phenylcyclopropyl substitution at an allene terminus (R^2) is conveniently installed. Interestingly, the cyclopropyl substituted vinylphosphonium salt **5c** could not be converted into allene enynes, in spite of its previously successful use in the construction of other allenes by trapping with simpler aldehydes.[6c] This is perhaps a reflection of the diminished trapping efficiency of *o*-alkynyl aromatic aldehydes as well as the relative instability of the cyclopropyl-containing allenic phosphorane, both as compared with the more routine simple aromatic derivatives.

(5) Compounds **4n** and **4o** were prepared in the usual manner, but isolated in crude form by filtration of the reaction mixture through a pad of silica gel. For each case, a single ^{13}C signal deriving from the labeled ylide carbon was observed at 208-209 ppm, verifying the presence of the desired allene unit. These samples were employed directly in the ^{13}C kinetics measurements described below. Crude samples of **2a** and **4a** prepared in the same way were found to give identical decomposition rate constants to purified samples of these allenes (data not shown).

(6) While all the other allene enynes reported here are oils, cyclopropyl compound **4f** is a crystalline solid. Single crystals were obtained and subjected to x-ray diffraction analysis, with the result shown in Fig. 2. To our knowledge, this is the first crystal structure of an allene enyne to be reported.

In the solid state, **4f** adopts an s-*trans* conformation (C2-C3-C7-C8 dihedral angle = 171.0°). Saito and coworkers predicted a similar structure for allene enyne **6** (R=H) and reported *ab initio* calculations showing that the s-*trans* conformation is 3.6 kcal/mol more stable than the reactive *s-cis* arrangement.[9] Additional substitution on the allene (R = CH_3, SOPh) raised the rate of cycloaromatization by more than an order of magnitude, an effect ascribed to a decrease in the s-*trans*/s-*cis* conformational energy difference.[9] Molecular mechanics calculations[10] predict that *s-cis* and *s-trans* conformations of **4f** are essentially equal in energy (ΔE = 0.07 kcal/mol), with dihedral angles of the two forms calculated to be 30° and 179°, respectively.[11] ^1H NMR NOE measurements in C_6D_6 solution show a 7.9% enhancement of the C3 allenic proton resonance (7.12 ppm) and a 2.8% enhancement of the C1 allenic proton resonance (5.13 ppm) upon irradiation of the t-butyl group (1.00 ppm). The former result is consistent with the presence of the s-*trans* conformation in solution as well as in the solid state. The latter NOE observation suggests that the s-*cis* conformation is also present in solution to a significant extent at 25°C.

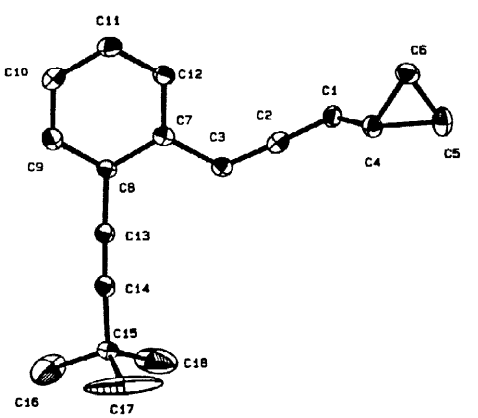
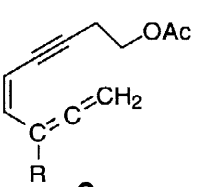


*Fig. 2. ORTEP drawing of the solid state structure of **4f**, showing 30% probability ellipsoids; C2-C3-C7-C8 dihedral 171.1°.*



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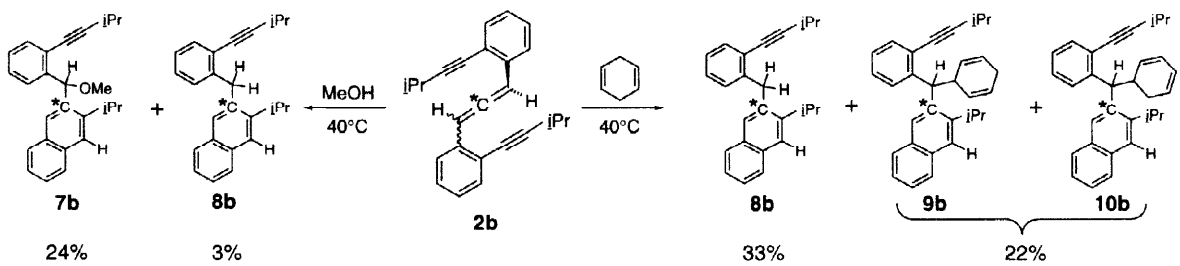
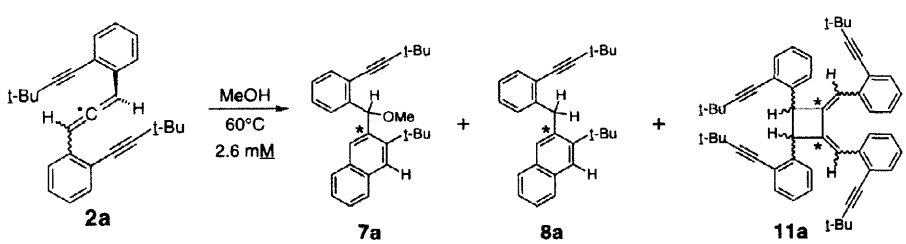
Cycloaromatization Studies

Product Isolation. Aromatic allene diynes **2** and allene enynes **4** were heated under nitrogen in methanol or 1,4-cyclohexadiene solvents to form naphthalenic products consistent with Myers-style cycloaromatizations of the allene enyne moiety. Cycloaromatization of the isopropyl substituted **2b** in methanol (31 mM allene) at 40°C provides the methyl ether **7b** as the major product in 24% yield, and the alkane **8b** as a minor product in 3% yield (Scheme 2). The rest of the mass balance (73%) is recovered from preparative thin layer chromatography plates as an inseparable collection of compounds displaying a complicated NMR spectrum with no dominant sets of resonances. Similarly, the n-butyl substituted **2c** undergoes cycloaromatization at room temperature in methanol solution (5 mM) to afford ether **7c**, analogous to **7b**, in 28% yield (not shown). No products corresponding to structure **8** were found by NMR or mass spectrometry. When allene **2b** is heated in 1,4-cyclohexadiene at 40°C, **8b** is isolated as the major product in 33% yield, along with a mixture of the solvent–trapped products **9b** and **10b** (combined 22% yield; Scheme 2). The product distribution for **2b** in both methanol and 1,4-cyclohexadiene is the same in 5 mM and 31 mM solutions. As was the case in methanol, the remaining material from the reaction in 1,4-cyclohexadiene is recovered from a preparative thin layer chromatograpy plate as a complex mixture.



Scheme 2

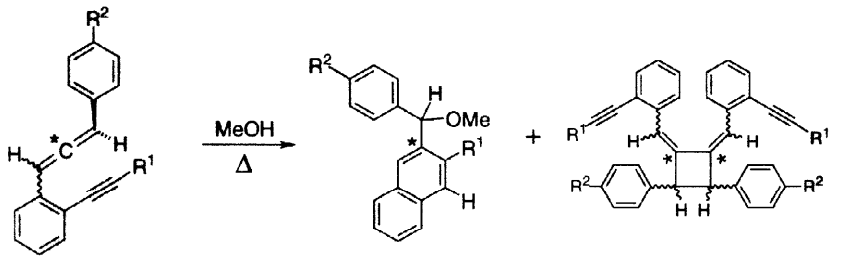
The tert-butyl substituted allene di(enyne) **2a** undergoes cycloaromatization only at higher temperatures, which allows [2+2] dimerization[12] to compete with ring closure. Thus, heating samples of **2a** in dilute (2.6 mM) methanol solution at 60°C under inert atmosphere results in cycloaromatization of the allene to yield the dipolar-derived ether **7a** in 37% yield, the radical-trapped product **8a** in 6% yield, and dimer **11a** in 6% yield (Scheme 3). Dimers are easily detected by chemical ionization mass spectrometry and by their enriched ^{13}C NMR signals (see below). The relative stereochemistry of the dimers was not determined. The extent of dimerization was found to be directly proportional to starting allene concentration, occurring at the expense of the cycloaromatization process (Scheme 3).



Concentration of **2a**	Isolated Yields **7a**	**8a**	**11a**
2.6 mM	37%	6%	6%
26 mM	27%	–	32%
80 mM	21%	–	44%

Scheme 3

Aromatic allene-ynes **4** provide naphthalenic products analogous to those described above for the cycloaromatization of allene diynes **2**, but in higher yields. For example, when heated at 40°C in methanol at 5 mM concentration for 24 hours, isopropyl substituted allenes **4g** and **4h** afforded the expected methyl ethers **12g** and **12h** in 61% and 49% yields, respectively (Scheme 4). For the related tert-butyl substituted **4a**, as in the case of diyne **2a**, cycloaromatization in methanol is competitive with allene dimerization. Accordingly, the reaction was studied under dilute conditions (2.6 mM), in which the main product was found to be ether **12a** (40% yield, Scheme 4). Trace amounts of dimeric species **13** were also detected by mass spectrometry in the complex mixture of the remaining products.



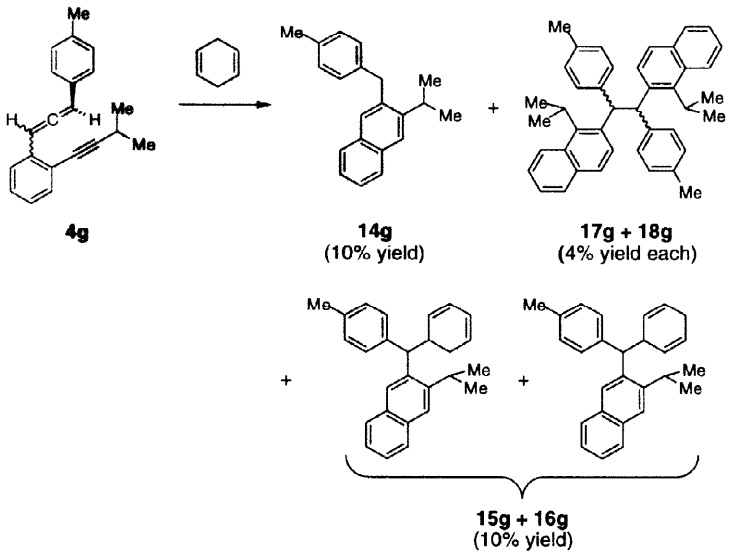
	R^1, R^2	Conc.	Yield	
a	t-Bu, Me	2.6 mM	**a** 40%	**a** trace
b	t-Bu, OMe	2.6 mM	**b** major	**b** minor
c	t-Bu, NMe_2	2.6 mM	**c** major	**c** minor
d	t-Bu, CF_3	2.6 mM	**d** major	**d** minor
g	i-Pr, Me	5 mM	**g** 61%	**g** trace
h	i-Pr, OMe	5 mM	**h** 49%	**h** trace

Scheme 4

Isolation of clean samples of the products described above allowed for the identification of characteristic signals in the ^{13}C NMR spectra. The ^{13}C-enriched central allene carbon becomes incorporated at position 2 in the naphthalenic cycloaromatization products, which for ethers **7** and **12** appears at 136-138 ppm. In contrast, allene dimers show the enriched ^{13}C resonance at 144-146 ppm, corresponding to an sp^2 center of the dialkylidenecyclobutane ring. Accordingly, the major products of allene decomposition in methanol may be identified from analysis of the ^{13}C NMR of the crude reaction mixtures in conjunction with mass spectrometry of fractions obtained by preparative thin layer chromatography. Minor constituents (<10%) are not resolved because the signal intensities of their ^{13}C-enriched sites are of a similar magnitude as some of the natural-abundance aromatic signals of the major products. The ratios (but not the absolute amounts) of the major products can be estimated from the intensities of the ^{13}C-enriched resonances. For instance, the cycloaromatization of **2b** in 1,4-cyclohexadiene (Scheme 2) gives a ratio of isolated yields of **8b** (33%) to **9b** + **10b** (22% combined) that is similar to the ratio of ^{13}C NMR resonances of the labeled carbon atoms in these structures (47% and 33% of the total labeled signal intensity, respectively).

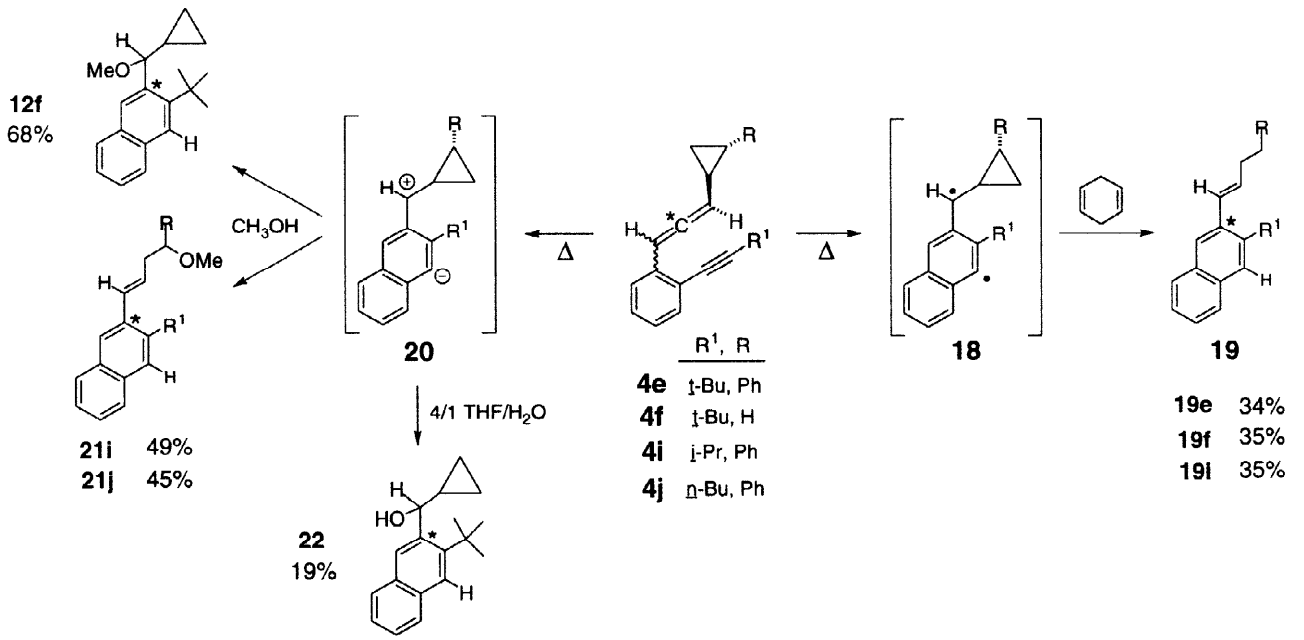
Thus, the t-butyl substituted compounds **4b**, **4c**, and **4d** were found to afford predominantly the cycloaromatized ethers **12b**, **12c**, and **12d**, respectively, in methanol at 2.6 mM (Scheme 4). These products were not isolated and characterized in detail, but were rather identified by their labeled ^{13}C NMR resonances at 138 ppm in the crude reaction mixture. In each case, the major bands from preparative thin layer chromatography showed the same ^{13}C labeled resonance and a parent ion mass value corresponding to the expected ether (**12b**, m/z = 336; **12c**, m/z = 349; **12d**, m/z = 374). Resonances at 144-145 ppm, indicating the formation of dimeric products, are also observed as minor components (<10%).

The cycloaromatization of allene-yne **4g** was also performed in 1,4-cyclohexadiene to examine the product distribution in a non-polar medium (Scheme 5). A 5 mM solution of the allene was heated at 40°C to form **14g** (10% yield), an inseparable mixture of **15g** and **16g** (10% yield), and the coupled products **17g** and **18g** (4% yield each). The identification of **17g** and **18g** as the *meso*- and *dl*-isomeric products of benzylic radical coupling and not allene [2+2] dimerization is made on the basis of the full ^{1}H and ^{13}C NMR spectra, with the notable observation of one-bond ^{13}C-^{13}C coupling of the benzylic resonance at approximately 50 ppm with the labeled carbon center in each compound. The percentages of the measured intensities for the ^{13}C labels in the ^{13}C NMR spectrum of the crude product mixture were 33% for **14g**, 37% for the mixture of **15g** and **16g**, and 29% for the mixture of **17g** and **18g**, again matching the relative isolated yields of these compounds.



Scheme 5

Lastly, the reactions of cyclopropyl-substituted allene enynes were studied under a variety of conditions: Scheme 6 shows the predominant products and isolated yields. These reactions were much slower than those of the aromatic-substituted cases discussed above, requiring extended heating at 105–110°C (see below for absolute rates). Compounds **4e**, **4f**, and **4i** in 1,4-cyclohexadiene yield naphthalenic products **19** as expected from a Myers style cycloaromatization. In these cases, the putative intermediate diradicals **18** are



Scheme 6

cyclopropylcarbinyl species, and undergo cyclopropane ring opening.[13] In addition, t-butyl-substituted allenes **4e** and **4f** also dimerize to a small extent (not shown), as indicated by the appropriate peaks in the mass spectra of the crude solutions and by trace peaks in ^1H and ^{13}C NMR spectra that are similar to those observed for dimer **11a** (Scheme 3). These dimeric compounds were not isolated. To minimize dimerization, cycloaromatization reactions of t-butyl cases were performed in 5 mM solution.

Allene enynes **4e**, **4f**, **4i**, and **4j** were also heated in methanol. In contrast to the isolation of discrete cycloaromatization products from 1,4-cyclohexadiene solution, phenylcyclopropyl allene **4e** produced an intractable mixture upon reaction in methanol under otherwise identical conditions. The ethers **12** usually found from cycloaromatization reactions in methanol were not detected by ^1H NMR, ^{13}C NMR, or mass spectrometric analysis of crude reaction mixtures. On the other hand, compounds **4i** and **4j**, bearing the phenylcyclopropyl group and smaller alkyne substituents, provide methyl ethers **21i** and **21j** in substantial yield. In contrast to a cyclopropyl thioether case examined by Myers,[3a] cyclopropane ring opening is observed here under polar conditions, with the products presumably arising from the benzylic cation derived from ring opening of dipolar intermediate **20**. The existence of such an intermediate is further supported by the isolation of ether **12f** from **4f** (5 mM methanol solution at 110°C for one week), in which the cyclopropyl ring remains intact. As was the case in 1,4-cyclohexadiene, the slow cycloaromatization of **4f** in methanol leads to the formation of small amounts of dimeric species. Lastly, **4f** was also heated in aqueous tetrahydrofuran (4:1 THF: H_2O) to afford naphthalenic alcohol **22** as the predominant species in the crude product mixture (19% isolated yield), presumably derived from a dipolar pathway (Scheme 6).

The following summary may be made of the observations presented above. In general, these parallel the results of Myers and coworkers,[3a] providing in some cases additional examples and in several cases slightly different results.

(1) Reactions conducted in 1,4-cyclohexadiene afford products consistent with H-atom or cyclohexadienyl trapping of intermediate diradicals. While the types of structures observed here are consistent with those described for simpler substrates,[3a] overall yields of identifiable products from cycloaromatization in the present cases are much less than the previous report. This may be due to the more highly stabilized nature of the benzylic radicals produced from our aromatic allene-ynes, which are expected to exhibit longer lifetimes and thus engage in a greater variety of side reactions. An example is provided by the observation of radical dimerization products **17g** and **18g** (Scheme 5) from the decomposition of allene **4g** in 1,4-cyclohexadiene solvent. Such a carbon radical recombination process is reported by Myers only for the reaction of 1,2,4-heptatrien-6-yne in methanol, where alternative radical quenching processes are slow.[3a] In our case, it appears that the more stable doubly benzylic radical formed in the cycloaromatization of **4g** is sufficiently robust in 1,4-cyclohexadiene to be able to recombine to form **17g** and **18g** in small amounts.

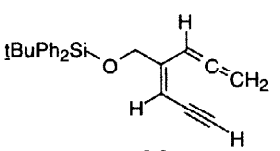
(2) Reactions of **2a-2c** conducted in methanol afford products (benzylic methyl ethers and benzylic hydrocarbons) proposed to arise from both dipolar (major) and diradical (minor) pathways, respectively, again closely related to the findings of the Myers group.[3a]

(3) For systems slow to undergo cycloaromatization, rates of allene [2+2] dimerization may become competitive at higher concentrations.

(4) Cyclopropyl-substituted allenes undergo cycloaromatization much more slowly than aryl-substituted allenes. Cycloaromatization in 1,4-cyclohexadiene is accompanied by cyclopropyl ring opening for both cyclopropyl- and phenylcyclopropyl-substituted cases. It is expected that ring opening of benzylic cyclopropylcarbinyl radicals such as **18f** (Scheme 6) is reversible,[13a] requiring high concentrations of 1,4-cyclohexadiene to trap the reactive primary ring-opened radical, as previously demonstrated by Myers.[3a] On the other hand, ring opening of benzylic phenylcyclopropylcarbinyl radical systems has been shown to be irreversible,[13b] presumably because of the resonance stabilization provided by the phenyl group to the ring-opened radical species. The production of the expected[13b,c] *trans*-alkene products ($J_{HH} \approx 15$ Hz) from such substrates therefore indicates that the trapping of radical **18** by the solvent is slower than the rate of cyclopropylcarbinyl ring opening. In methanol, the simple cyclopropyl ring of **4f** remains intact upon cycloaromatization, whereas phenylcyclopropyl analogues undergo cyclopropane ring opening, presumably via an intermediate stabilized benzylic cation.

(5) Cycloaromatization of **4e** is inhibited both by the presence of a t-butyl group on the alkyne and a nonaromatic group on the allene. This compound appears to decompose by other pathways in methanol solution, as shown by analysis of the crude product mixture by ^{13}C NMR (complex spectrum lacking the characteristic signal for a methyl ether) and mass spectrometry (lack of peaks of appropriate molecular weights for cycloaromatized products). Allene dimerization is not a dominant process in this case.

(6) The cycloaromatization of **4f** in aqueous THF shows no evidence of radical trapping by THF or radical coupling, in contrast to Myers' observation that such products are produced exclusively (30% isolated yield) from the reaction of **23** in the same solvent mixture.[3a] Thus, dipolar character is favored by one or more of the following factors: use of an aromatic group instead of an alkene moiety between allene and alkyne units, monosubstitution at the allene terminus, or substitution at the alkyne terminus. The exclusive isolation of dipolar-derived products from allenic thioether **24** in 4/1 THF/H_2O[3a] also shows that the reaction mechanism can be affected by substitution of polar groups on the allene enyne skeleton



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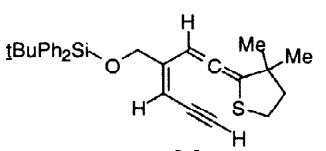

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Kinetics. The kinetics of decomposition of allene di(enynes) **2** and allene enynes **4** were measured to determine the effect of various substitution patterns on the rate of cycloaromatization. In all cases, the disappearance of an allene enyne signal was followed against a suitable internal standard, and the rates of allene enyne disappearance are reported as rates of cycloaromatization in cases where the isolated products show cycloaromatization to be the predominant process. This is confirmed in ^{13}C NMR kinetic studies, in which the observed labeled product resonance(s) match those of the isolated compounds discussed above.

The rates of cycloaromatization of allene enynes **2b** and **2c** were measured in methanol or 1,4-cyclohexadiene solutions (80 mM initial concentration). The substrates were prepared with ^{13}C enrichment (99%) at the central allene carbon, and the disappearance of this allene resonance was monitored against *p*-dioxane internal standard in the ^{13}C NMR. Representative spectra for the cycloaromatization of **2b** in methanol are shown in Fig. 3, with central allene carbon label at 209 ppm and dioxane at 66.2 ppm. The top spectrum shows the sample after 10 minutes reaction time, and the bottom spectrum shows the same sample

after 3.7 half lives (310 minutes). Note the disappearance of the allene resonance and the growth of the labeled aromatic carbon of **7b** at 137.4 ppm. The ratio of the peak heights of the allene and *p*-dioxane resonances is directly proportional to the allene concentration, so a plot of the natural logarithm of that ratio vs. time affords a line with slope equal to the first order rate constant, as shown at the right of Fig. 3. Comparing repeat runs for several cases, an average error of 7% was calculated for these rate measurements.

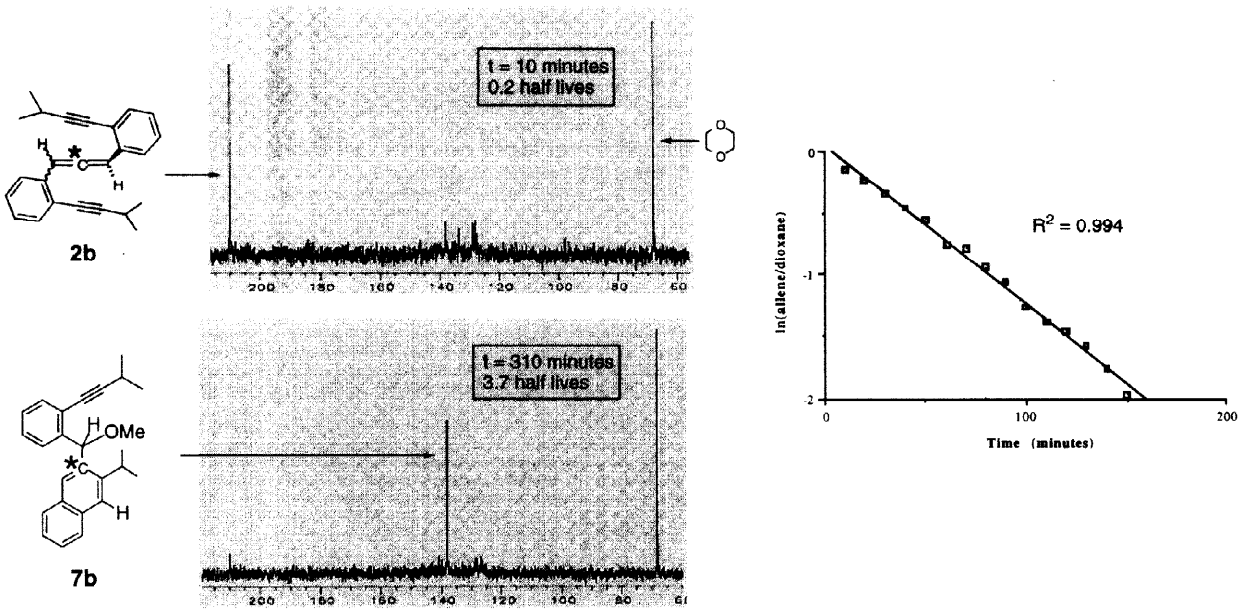


Fig. 3. ^{13}C *NMR spectra for the cycloaromatization of* **2b** *(80 mM) in methanol at 28.6°C.*

In contrast with **2b** and **2c**, the rate of disappearance of allene **2a** may not be equated with the rate of its cycloaromatization at higher concentrations, since predominantly dimeric products are formed. The disappearance of **2a** follows clean second-order kinetics at a starting concentration of 240 mM, and only the [2+2] dimer is detected in the ^{13}C NMR spectrum of the crude product. Attempts to measure the rate of cycloaromatization of **2a** by ^{13}C NMR at concentrations in which cycloaromatization predominates over dimerization were unsuccessful due to the poor signal strength of the dilute allene. Thus, rates were measured under these conditions by following the disappearance of **2a** by reverse-phase HPLC using 1-methoxynaphthalene as an internal standard. For example, the first order disappearance of **2a** (starting concentration of 2.6 mM, which was shown in Scheme 3 to produce mostly cycloaromatization products) versus 1-methoxynaphthalene at 60°C is shown in Fig. 4.

Activation parameters for the cycloaromatization reaction were determined[14] for four compounds (**2a**, **2b**, **4g**, and **4n** in methanol, and **2b** and **4g** in 1,4-cyclohexadiene) by plotting ln(k/T) vs. (1/T), as shown in the example of Fig. 5. The results are summarized in Table 2, deriving from rate measurements summarized in the Experimental Section (Table 7). The values reported by Myers for the parent structure (Z)-1,2,4-heptatrien-6-yne (**25**) are listed for comparison. Rate constants at fewer temperatures were also measured for the following allenes: **2c**, **4h**, **4k**, **4l**, **4o**, and the cyclopropyl-substituted cases **4e**, **4f**, **4i**, and **4j** (Table 7).

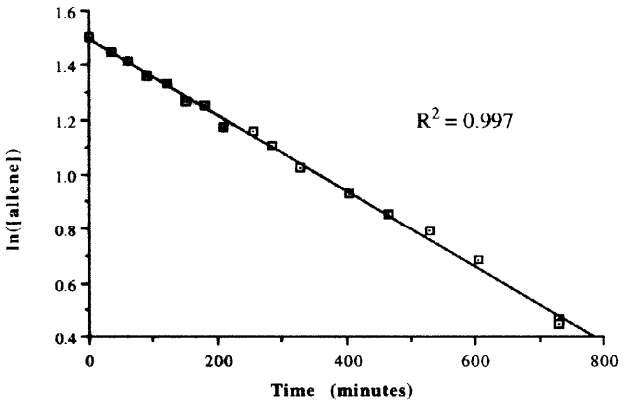


Fig. 4. Kinetics of cycloaromatization of 2a (2.6 mM) in methanol at 60°C, determined by HPLC analysis against 1-methoxynaphthalene internal standard.

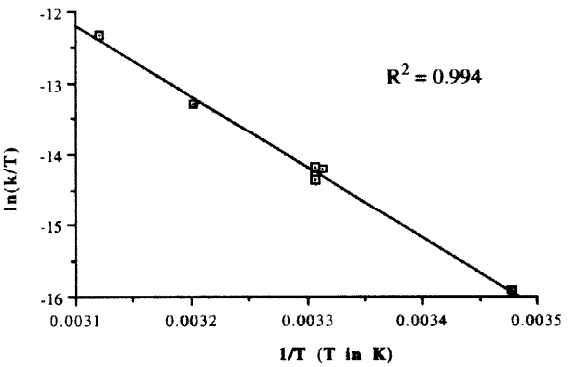


Fig. 5. Eyring plot for the cycloaromatization of 2b in methanol.

Note that **4k** and **4l** bear chiral centers at the propargylic position, and that **4g** and **4h** differ only in the nature of the substituent at the *para* position of the phenyl ring. Compound **4e** produces a complex mixture of products in methanol (see above), but its decomposition kinetics are cleanly first order.

Table 2. Activation Parameters for Cycloaromatization Reactions of Allene Enynes

entry	allene	solvent	$\Delta H^{\ddagger}$ (kcal/mol)	$\Delta S^{\ddagger}$ (e.u.)	Range (°C)	R^2
1	**2a**	MeOH	21.3 ± 0.6	-15.9 ± 1.7	60.0 - 85.0	0.997
2	**2b**	MeOH	19.6 ± 0.5	-10.6 ± 2.0	14.4 - 47.2	0.994
3	**2b**	1,4-CHD	18.2 ± 0.6	-15.6 ± 1.6	14.4 - 47.2	0.997
4	**4g**	MeOH	20.4 ± 0.4	-10.9 ± 1.1	27.9 - 55.2	0.999
5	**4g**	1,4-CHD	19.4 ± 0.6	-14.3 ± 1.9	28.3 - 55.9	0.997
6	**4n**	MeOH	17.6 ± 0.7	-19.9 ± 2.3	27.0 - 61.4	0.991
7	**25** [3a]	1,4-CHD	21.8 ± 0.5	-11.6 ± 1.5	39 - 100	

Lastly, the rates of cycloaromatization of aryl substituted allene enynes **4a-d** bearing a t-butyl group at the alkyne terminus and different *p*-substituted aryl groups at the allene terminus, were also measured. Because allene dimerization occurs in concentrated solutions, these compounds were studied under dilute conditions (2.6 mM) by the HPLC method, as summarized in Table 3.

Table 3. Rates of Cycloaromatization at 85°C of Aryl-Substituted Allene Enynes Bearing t-Butyl Groups.

compound	solvent	*para* substituent	k (s^{-1})	$t_{1/2}$ (min)	# $t_{1/2}$s
4a	MeOH	Me	$(5.7 \pm 0.3) \times 10^{-5}$	203	2.2
4b	MeOH	MeO	$(3.5 \pm 0.3) \times 10^{-5}$	333	1.0
4c	MeOH	Me_2N	$(6.5 \pm 0.4) \times 10^{-5}$	177	1.7
4d	MeOH	CF_3	$(3.3 \pm 0.3) \times 10^{-5}$	354	1.0
4d	1,4-CHD	CF_3	$(4.2 \pm 0.5) \times 10^{-5}$	275	1.8

$t_{1/2}$ = half life; # $t_{1/2}$s = number of half lives

DISCUSSION

Synthesis of Aromatic Allene-Ynes

The synthesis of aromatic allene enynes from *o*-alkynyl aromatic aldehydes has been accomplished via titanium substituted ylides by both one-pot and two-step procedures. In the synthesis of mixed allenes, only alkynes bearing bulky substituents may be introduced in the preparation of the vinylphosphonium salt. In contrast, the incorporation of the alkyne fragment in the second ("trapping") aldehyde allows a range of primary, secondary, and tertiary substituents at the propargylic position to be tolerated. While many of these products may be obtained in comparable or higher yields by other procedures, the titanated ylide method represents a uniquely direct route to a large variety of allene enynes in a short period of time.

Steric Effects in Cycloaromatization

The nature of the substituent at the alkyne terminus of allene enynes has a dramatic effect on the rate of cycloaromatization. For example, the half-lives of aromatic allene diynes **2a-c** at 29.2 degrees are shown in Table 4 to differ by a factor of 244 on going from a t-butyl to an isopropyl substituent, and a factor of 416 on going from t-butyl to n-butyl. Similar rate differences are found for t-butyl vs. i-Pr substitution in allene enynes **4a** and **4g** (203-fold), and indirectly in the comparison of **4e** to **4i** in MeOH [the former compound decomposes by non-cycloaromatization pathways more slowly at 95.2°C than the latter compound cycloaromatizes at 56.4°C (Table 7, Experimental Section)]. The relatively small rate differences for i-Pr vs. n-Bu substitution are also demonstrated by allene enynes **4i** and **4j** (factor of 1.4, Table 4). In an attempt to understand these relative rates, MM2 energy-minimized structures of representative aromatic allene diynes were generated;[10] examples are shown in Fig. 6.

Table 4. Half Lives for Allene Enyne Cycloaromatizations in Methanol.

allene	alkyne substituent	$t_{1/2}$ (min)	T (°C)
2a	t-Bu	14164 [a]	29.2
2b	i-Pr	58 [a]	29.2
2c	n-Bu	34 [b]	29.2
4a	t-Bu	203 [b]	85.0
4g	i-Pr	1 [a]	85.0
4i	i-Pr	230 [b]	56.4
4j	n-Bu	162 [b]	56.1

(a) calculated from activation parameters of Table 2; (b) from results in Table 7

Molecular mechanics calculations show a strong preference for the aromatic rings to be coplanar with the adjacent allene C(H)=C unit, which would also be expected to be favored for stereoelectronic reasons. The presence of a styrene-like band in the 230-240 nm region of the electronic spectra of diarylallenes, including those reported here, verify that this orbital overlap occurs in solution. The coplanar arrangement of arene and adjacent allene fragments thus defines two types of conformations, described as s-*cis* and s-*trans* by the dihedral angle about the arene–allene single bond (see discussion of **4f** and **6**, above). A dihedral angle

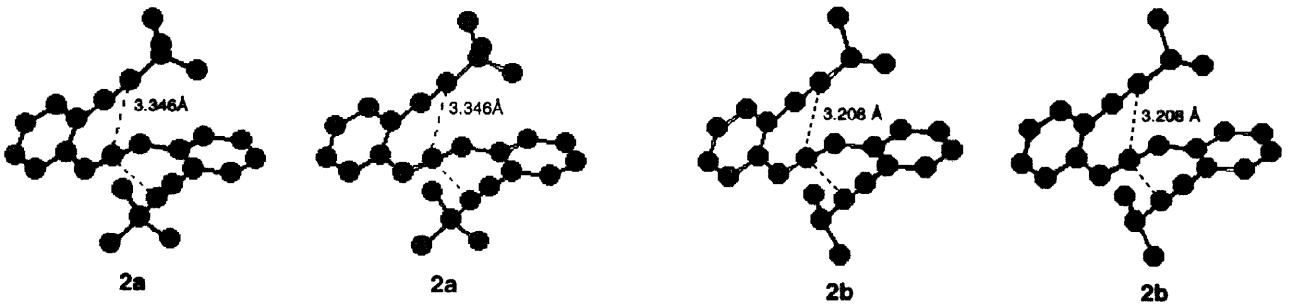


*Fig. 6. Stereoscopic representations of calculated minimum energy conformations of **2a** and **2b**. Dotted lines connect the reactive centers for cycloaromatization; H atoms are omitted for clarity.*

of approximately 0° brings the reactive centers (the central carbon of the allene, designated C1, and the outer carbon of the alkyne, designated C6) closest to each other and is therefore required for cycloaromatization. If both dihedral angles of an aromatic allene di(enyne) are near 0°, the molecule adopts a compact, L-shaped conformation when viewed down the allene axis. A dihedral angle of about 180° produces an extended structure with the alkyne unit as far as possible from the allene.

For **2a-c**, the calculated minimum energy conformations are the "L-shaped" structures, with dihedral angles of 0±2° (Fig. 6). The distance between the reactive centers is calculated to be significantly greater for the stable t-butyl case (3.346 Å) than for the more reactive isopropyl or n-butyl compounds (3.208 Å, 3.212 Å). Analogous minimum-energy structures (not shown) are calculated for the related compounds **4a** (3.339 Å), **4g** (3.222 Å), **4i** (3.245 Å), **4j** (3.239 Å), and **4n** (3.196 Å). Therefore, cycloaromatization rate appears to be inversely proportional to the distance between the reactive centers in the ground state. A correlation of this type was initially proposed for cyclic enediynes,[1a,15] but was later shown to be a function of ring strain energies.[16,17] For acyclic aromatic allene-yne compounds of the type described here, those which adopt ground-state geometries with reactive centers closer than 3.18-3.19 Å are unlikely to be stable toward cycloaromatization at room temperature, whereas compounds with ground-state distances longer than about 3.25-3.3 Å should resist cyclization upon heating.[18] Rates of cycloaromatization for structures of the intermediate distance range are hard to predict, since entropic differences can make a substantial contribution to relative rate. For example, a comparison of the activation parameters for **2a** and **2b** shows that the relative rate difference of 244 for these compounds at 29.2°C is due to both enthalpic and entropic factors in approximately equal amounts.[19] In contrast, allenes **4n** and **4g** react at approximately equivalent rates due to compensating enthalpic and entropic parameters.

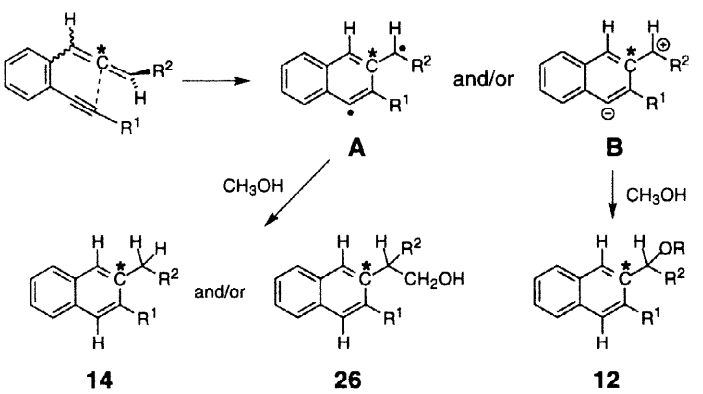
It should be noted that kinetics measurements for **4k** and **4l**, which are obtained as approximately equal mixtures of diastereomers, showed no break in the linear plots around 50% conversion, indicating that little or no kinetic resolution occurs in the cycloaromatizations of **4k** or **4l**. Indeed, unreacted **4k** and **4l**, isolated after approximately 80% completion in the cycloaromatization reaction, showed no change in diastereomeric composition.[20] This is consistent with the very small differences in C1-C6 distances calculated for the competing diastereomers. Although **4l** bears very different groups (methoxy and isopropyl) at the propargylic position, these moieties are directed away from the allene fragment and so experience little differential diastereotopic interaction with the rest of the structure.

Cyclopropyl Ring Opening

Ring opening of allene-terminal cyclopropyl groups occurs under both polar and nonpolar conditions, presumably after cycloaromatization takes place. Phenylcyclopropyl-substituted allenes **4e**, **4i**, and **4j** provide cyclopropyl ring-opened products exclusively. In contrast, the unsubstituted cyclopropylallene **4f** affords the cyclopropyl ether in methanol but the ring-opened alkene in 1,4-cyclohexadiene, which may be related to the relative rates of trapping of ring-opened intermediates in the polar (methanol) vs. diradical (1,4-cyclohexadiene) manifolds. The case of t-butyl phenylcyclopropyl allene **4e** is curious, in that it provides a normal yield of ring-opened alkene in 1,4-cyclohexadiene, but no cycloaromatization products can be detected in methanol, in spite of the first-order kinetics measured for decomposition in that solvent. The cycloaromatization rate of **4f** in methanol, from which a good yield of ether **12f** is isolated, is very similar to that of **4e**, as expected since both structures bear a *tert*-butyl group at the alkyne terminus. Although it is possible that **4e** undergoes a different reaction, the coincident decomposition rates for **4e** and **4f** suggests that both are cycloaromatized, but that trapping of the resulting intermediate(s) from the former structure is not clean under the rather forcing conditions required.

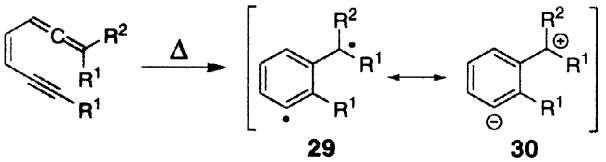
Substituent Electronic Effects in Cycloaromatization

We frame our discussion of electronic effects in terms first applied to allene enyne cycloaromatization by Myers and coworkers.[3a] The process can proceed through diradical (**A**) or dipolar (**B**) intermediates of the kind shown in Scheme 7, or structures that combine elements of both extremes. In each case, the naphthalene C4 position is highly reactive and will capture an H atom from an H• or H^+ donor. Thus, substitution at the benzylic position provides the more informative probe of the character of the cycloaromatization intermediate. Using methanol as an example, the formation of ethers (**12**) is regarded as a signature of a pathway involving significant carbocation character (**B**), whereas hydrocarbon structure **14** or alcohol **26** signals reaction through a diradical intermediate (**A**). It should be emphasized that the nature of the naphthalene intermediate thus disclosed does not necessarily provide information on the nature of the cycloaromatization transition state.



Scheme 7

The cycloaromatization of allene enynes, exemplified by (Z)-1,2,4-heptatrien-6-yne (**25**), was proposed to proceed through a common transition state in nonpolar and polar solvents, leading to a diradical intermediate (**29**) in 1,4-cyclohexadiene or a polar diradical intermediate in methanol, the latter species being best described as a linear combination of the limiting structures **29** and **30** (Scheme 8).[21] The methyl-substituted analogue **27** was found to react in cyclohexadiene 6.5 times faster than **25** at 77-78°C, an effect ascribed to electron donation by the CH_3 group into an electron-deficient transition state leading to the isolation of products derived from radical trapping.[3a] The rate of cycloaromatization of the thioether analogue



29 **30**

25 $R^1 = R^2 = H$ **27** $R^1 = H$, $R^2 = CH_3$
28 $R^1 = CH_2OSiMe_2tBu$, $R^2 = P(O)Ph_2$

Scheme 8

24 was found to be approximately 1400 times faster than that calculated for **25** (10°C, cyclohexadiene solvent), a result also consistent with a polarized transition state.

Consistent with expectations based on the Myers model, our study reveals a substantial difference in cycloaromatization rate of aryl-substituted allenes relative to cyclopropyl-substituted systems. This was observed qualitatively in studies of product structures described above for allenes **4e**, **4f**, **4i**, and **4j**, and confirmed by kinetics measurements. Thus, in methanol, allene **4i** at 57.2°C reacts at a rate (5.23×10^{-5} s^{-1}) 17 times less than that of the aromatic allene analogue **4g** (8.9×10^{-4} s^{-1}, calculated from activation parameters in Table 2, and in 1,4-cyclohexadiene the rate difference is approximately 25-fold at 56°C (Table 7, Experimental Section). Similarly, aromatic allene enynes bearing n-alkyl substituents at the alkyne terminus (such as **4m** and the n-butyl analogue of **4a**) were isolated in poor yields and found to be unstable at room temperature due to facile cycloaromatization, whereas phenylcyclopropyl compound **4j** was easily isolated and showed a half-life of almost 3 h at 56°C.

The cycloaromatization rate difference between aliphatic- and aromatic-substituted allenes is consistent with an early transition state wherein the incipient benzylic radical or carbocation is orthogonal to, and therefore not in conjugation with, the developing aromatic system.[22] Thus, the *p*-tolyl substituent of **4g** provides the only available benzylic stabilization to the transition state structure, which is not available to allene **4i**.[23]

The degree of electronic stabilization of radical and/or cationic character at the developing benzylic position was further probed with the series of *para*-substituted aromatic allene enynes listed in Table 3. Substituent effects on benzylic radicals have been described in the most appropriate fashion by Creary,[24,25] who measured rate constants (k) as a function of aryl substituent (X) for the thermal rearrangement of 2-methylene-arylcyclopropanes to 2-isopropylidene-arylcyclopropanes through a diradical intermediate. The Creary $\sigma_c^{\bullet}$ scale was defined analogous to Hammett[26] σ values: for each substituent, $\rho\sigma_c^{\bullet} = \log(k/k_0)$, where k_0 is the rate constant for the rearrangement for the unsubstituted aryl compound (X = H) and the reaction constant ρ is assigned a value of 1.0. We suggest that S_N1 solvolyses of benzylic halides represent the best model reactions available for Hammett constants describing benzylic cation formation. Three examples provide a range of reaction constant (ρ) values: $ArCH_2Cl + H_2O$ in water ($\rho = -1.3$);[27a] Ar^1Ar^2CHCl + MeOH in MeOH ($\rho = -4.1$);[27b] and $ArPh_2CCl$ + EtOH in EtOH/Et_2O ($\rho = -2.9$).[27b] If one assumes that the developing naphthyl ring does not participate in stabilization of the (orthogonal) benzylic center (*vide supra*), then the first of these ($\rho = -1.3$) should be the most valid for the present application.

Values of the product of the substituent and reaction constants for the above radical and cation model reactions for each substituent used in our study are shown in Table 5, along with the expected relative rates for purely polar (σ^+) and purely radical ($\sigma_c^{\bullet}$) mechanisms derived from these models. The observed rates are remarkably insensitive to the nature of the aromatic substituent, showing a much smaller rate enhancement for the dimethylamino substituent than is predicted by either model. This provides further support for the notion

of a transition state reached early on the reaction coordinate.[22] Although the fit to expected values is poor, the roughly equivalent rates appear to correlate better with the trend expected for a diradical-like process, particularly for the trifluoromethyl case (**4d**).

Table 5. Observed (Table 3) and Calculated ($\rho\sigma_c^{\bullet}$ and $\rho\sigma^{+}$) Relative Rates of Cycloaromatization of t-Butyl Substituted Allene Enynes in Methanol with Respect to **4a**

compound	substituent	$\rho\sigma_c^{\bullet}$ [22]	$\rho\sigma^{+}$ [24,25]	k_{rel} ($\rho_c\sigma^{\bullet}$)	k_{rel} ($\rho\sigma^{+}$)	k_{rel} (obs)
4a	*p*-Me	0.11	0.44	1.0	1.0	1.0
4b	*p*-OMe	0.24	0.70	1.3	1.8	0.6*
4c	*p*-NMe_2	0.90	1.6	6.2	14	1.2
4d	*p*-CF_3	0.08	-1.4	0.9	0.014	0.6

* A similar value is obtained by comparison the observed rate of methoxy allene **4h** at 34.1°C (Table 7, Experimental Section) to the rate of methyl allene **4g** calculated at the same temperature from its measured activation parameters, giving a relative rate of 0.9.

Finally, the electronic effect of *para*-substituents on an aromatic ring at the alkyne terminus was briefly investigated by comparing the cycloaromatization rates of compounds **4n** and **4o**. Using activation parameters determined for **4n** to calculate rates at the temperatures used for **4o**, relative rates (**4o**/**4n**) of 0.9 (28.9°C) and 1.6 (42.7°C) are observed. This suggests that substituents on the alkyne make little electronic contribution to transition state stabilization, in contrast to the change in mechanism and reaction energetics reported for allenic phosphine oxides.[1e,23] It should be noted that, although standard labeled naphthalenic ^{13}C NMR resonances were observed for the dominant products from cycloaromatization of **4n** and **4o**, these products were not characterized in detail. It has been reported that different cyclization products arise from certain aryl-substituted allene enynes.[5]

Myers and coworkers based their hypothesis of a common diradical transition state in polar and nonpolar solvents on the observation of idential rates of cycloaromatization of **25** in CD_3OH and 1,4-cyclohexadiene at a single temperature. We find not a set of identical rates in different solvents, but rather a consistent trend that substantiates the same conclusion. Thus, a comparison of activation parameters for two isopropyl-substituted allenes (**2b** and **4g**) in the two solvents shows a small but significant solvent dependence: in both cases, $\Delta H^{\ddagger}$ is approximately 1 kcal/mol greater in methanol than in 1,4-cyclohexadiene and $\Delta S^{\ddagger}$ is approximately 4 eu more negative in the nonpolar solvent (Table 2). In addition, both **4k** and **4i** react approximately twice as fast in methanol as in 1,4-cyclohexadiene at similar temperatures (Table 7, Experimental Section). The consistent trend of the comparative rates and activation parameters, as well as the relatively small differences in these numbers, gives further support to the proposal of a common cycloaromatization transition state in both polar and nonpolar solvents. Such a transition state is likely to be a linear combination of the two extremes (Scheme 8), with some polar character providing stabilization in methanol and thus lowering the enthalpy of activation in that solvent. The magnitude of the difference in activation entropy is not large enough to permit an unambiguous explanation of its source.

The reaction medium has an important role in determining the mechanistic course after the transition state: polar solvents lead to dipolar-derived products, whereas nonpolar solvents favor the production of

diradical-derived products. Similar dichotomous reactivity has been reported for the cycloaromatization of a cyclic allene enyne sulfone,[28] and the phenomenon has important implications for the use of simple allene enyne compounds as polynucleotide cleavage agents. While strongly electrophilic dipolar intermediates can induce DNA damage, principally by alkylation of polynucleotide bases,[23,29] diradicals are in general more potent because of their extremely high reactivities and their potential for accomplishing simultaneous double-strand scission. Thus, simple allene enynes suffer two disadvantages when compared to ene-diynes, including neocarzinostatin and related natural products: the σ,σ-diradicals produced by the enediynes are of substantially higher energy than the σ,π-diradicals produced by cyclization of allene enynes, and σ,σ-diradical species do not have an easily-accessible dipolar form, and so are not passivated in the presence of polar solvents in this way. Thus, efforts to employ simple allene enyne compounds as radical-based DNA cleavage agents should also include means to accomplish polynucleotide binding before cycloaromatization in a manner that insulates the incipient diradical from its aqueous environment.

Experimental Section

General Methods. ^{1}H,^{13}C, and ^{31}P NMR spectra were recorded at 300, 75.2, and 121.7 MHz, respectively, on either a GE GN-300 or QE-300 instrument. ^{1}H spectra were referenced to residual protons in the solvent, ^{13}C spectra to solvent peaks, and ^{31}P spectra to external H_3PO_4. IR spectra were recorded on a Mattson Cygnus 1000 instrument. Electronic spectra were recorded in quartz solution cells using a Hewlett–Packard 8452A diode array spectrophotometer. Melting points were measured on samples in unsealed capillary tubes and are uncorrected. Elemental analyses were performed on a Perkin-Elmer Model 2400 CHN Analyzer, using acetanilide as the calibration standard. We were unable to obtain satisfactory analyses on product oils; in these cases ≥95% purity is determined by ^{1}H and ^{13}C NMR spectroscopy. High resolution mass spectrometry was performed at The Pennsylvania State University and at the University of Texas at Austin. THF, hexane, and toluene were purified by distillation from Na benzophenone-ketyl; triethylamine was dried by refluxing over potassium hydroxide and distilled. Anhydrous methanol was purchased from Aldrich and used as received; 1,4-cyclohexadiene was purchased from Aldrich and dried by bulb-to-bulb vacuum transfer or distillation from freshly-cast sodium mirror. $Ti(O\underline{i}Pr)_4$ was vacuum distilled and stored under nitrogen. $NaN(SiMe_3)_2$ was obtained either as a solid or in THF solution from Lancaster Chemical Co. or Aldrich Chemical Co. Solid phenyllithium (92% pure by titration), prepared from n-BuLi and bromobenzene, was prepared as previously described.[6c] $(Me_2N)_3P{=}CH_2$ was prepared as previously described;[6c] when desired, $^{13}CH_3I$ (99% enrichment, Cambridge Isotope Laboratories) was used to provide a label at the central allene carbon. Note that the methylide may be generated and used *in situ* from these commercially-available reagents by deprotonation of the intermediate methylphosphonium salt with one equivalent of $NaN(SiMe_3)_2$.[6a] $TiCl_2(O\underline{i}Pr)_2$ was prepared by mixing equimolar hexane solutions of $TiCl_4$ and $Ti(O\underline{i}Pr)_4$. All other reagents were purchased from commercial suppliers and used as received. All manipulations involving ylide species were conducted under dry nitrogen atmosphere, either in an MBraun glovebox (Innovative Technologies, Cambridge, MA) or using standard Schlenk techniques. Abbreviations: CI-MS (chemical ionization mass spectrometry, using methane as reagent gas), HRMS (high resolution mass spectrometry).

Preparation of aldehydes 1. 2-Alkynylbenzaldehydes **1** were prepared by palladium-catalyzed coupling[30] of monosubstituted alkynes with 2-bromobenzaldehyde or the ethylene glycol ketal of 2-iodobenzaldehyde, as follows.

1a A deoxygenated solution of *o*-bromobenzaldehyde (8.4 g, 45 mmol) in triethylamine (80 mL) was treated with triphenylphosphine (0.47 g, 1.8 mmol), palladium acetate (0.20 g, 0.9 mmol) and copper(I) iodide (0.17 g, 0.9 mmol). After 10 minutes, 3,3-dimethyl-1-butyne (5.7 g, 69 mmol) was added via syringe. The reaction was heated at reflux for 6 hours, and then cooled to room temperature. The solution was then filtered in air and partitioned between diethyl ether and water. The organic layer was dried ($MgSO_4$), evaporated, and the resulting 2-alkynylbenzaldehyde was purified by column chromatography on silica gel (EtOAc/petroleum ether), to yield **1a** (7.7 g, 41 mmol, 92%) as a light yellow oil. ^1H NMR ($CDCl_3$, δ) 10.54 (s, 1H), 7.88 (d, J = 7.2 Hz, 1H), 7.47-7.54 (m, 2H), 7.34-7.40 (m, 1H), 1.35 (s, 9H); ^{13}C NMR ($CDCl_3$, δ) 191.3, 135.3, 133.0, 132.6, 127.3, 126.0, 105.4, 74.4, 30.2, 27.8; CI-MS m/z = 187 ($[M+1]^+$).

1b (prepared as for **1a** above, 90% yield as a yellow oil): ^1H NMR ($CDCl_3$, δ) 10.54 (s, 1H), 7.88 (d, J = 8.4 Hz, 1H), 7.47-7.54 (m, 2H), 7.35-7.40 (m, 1H), 2.84 (h, J = 6.9 Hz, 1H), 1.29 (d, J = 6.9 Hz, 6H) ; ^{13}C NMR ($CDCl_3$, δ) 192.6, 136.3, 134.1, 133.6, 128.3, 127.2, 103.7, 75.9, 23.2, 21.8; CI-MS m/z = 173 ($[M+1]^+$).

1c (prepared as for **1a** above, 86% yield as a yellow oil): ^1H NMR ($CDCl_3$, δ) 10.55 (s, 1H), 7.89 (d, J = 7.8 Hz, 1H), 7.50-7.53 (m, 2H), 7.37-7.40 (m, 1H), 2.50 (t, J = 6.9 Hz, 2H), 1.62-1.66 (m, 2H), 1.50-1.54 (m, 2H), 0.97 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, δ) 192.6, 136.4, 134.1, 133.7, 128.4, 128.3, 127.3, 98.6, 76.7, 31.0, 22.5, 19.7, 14.0; CI-MS m/z = 187 ($[M+1]^+$).

1d A solution of 2-(2-iodophenyl)-1,3-dioxolane (2 g, 7.3 mmol) in 100 mL diethylamine was deoxygenated by bubbling with nitrogen for 20 minutes, and then treated with $Pd(PPh_3)_2Cl_2$ (25 mg, 40 mmol) and 3-methyl-1-hexyne (2.1 g, 22 mmol). The solution was again purged with nitrogen (10 minutes), copper(I) iodide (0.08 mmol, 14 mg) was added, and the the mixture was heated at reflux for seven days under inert atmosphere. Workup was performed as above, followed by silica gel chromatography (EtOAc/CH_2Cl_2) to give 2-(3-methyl-1-hexynylphenyl)-1,3-dioxolane (1.7 g, 7.0 mmol, 97%) as a yellow oil. ^1H NMR ($CDCl_3$, δ) 7.57-7.60 (m, 1H), 7.44-7.46 (m, 1H), 7.27-7.33 (m, 2H), 6.23 (s, 1H), 4.05-4.19 (m, 4H), 2.72-2.76 (m, 1H), 1.29-1.75 (m, 4H), 1.30 (d, J = 6.9 Hz, 3H), 0.99 (t, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, δ) 139.1, 132.8, 129.3, 128.0, 126.3, 123.9, 102.5, 100.2, 78.2, 65.9, 39.6, 26.9, 21.5, 21.0, 14.4. Hydrolysis of the ketal (10:1 THF/1N aqueous HCl, 4h, room temperature), followed by extraction and column chromatography (petroleum ether/CH_2Cl_2) gave aldehyde **1d** (1.3 g, 6.5 mmol, 92% yield) as a yellow oil. ^1H NMR ($CDCl_3$, δ) 10.56 (s, 1H), 7.90 (d, J = 7.8 Hz, 1H), 7.51-7.54 (m, 2H), 7.39-7.41 (m, 1H), 2.72-2.78 (m, 1H), 1.50-1.65 (m, 4H), 1.31 (d, J = 6.9 Hz, 3H), 0.98 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, δ) 192.7, 136.3, 134.1, 133.7, 128.4, 128.2, 127.3, 103.0, 76.8, 39.4, 27.0, 21.3, 21.1, 14.3; CI-MS m/z = 201 ($[M+1]^+$).

1e 4-Methyl-1-pentyn-3-ol and 2-(2-iodophenyl)-1,3-dioxolane were coupled as for **1d**, and the crude product was purified by column chromatography (EtOAc/petroleum ether). The crude 2-(3-hydroxy-4-methyl-1-pentynylphenyl)-1,3-dioxolane was obtained as a yellow oil (1.0 g, 4.1 mmol, 57% yield). ^1H NMR ($CDCl_3$, δ) 7.55 (dd, J = 7.5 Hz, J = 1.8 Hz, 1H), 7.42 (dd, J = 7.2 Hz, J = 1.5 Hz, 1H), 7.23-7.33 (m, 2H), 6.19 (s, 1H), 4.37 (d, J = 5.7 Hz, 1H), 3.97-4.12 (m, 4H), 3.65 (br s, 1H), 1.90-2.00 (m, 1H), 1.06 (d, J = 6.6 Hz, 3H), 1.02 (d, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, δ) 139.3, 133.0, 129.4, 128.8, 126.3, 122.6, 102.2, 94.8, 82.7, 68.5,

65.8, 35.1, 18.7, 17.9; CI-MS m/z = 247 ($[M+1]^+$). The propargylic alcohol was then methylated (powdered KOH, DMSO, CH_3I) and purified by column chromatography (petroleum ether/ethyl acetate) to give the corresponding methyl ether in 83% yield. ^1H NMR ($CDCl_3$, δ) 7.61 (dd, J = 7.2 Hz, J = 1.5 Hz, 1H), 7.50 (dd, J = 6.9 Hz, J = 1.2 Hz, 1H), 7.28-7.39 (m, 2H), 6.21 (s, 1H), 3.97-4.21 (m, 4H), 4.01 (d, J = 6.3 Hz, 1H), 3.51 (s, 3H), 2.00-2.10 (m, 1H), 1.11 (d, J = 6.9 Hz, 3H), 1.08 (d, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, δ) 139.4, 133.1, 129.4, 128.8, 126.4, 122.7, 102.3, 92.4, 84.2, 78.0, 65.9, 57.3, 33.6, 19.0, 18.3. Ketal hydrolysis as for **1d** provided **1e** in 86% yield after purification. ^1H NMR ($CDCl_3$, δ) 10.53 (s, 1H), 7.88 (d, J = 7.5 Hz, 1H), 7.49-7.56 (m, 2H), 7.38-7.40 (m, 1H), 3.98 (d, J = 5.7 Hz, 1H), 3.47 (s, 3H), 2.00-2.07 (m, 1H), 1.05 (apparent t (d of doublets), 6.6 Hz separation, 6H); ^{13}C NMR ($CDCl_3$, δ) 191.7, 136.4, 134.1, 134.0, 129.0, 127.5, 126.8, 95.0, 82.5, 77.9, 57.5, 33.5, 19.0, 18.3; CI-MS m/z = 217 ($[M+1]^+$).

1f This aldehyde was prepared from propargyl alcohol and 2-(2-iodophenyl)-1,3-dioxolane in analogous fashion to **1e**. Alkyne coupling provided the substituted propargylic alcohol (60% yield) as a yellow oil. ^1H NMR ($CDCl_3$, δ) 7.57 (dd, J = 7.2 Hz, J = 1.5 Hz, 1H), 7.43 (dd, J = 7.2 Hz, J = 1.5 Hz, 1H), 7.26-7.36 (m, 2H), 6.19 (s, 1H), 4.46 (s, 2H), 4.00-4.16 (m, 4H), 3.17 (br s, 1H); ^{13}C NMR ($CDCl_3$, δ) 139.4, 133.1, 129.5, 129.0, 126.5, 122.3, 102.3, 92.8, 82.9, 66.0, 51.8. Methylation gave the corresponding methyl ether (96% yield) as a yellow oil. ^1H NMR ($CDCl_3$, δ) 7.47 (dd, J = 7.2 Hz, J = 1.5 Hz, 1H), 7.38 (dd, J = 7.2 Hz, J = 1.8 Hz, 1H), 7.20-7.27 (m, 2H), 6.08 (s, 1H), 4.26 (s, 2H), 3.90-4.10 (m, 4H), 3.36 (s, 3H). Lastly, ketal hydrolysis gave **1f** as a yellow oil in 96% yield. ^1H NMR ($CDCl_3$, δ) 10.53 (s, 1H), 7.46-7.52 (m, 2H), 7.35-7.40 (m, 1H), 4.36 (s, 2H), 3.45 (s, 3H); ^{13}C NMR ($CDCl_3$, δ) 191.8, 136.5, 134.2, 133.9, 129.3, 127.6, 126.5, 92.7, 82.4, 60.7, 58.3; CI-MS m/z = 175 ($[M+1]^+$).

1g Coupling of phenylacetylene and 2-bromobenzaldehyde was performed in the manner of **1a** above to give 2-(phenylethynyl)benzaldehyde (**1g**) as a brown oil after workup (93% yield), which was used without further purification. ^1H NMR ($CDCl_3$, δ) 10.63 (s, 1H), 7.91 (d, J = 7.9 Hz, 1H), 7.58-7.47 (m, 5H), 7.38-7.28 (m, 3H); ^{13}C NMR ($CDCl_3$, δ) 190.9, 135.4, 133.4, 133.0, 131.4, 131.2, 128.2, 128.0, 126.8, 126.3, 121.9, 96.0, 84.7; CI-MS m/z = 207 ($[M+1]^+$).

1h Coupling of (4-methoxyphenyl)acetylene and 2-bromobenzaldehyde was performed in the manner of **1a** above to give 2-(4-methoxyphenylethynyl)benzaldehyde (**1h**) as a yellow oil after workup (95% yield), which was used without further purification. ^1H NMR ($CDCl_3$, δ) ^1H NMR ($CDCl_3$, δ) 10.58 (s, 1H), 7.93 (d, J = 4 Hz, 1H), 7.6-7.4 (m, 6H), 3.46 (s, 3H); CI-MS m/z = 237 ($[M+1]^+$).

One-pot preparation of allene diynes. A representative procedure is as follows.

2a. Under a dry nitrogen atmosphere, a solution of $TiCl_2(OiPr)_2$ (150 mg, 0.6 mmol) in 5 mL THF was treated with $(Me_2N)_3P{=}CH_2$ (113 mg, 0.6 mmol) in 2 mL THF, followed immediately by $NaN(SiMe_3)_2$ (0.86 mL of a 2.1 M THF solution, 1.8 mmol). To the stirred red-brown mixture was added aldehyde **1a** (0.71g, 3.8 mmol) in 1 mL THF. The allene is readily identified by thin layer chromatography as the only product of the reaction less polar than the starting aldehyde, and by its characteristic purple color upon development with *p*-anisaldehyde stain. After one hour, the reaction mixture was opened to air and partitioned between diethyl ether and 10% aqueous tartaric acid. The organic layer was dried ($MgSO_4$), evaporated, and chromatographed on silica gel (petroleum ether/CH_2Cl_2) to afford **2a** as a pale yellow oil (93 mg, 0.25 mmol, 40%). ^1H NMR ($CDCl_3$, δ) 7.51 (d, J = 7.5 Hz, 2H), 7.45 (d, J = 7.5 Hz, 2H), 7.05-7.25 (m, 6H) 1.41 (s, 18H);^{13}C NMR

($CDCl_3$, δ) 209.8, 135.1, 132.9, 128.3, 127.4, 127.0, 122.6, 104.3, 97.1, 77.7, 31.6, 28.7; IR (CH_2Cl_2, cm^{-1}) 3050, 2970, 2930, 2868, 2233, 1934, 1595, 1473, 1446, 1363, 1292, 1205, 900, 796; UV-Vis (CH_2Cl_2, nm) 238, 274, 282. The product is unambiguously identified as the allene by the characteristic chemical shift of the central allene carbon (labeled when $^{13}CH_3I$ is used to generate the phosphorus methylide) at 208-209 ppm. Upon ^{13}C enrichment, the allenic signal at 97.1 ppm and the aromatic *ipso* resonance at 122.6 ppm in the ^1H-decoupled ^{13}C NMR spectrum are replaced by doublets ($^1J_{CC}$ = 101 Hz, and $^2J_{CC}$ = 6 Hz, respectively).

2b. Using aldehyde **1b**, the above procedure provided **2b** in only 7% yield. The yields were improved to 30% by cooling the solutions of titanated ylide (composed of $TiCl_2(OiPr)_2$, $(Me_2N)_3P{=}CH_2$ and $NaN(SiMe_3)_2$) and aldehyde to approximately -20°C prior to mixing them to initiate the reaction. The reaction mixture was then allowed to stand at ambient temperature for 45 minutes, and was then cooled to 0°C. Workup and chromatography was performed as above, except that all manipulations were conducted in a cold room at 4°C, and rotary evaporation was performed with the sample immersed in an ice/water bath. Allene **2b** was isolated as a light yellow oil. ^1H NMR ($CDCl_3$, δ) 7.49 (d, J = 7.5 Hz, 2H), 7.43 (d, J = 7.5 Hz, 2H), 7.13-7.24 (m, 6H), 2.86 (h, J = 6.6 Hz, 2H), 1.32 (d, J = 6.6 Hz, 12H);^{13}C NMR ($CDCl_3$, δ) 209.7, 135.2, 132.9, 128.2, 127.3, 127.1, 122.5, 101.5, 97.1, 78.3, 23.5, 21.2. ^{13}C enrichment at the central allene carbon gave rise to splitting of the resonance assigned to the outer allene carbons at 97.1 ppm ($^1J_{CC}$ = 102 Hz).

2c. Using aldehyde **1c** in a procedure analogous to that above for **2b** (including workup and chromatography at 4°C), the n-butylallene **2c** was isolated as a light yellow oil in 6% yield. For the ^{13}C-enriched compound, ^1H NMR ($CDCl_3$, δ) 7.46 (d, J = 7.8 Hz, 2H), 7.41 (d, J = 7.5 Hz, 2H), 7.11-7.22 (m, 6H), 2.46 (t, J = 6.9 Hz, 2H), 1.46-1.64 (m, 4H), 0.96 (t, J = 7.2 Hz, 3H) ;^{13}C NMR ($CDCl_3$, δ) 209.8, 135.2, 132.9, 128.2, 127.3, 127.1, 122.3, 97.0 ($^1J_{CC}$ = 102 Hz), 96.2, 79.1, 31.3, 22.5, 19.8, 14.1; IR (CH_2Cl_2, cm^{-1}) 3048, 2958, 2933, 2874, 2225, 1886, 1695, 1595, 1467, 1267, 906, 717; UV-Vis (CH_2Cl_2, nm) 234, 272, 282.

Synthesis of vinylphosphonium salts. Unless otherwise described, vinylphosphonium salts were prepared by the following procedure.

3a. A solution of $TiCl_2(OiPr)_2$ (1.3 g, 5.4 mmol) in 100 mL of THF was treated with $(Me_2N)_3P{=}CH_2$ (0.957 g, 5.4 mmol), followed immediately by $NaN(SiMe_3)_2$ (5.4 mmol). To the resulting red-brown mixture was added aldehyde **1a** (2.5 g, 13.4 mmol). After 2–3 hours at room temperature, the slow precipitation of vinylphosphonium salt was accelerated by the addition of 50 mL hexane, and the reaction mixture was allowed to settle overnight. Vinylphosphonium chloride salt **3a•Cl** was isolated by filtration and washed with a small amount of hexane. Excess aldehyde may be recovered from the filtrate by chromatography. After brief drying under vacuum, **3a•Cl** was dissolved in water, filtered to remove a brown insoluble solid, and the resulting solution was treated with an aqueous solution of $NaBPh_4$ (1.8 g, 5.4 mmol), causing immediate precipitation of **3a•BPh$_4$**. In some cases, the precipitation of vinylphosphonium tetraphenylborates may be aided by the addition of saturated aqueous sodium chloride to the aqueous mixture. The white solid was filtered, rinsed well (8 x 20 mL) with water to remove excess $NaBPh_4$, and then dried in a vacuum dessicator for two days prior to use (1.7 g, 2.5 mmol, 47% yield based on methylide). For **3a•Cl**: ^1H NMR (D_2O, δ) 7.80 (d, J = 7.8 Hz, 1H), 7.50 (dd, J = 18.3 Hz, J_{PH} = 23.1 Hz, 1H), 7.31-7.36 (m, 1H), 7.05-7.15 (m, 2H), 6.71 (dd, J = 18.3 Hz, J_{PH} = 20.7 Hz), 2.69 (d, $^3J_{PH}$ = 9.9 Hz, 18H), 1.26 (s, 9H);^{13}C NMR (D_2O, δ) 148.5

(d, $^2J_{PC}$ = 6.7 Hz), 134.9 (d, $^3J_{PC}$ = 22.0 Hz), 133.0, 131.3, 129.4, 127.3, 124.5, 109.9 (d, $^1J_{PC}$ = 161.0 Hz), 106.0, 77.1, 36.7 (d, $^2J_{PC}$ = 3.4 Hz), 31.1, 28.4. When the salt is prepared with $(Me_2N)_3P{=}^{13}CH_2$, the ^{1}H NMR resonance at 6.71 ppm is replaced by one at 6.67 ppm (ddd , $^1J_{CH}$ = 161.6 Hz, J = 17.4 Hz, $^2J_{PH}$ = 21.3 Hz). For **3a•BPh$_4$**: ^{1}H NMR (CD_3CN, δ) 7.72-7.85 (m, 2H), 7.40-7.47 (m , 4H), 7.20-7.28 (m , 8H), 6.95-7.00 (m, 8H), 6.80-6.85 (m, 3H), 6.62 (dd, J = 18.3 Hz, J_{PH} = 20.7 Hz), 2.76 (br d, $^3J_{PH}$ = 10.2 Hz, 18H), 1.34 (s, 9H); ^{31}P NMR (CD_3CN, δ) 50.7, IR (KBr, cm^{-1}) 3051, 2966, 2233, 1589, 1477, 1302, 1168, 993, 856, 707; UV-Vis (CH_2Cl_2, nm) 244, 286, 330. Anal. Calcd for $C_{44}H_{53}N_3BP$: C, 79.39; H, 8.02; N, 6.31. Found: C, 79.10; H, 7.97; N, 6.56.

3b. Prepared with 99% ^{13}C enrichment; **3b•**BPh_4 was isolated as a white solid in 43% yield. For **3b•Cl**: ^{1}H NMR (D_2O, δ) 7.77 (d, J = 8.1 Hz, 1H), 7.48 (dd, J = 17.7 Hz, $^3J_{PH}$ = 23.1 Hz, 1H), 7.34 (t, J = 7.2 Hz, 1H), 7.03-7.12 (m, 2H), 6.70 (ddd, $^1J_{CH}$ = 161.7 Hz, J = 17.7 Hz, $^2J_{PH}$ = 21.6 Hz), 2.73 (h, J = 6.9 Hz, 1H), 2.67 (d, $^3J_{PH}$ = 10.2 Hz, 18H), 1.19 (d, J = 6.9 Hz, 6H); ^{13}C NMR (D_2O, δ) 148.6 (dd, $^1J_{CC}$ = 68.2 Hz, $^2J_{PC}$ = 7.2 Hz), 134.9 (d, $^3J_{PC}$ = 22.3 Hz), 132.9, 131.3, 129.3, 127.2, 124.6 (d, $^4J_{PC}$ = 3.9 Hz), 109.9 (d, $^1J_{PC}$ = 160.6 Hz), 103.4, 77.6, 36.7 (d, $^2J_{PC}$ = 3.3 Hz), 23.2, 21.5. **3b•**BPh_4: ^{1}H NMR (CD_3CN, δ) 7.72-7-86 (m, 2H), 7.38-7.50 (m, 4H), 7.21-7.27 (m, 8H), 6.92-7.00 (m, 8H), 6.79-6.84 (m, 3H), 6.68 (ddd, $^1J_{CH}$ = 161.7 Hz, J = 17.7 Hz, $^2J_{PH}$ = 22.2 Hz), 2.88 (h, J = 6.9 Hz), 2.76 (d, $^3J_{PH}$ = 9.6 Hz, 18H), 1.26 (d, J = 6.6 Hz, 6H); IR (KBr, cm^{-1}) 3051, 2995, 2228, 1581, 1479, 1300, 1167, 991, 742, 732, 607; UV-Vis (CH_2Cl_2, nm) 244, 286, 326; ^{31}P NMR (CH_2Cl_2, δ) 50.7 (d, $^1J_{PC}$ = 163.7 Hz). Anal. Calcd for $C_{43}H_{51}N_3BP$: C, 79.25; H, 7.89; N, 6.45. Found: C, 78.94; H, 7.92; N, 6.51.

3d. Prepared with 99% ^{13}C enrichment; **3d•**BPh_4 was isolated as a white solid in 51% yield. For **3d•**Cl: ^{1}H NMR (D_2O, δ) 7.92 (d, J = 8.1 Hz, 1H), 7.48 (dd, J = 17.9 Hz, J_{PH} = 22.5 Hz, 1H), 7.38 (t, J = 7.5 Hz, 1H), 7.00-7.09 (m, 2H), 6.83 (ddd, $^1J_{CH}$ = 162.0 Hz, J = 18.0 Hz, $^2J_{PH}$ = 21.0 Hz), 2.68 (d, $^3J_{PH}$ = 9.9 HZ, 18H), 2.55-2.70 (m, 1H), 1.36-1.48 (m, 4H), 1.19 (d, J = 6.6 Hz, 3H), 0.93 (t, J = 6.6 Hz, 3H); ^{13}C NMR (D_2O, δ) 148.0 (dd, $^1J_{CC}$ = 67.1 Hz, $^2J_{PC}$ = 6.6 Hz), 135.2 (d, $^3J_{PC}$ = 22.0 Hz), 132.7, 130.9, 129.6, 127.7, 124.6 (d, $^4J_{PC}$ = 3.8 Hz), 110.6 (d, $^1J_{PC}$ = 160.3 Hz), 101.7, 78.8, 39.4, 36.7 (d, $^2J_{PC}$ = 3.5 Hz), 26.8, 21.5, 21.1, 14.3. For **3d•BPh$_4$**: IR (KBr, cm^{-1}) 3052, 2964, 2224, 1583, 1496, 1302, 1170, 993, 742, 707, 613; UV-Vis (CH_2Cl_2, nm) 244, 286, 330; ^{31}P NMR (CH_2Cl_2, δ) 51.1 (d, $^1J_{PC}$ = 168.0 Hz).

3e. Prepared with 99% ^{13}C enrichment; **3e•**BPh_4 was isolated as a white solid in 44% yield. For **3e•**Cl: ^{1}H NMR (D_2O, δ) 7.81 (d, J = 8.1 Hz, 1H), 7.59 (dd, J = 18.0 Hz, J_{PH} = 22.5 Hz, 1H), 7.43 (t, J =7.5 Hz, 1H), 7.26-7.34 (m, 2H), 6.72 (ddd, $^1J_{CH}$ = 161.7 Hz, J = 18.0 Hz, $^2J_{PH}$ = 21.9 Hz, 1H), 4.05 (d, J = 5.4 Hz, 1H), 3.40 (s, 3H), 2.73 (d, $^3J_{PH}$ = 9.9 Hz, 18H), 1.90-2.05 (m, 1H), 0.95 (d, J = 6.9 Hz, 3H), 0.94 (d, J = 6.6 Hz, 3H). For **3e•BPh$_4$**: ^{1}H NMR (CD_3CN, δ) 7.81-7.85 (m, 1H), 7.81 (dd, J = 17.7 Hz, J_{PH} = 22.8 Hz, 1H), 7.45-7.58 (m, 3H), 7.24-7.27 (m, 8H), 6.96-7.00 (m, 8H), 6.66 (dd, $^1J_{CH}$ = 161.7 Hz, J = 17.7 Hz, $^2J_{PH}$ = 21.9 Hz, 1H), 4.05 (d, J = 5.4 Hz, 1H), 3.42 (s, 1H), 2.74 (d, $^3J_{PH}$ = 9.9 Hz, 18H), 1.97-2.08 (m, 1H), 1.04 (d, J = 6.9 Hz, 3H), 1.02 (d, J = 6.9 Hz, 3H); ^{13}C NMR (CH_2Cl_2, δ) 163.5 (q, $^1J_{BC}$ = 49.2 Hz), 150.0 (dd, $^1J_{CC}$ = 68.0 Hz, $^2J_{PC}$ = 6.6 Hz), 135.4, 133.5 (d, $^3J_{PC}$ = 22.0 Hz), 132.9, 131.2, 128.7, 125.9, 125.1, 123.6, 121.3, 106.6 (d, $^1J_{PC}$ = 163.3 Hz), 94.2, 82.8, 77.0, 56.5, 36.2, 32.6, 17.9, 17.2; IR (CH_2Cl_2, cm^{-1}) 3057.4, 2984.1, 2824.0, 2305.0, 1581.7, 1477.6, 1302.0, 1172.8, 1302.0, 1172.8, 1089.9, 997.3, 854.5; UV-Vis (CH_2Cl_2, nm) 242, 288, 326; ^{31}P NMR (CH_2Cl_2, δ) 50.7 (d, $^1J_{PC}$ = 164.7 Hz).

3f. Prepared by an older procedure than the one described above, employing $TiCl_3(O\underline{i}Pr)$ instead of $TiCl_2(O\underline{i}Pr)_2$, **3f**•$BPh_4$ was isolated as a white solid in 41% yield. For **3f**•Cl: ^1H NMR (D_2O, δ) 7.70 (d, J = 7.2 Hz, 1H), 7.57 (dd, J = 18.1 Hz, J_{PH} = 23.1 Hz, 1H), 7.37-7.44 (m, 3H), 6.69 (dd, J = 18.3 Hz, J_{PH} = 21.3 Hz, 1H), 4.36 (s, 2H), 3.42 (s, 3H), 2.72 (d, $^3J_{PH}$ = 9.9 Hz, 18H); ^{13}C NMR (D_2O, δ) 148.9 (d, $^2J_{PC}$ = 7.0 Hz), 135.5 (d, $^3J_{PC}$ = 22.4 Hz), 133.3, 131.5, 130.1, 127.0, 122.9, 110.2 (d, $^1J_{PC}$ = 160.4 Hz), 91.6, 84.2, 60.3, 57.9, 36.6 (d, $^2J_{PC}$ = 3.6 Hz). For **3f**•BPh_4: ^1H NMR (CD_3CN, δ) 7.72 (m, 2H), 7.45-7.56 (m, 4H), 7.20-7.43 (m, 8H), 6.95-6.99 (m, 8H), 6.79-6.93 (m, 3H), 6.69 (dd, J = 18.0 Hz, J_{PH} = 21.9 Hz, 1H), 4.35 (s, 2H), 3.38 (s, 3H), 2.74 (d, $^3J_{PH}$ = 9.9 Hz, 18H); ^{31}P NMR (CD_3CN, δ) 51.8.

5a, **5b**, **and 5c**. Complete characterization of these tetraphenylborate salts is reported in reference 6c. They were isolated here in yields of 66%, 70%, and 22%, respectively. **5d**•BPh_4 was prepared in fully ^{13}C-enriched form from *trans*-2-phenylcyclopropane carboxaldehyde by the above procedure (but using only two equivalents of aldehyde) as a white solid in 33% yield. For **5d•Cl**: ^1H NMR (D_2O, δ) 7.23-7.28 (m, 2H), 7.10-7.13 (m, 3H), 6.30 (ddd, $^3J_{PH}$ = 21.0 Hz, J = 16.8 Hz, $^2J_{CH}$ = 9.3 Hz, 1H), 5.77 (ddd, $^2J_{PH}$ = 23.1 Hz, J = 16.8 Hz, $^1J_{CH}$ = 159.6 Hz, 1H), 2.68 (d, $^3J_{PH}$ = 9.9 Hz, 18H), 2.31-2.37 (m, 1H), 1.90-1.94 (m, 1H), 1.49-1.56 (m, 1H), 1.40-1.47 (m, 1H); ^{13}C NMR (D_2O, δ) 159.0 (dd, $^1J_{CC}$ = 66.1 Hz, ^2JP_C = 5.1 Hz), 140.8, 128.3, 125.9, 125.5, 106.4 (d, $^1J_{PC}$ = 162.6 Hz), 35.8 (d, $^2J_{PC}$ = 2.8 Hz), 28.7, 26.5, 18.3. For **5d•BPh_4**: IR (KBr, cm^{-1}) 3049, 2995, 1616, 1479, 1300, 1172, 993, 823, 705; UV-Vis (CH_2Cl_2, nm) 234; ^{31}P NMR (CH_2Cl_2, δ) 49.4 (d, $^1J_{PC}$ = 158.0 Hz).

Synthesis of allene ynes from vinylphosphonium salts. A representative procedure is as follows.

4a. A solution of **3a**•BPh_4 (400 mg, 0.6 mmol, 99% ^{13}C labeled) in 60 mL was cooled to -78°C under a nitrogen atmosphere and treated with PhLi (137 mg, 1.5 mmol, in 10 mL THF) by syringe, causing an immediate color change to yellow-orange indicating the formation of the intermediate allenic phosphorane. After 30 minutes at –78°C, a cooled, degassed solution of 4-methylbenzaldehyde (576 mg, 4.8 mmol, in 10 mL THF) was added rapidly by syringe, resulting in immediate discharge of the orange color to give a pale yellow solution. The reaction mixture was allowed to warm to room temperature over 4 hours, and was then partitioned between water and diethyl ether. Following extraction, drying of the organic layer ($MgSO_4$), and rotary evaporation, the crude product was purified by column chromatography (petroleum ether/CH_2Cl_2) to isolate the nonpolar allene **4a** (117 mg, 0.4 mmol) in 68% yield. Unless otherwise indicated, all allenes were isolated as yellow oils and yields are given of isolated compounds after chromatography. ^1H NMR ($CDCl_3$, δ) 7.57 (d, J = 7.5 Hz, 1H), 7.53 (d, J = 7.2 Hz, 1H), 7.38 (d, J = 7.8 Hz, 2H), 7.20-7.30 (m, 5H), 6.71 (dd, J = 4.2 Hz, $^2J_{CH}$ = 6.6 Hz, 1H), 2.45 (s, 3H), 1.49 (s, 9H);^{13}C NMR ($CDCl_3$, δ) 207.9, 134.4, 132.0, 130.1, 128.3 (d, $^2J_{CC}$ = 6.2 Hz), 129.1, 127.3, 126.5, 126.4, 126.4, 126.1, 126.0, 121.6 (d, $^2J_{CC}$ = 5.8 Hz), 103.3, 97.8 (d, $^1J_{CC}$ = 101.2 Hz), 96.1 (d, $^1J_{CC}$ = 101.2 Hz), 76.8, 30.7, 27.9, 20.8; IR (CH_2Cl_2, cm^{-1}) 3026, 2970, 2928, 2868, 2233, 1595, 1512, 1485, 1363, 1292, 1205, 887, 827; UV-Vis (CH_2Cl_2, nm) 232, 242, 268.

4b. Prepared from **3a**•BPh_4 and 4-methoxybenzaldehyde in 53% yield (20 mg, 0.07 mmol). ^1H NMR ($CDCl_3$, δ) 7.45 (d, J = 7.8 Hz, 1H), 7.40 (d, J = 7.2 Hz, 1H), 7.29 (d, J = 8.7 Hz, 2H), 7.11-7.20 (m, 3H), 6.87 (d, J = 8.7 Hz, 1H), 6.58 (dd, J = 4.2 Hz, $^2J_{CH}$ = 6.6 Hz, 1H), 3.81 (s, 3H), 1.36 (s, 9H); ^{13}C NMR ($CDCl_3$, δ)

207.5, 103.3, 99.2 (d, $^1J_{CC}$ = 91.6 Hz), 96.0 (d, $^1J_{CC}$ = 91.4 Hz), 76.7, 54.9, 30.7, 27.8; IR (CH_2Cl_2, cm^{-1}) 3061, 2968, 2931, 2229, 1886, 1635, 1510, 1248, 1173, 1031, 837; UV-Vis (CH_2Cl_2, nm) 236, 274, 368.

4c. Prepared from **3a**•BPh_4 and 4-dimethylaminobenzaldehyde in 13% yield (25 mg, 0.08 mmol). ^1H NMR ($CDCl_3$, δ) 7.48 (d, J = 7.5 Hz, 1H), 7.40 (d, J = 7.5 Hz, 1H) 7.26 (d, J = 8.7 Hz, 2H), 7.09-7.20 (m, 3H), 6.71 (d, J = 8.7 Hz, 1H), 6.59 (dd, J = 4.2 Hz, $^2J_{CH}$ = 6.6 Hz, 1H), 2.96 (s, 6H), 1.38 (s, 9H); ^{13}C NMR ($CDCl_3$, δ) 207.5, 135.0, 131.9, 127.5, 127.4, 127.2, 126.1, 126.0, 120.6, 97.7 (d, $^1J_{CC}$ = 101.2 Hz), 95.9 (d, $^1J_{CC}$ = 101.3 Hz), 84.0, 76.8, 40.1, 30.7; IR (CH_2Cl_2, cm^{-1}) 3049, 2968, 2808, 2231, 1884, 1608, 1521, 1483, 1356, 1265, 1165, 725; UV-Vis (CH_2Cl_2, nm) 236, 268, 298.

4d. Prepared from **3a**•BPh_4 and five equivalents of 4-trifluoromethylbenzaldehyde as a trapping agent, in 30% yield (86 mg, 0.26 mmol). ^1H NMR ($CDCl_3$, δ) 7.57 (d, J = 8.1 Hz, 2H), 7.41-7.47 (m, 4H), 7.16-7.22 (m, 3H), 6.64 (dd, J = 4.2 Hz, J = 6.0 Hz, 1H), 1.372 (s, 9H); ^{13}C NMR ($CDCl_3$, δ) 209.0, 127.4, 126.9, 126.8, 126.7, 126.6, 126.2, 126.1, 125.3 (q, $^3J_{CF}$ = 3.6 Hz), 122.0, 121.9, 103.7, 97.2 (d, $^1J_{CC}$ = 101.2 Hz), 97.1 (d, $^1J_{CC}$ = 103.2 Hz), 89.8, 30.6, 27.8. (Note that the carbons α and β to the fluorines were not detected, but the γ carbon was found to exhibit the same $^3J_{CF}$ coupling constant as the equivalent carbon in the parent aldehyde.) IR (CH_2Cl_2, cm^{-1}) 2970, 2930, 2868, 2233, 1888, 1633, 1325, 1167, 1124, 1066, 848; UV-Vis (CH_2Cl_2, nm) 234, 242, 270.

4e. Prepared from **3a**•BPh_4 and four equivalents of *trans*-2-phenylcyclopropyl carboxaldehyde as a trapping agent, in 68% yield as an equimolar mixture of diastereomers (182 mg, 0.60 mmol). ^1H NMR ($CDCl_3$, δ) 7.51 (t, J = 6.3 Hz, 1H), 7.43 (d, J = 7.5 Hz, 1H), 7.28-7.35 (m, 2H), 7.22-7.25 (m, 2H), 7.13-7.19 (m, 3H) 6.87-6.93 (m, 1H), 5.65-5.75 (m, 1H), 2.01-2.10 (m, 1H), 1.66-1.77 (m, 1H), 1.42 (s, 9H), 1.18-1.34 (m, 2H); ^{13}C NMR ($CDCl_3$, δ) 205.8 & 205.7 (two diastereomers), 135.7, 132.3, 129.6, 128.4, 127.6, 126.5, 126.3, 126.1, 125.7, 122.0, 103.5, 98.3 (d, $^1J_{CC}$ = 102.2 Hz) & 98.2 (d, $^1J_{CC}$ = 102.3 Hz) (two diastereomers), 95.0 (d, $^1J_{CC}$ = 101.0 Hz), 77.3, 31.2, 28.3, 25.83 & 25.81 (two diastereomers), 21.8 & 21.4 (two diastereomers), 17.2 & 17.1 (two diastereomers); IR (CH_2Cl_2, cm^{-1}) 3068, 3030, 2970, 2930, 2868, 2234, 1896, 1604, 1496, 1445, 1363, 1294, 1205, 883; UV-Vis (CH_2Cl_2, nm) 236, 268.

4f. Prepared from **3a**•BPh_4 and four equivalents of cyclopropyl carboxaldehyde as a trapping agent, isolated as a white crystalline solid in 68% yield (56 mg, 0.24 mmol). ^1H NMR ($CDCl_3$, δ) 7.46 (d, J = 7.8 Hz, 1H), 7.39 (d, J = 7.2 Hz, 1H), 7.23 (t, J = 7.5 Hz, 1H), 7.12 (t, J = 8.1 Hz, 1H), 6.81 (dd, J = 3.6 Hz, $^2J_{CH}$ = 6.6 Hz, 1H), 5.48 (ddd, $^2J_{CH}$ = 6.6 Hz, J = 6.9 Hz, J = 3.0 Hz, 1H), 1.42-1.47 (m, 1H), 1.39 (s, 9H), 0.77-0.83 (m, 2H), 0.48-0.52 (m, 2H); ^{13}C NMR ($CDCl_3$, δ) 205.5, 132.2, 128.7, 127.6, 126.3, 126.1, 121.8, 103.3, 99.2 (d, $^1J_{CC}$ = 102.2 Hz), 94.3 (d, $^1J_{CC}$ = 100.8 Hz), 77.2, 31.1, 28.2, 9.4, 7.0, 6.8; IR (CH_2Cl_2, cm^{-1}) 3084, 2970, 2930, 2868, 2233, 1896, 1595, 1485, 1363, 1294, 1205, 931; UV-Vis (CH_2Cl_2, nm) 236, 268.

Crystals suitable for x-ray diffraction were obtained by slow evaporation at −10°C of a methylene chloride solution. Pertinent bond lengths (Å) and angles include: C1-C2 1.299(7), C2-C3 1.324(7), C13-C14 1.194(7), C1-C2-C3 177.6(5)°, C4-C1-C2 124.4(5)°, C2-C3-C7 123.2(5)°, C8-C13-C14 177.8(5)°, C13-C14-C15 177.5(5).

4g. Prepared from **5a**•BPh_4 and **1b**, in 30% yield (135 mg, 0.50 mmol). ^1H NMR ($CDCl_3$, δ) 7.53 (d, J = 7.5 Hz, 1H), 7.50 (d, J = 7.5 Hz, 1H), 7.34 (d, J = 7.8 Hz, 2H), 7.17-7.27 (m, 5H), 6.67 (dd, J = 4.2 Hz, $^1J_{CH}$ = 6.6 Hz, 1H), 2.92 (h, J = 6.6 Hz, 1H), 2.41 (s, 3H), 1.38 (d, J = 6.6 Hz, 6H); ^{13}C NMR ($CDCl_3$, δ) 207.9, 130.1, 129.0, 128.7, 127.3, 126.5, 126.45, 126.39, 126.1, 121.6, 100.6, 97.7 (d, $^1J_{CC}$ = 101.4 Hz), 96.1 (d,

$^1J_{CC}$ = 101.2 Hz), 77.5, 22.7, 21.0, 20.8; IR (CH_2Cl_2, cm^{-1}) 3026, 2972, 2930, 2872, 2225, 1886, 1695, 1595, 1512, 1485, 1321, 1105, 887; UV-Vis (CH_2Cl_2, nm) 234, 242, 248, 268.

4h. Prepared from **5b**•BPh_4 and **1b**, in 42% yield (83 mg, 0.29 mmol). ^1H NMR ($CDCl_3$, δ) 7.42-7.49 (m, 1H), 7.31(d, J = 7.8 Hz, 2H), 7.12-7.23 (m, 4H), 6.98 (d, J = 7.5 Hz, 2H), 6.60-6.63 (m, 1H), 3.81 (s, 3H), 2.80 (h, J = 6.9 Hz, 1H), 1.33 (d, J = 6.9 Hz, 6H); ^{13}C NMR ($CDCl_3$, δ) 207.6, 132.0, 130.1, 127.70, 127.64, 127.3, 126.7, 126.4, 126.1, 125.3, 121.5, 100.5, 97.4 (d, $^1J_{CC}$ = 89.2 Hz), 96.1 (d, $^1J_{CC}$ = 89.2 Hz), 77.4, 54.9, 22.7, 21.0; IR (CH_2Cl_2, cm^{-1}) 3061, 2972, 2935, 2839, 2225, 1693, 1606, 1510, 1249, 1172, 1031, 837, 715; UV-Vis (CH_2Cl_2, nm) 234, 272.

4i. Prepared from **5d**•BPh_4 and **1b**, in 33% yield (48 mg, 0.16 mmol). ^1H NMR ($CDCl_3$, δ) 7.40-7.55 (m, 2H), 7.20-7.35 (m, 3H), 7.10-7.20 (m, 4H), 6.89-6.90 (m, 1H), 5.70-5.80 (m, 1H), 2.80-2.85 (m, 1H), 2.00-2.15 (m, 1H), 1.60-1.75 (m, 1H), 1.35 (d, J = 6.6 Hz, 6H), 1.13-1.25 (m, 1H); ^{13}C NMR ($CDCl_3$, δ) 206.2 and 206.0 (two diastereomers), 132.8, 128.8, 128.2, 127.0, 126.8, 126.6, 126.0, 122.4, 101.2, 98.63 (d, $^1J_{CC}$ = 102.8 Hz) and 98.56 (d, $^1J_{CC}$ = 102.4 Hz) (two diastereomers), 95.4 (d, $^1J_{CC}$ = 101.5 Hz), 77.8, 26.3, 23.6, 22.2, 21.9 and 21.8 (two diastereomers), 17.6 and 17.5 (two diastereomers); IR (CH_2Cl_2, cm^{-1}) 3030, 2972, 2225, 1896, 1604, 1485, 1444, 1321, 1105, 863; UV-Vis (CH_2Cl_2, nm) 236, 268.

4j. Prepared from **5d**•BPh_4 and **1c**, in 14% yield (44 mg, 0.14 mmol). ^1H NMR ($CDCl_3$, δ) 7.44-7.48 (m, 1H), 7.40 (d, J = 7.5 Hz, 1H), 7.10-7.32 (m, 7H), 6.85-6.89 (m, 1H), 5.62-5.73 (m, 1H), 2.39-2.51 (m, 2H), 1.90-2.04 (m, 2H), 1.49-1.71 (m, 4H), 1.15-1.29 (m, 3H), 0.89-1.01 (m, 3H); IR (CH_2Cl_2, cm^{-1}) 3030, 2931, 2872, 2220, 1896, 1604, 1485, 1460, 1105, 1039, 883; UV-Vis (CH_2Cl_2, nm) 236, 270.

4k. Prepared from **3d**•BPh_4 and eight equivalents of 4-methylbenzaldehyde in 25% yield (45 mg, 0.15 mmol). In contrast to analogous reactions of all other aromatic vinylphosphonium salts, treatment of **3d**•BPh_4 with PhLi produced a dark red solution, the color of which does not completely disappear upon addition of trapping aldehyde. Instead, the reaction mixture turns dark green immediately and then dark brown over time. ^1H NMR ($CDCl_3$, δ) 7.45-7.52 (m, 2H), 7.28-7.35 (m, 2H), 7.10-7.28 (m, 5H), 6.64 (dd, J = 4.2 Hz, J_{CH} = 6.6 Hz, 1H) 2.65-2.80 (m, 1H), 2.39 (s, 3H), 1.50-1.75 (m, 4H), 1.34 (d, J = 6.9 Hz, 3H), 1.02 (t, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, δ) 208.8, 131.4, 129.9, 129.6, 127.8, 127.4, 126.9, 126.7, 125.3, 98.5 (d, $^1J_{CC}$ = 103.0 Hz), 97.1 (d, $^1J_{CC}$ = 103.2 Hz), 86.2, 79.7, 39.4, 26.6, 21.5, 21.1, 14.2.

4l. Prepared from **5a**•BPh_4 and **1e**, in 28% yield (33 mg, 0.10 mmol). ^1H NMR ($CDCl_3$, δ) 7.52 (d, J = 8.1 Hz, 1H), 7.27-7.31 (m, 3H), 7.16-7.22 (m, 4H), 6.65 (d, J = 6.6 Hz, 1H), 4.04 (d, J = 5.7 Hz, 1H), 3.55 (s, 3H), 2.38 (s, 3H), 2.10-2.20 (m, 1H), 1.16 (d, J = 6.6 Hz, 6H), 1.13 (s, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, δ) 208.5, 137.2, 135.4, 132.8, 130.3, 129.5, 128.5, 126.94, 126.89, 126.7, 121., 98.4, 9.5, 92.1, 84.6, 57.0, 33.2, 21.2, 18.7, 18.0.

4m. Prepared from **5a**•BPh4 and **1f**, in 7% yield (10 mg, 36 mmol). 1H NMR (CDCl3, δ) 7.08-7.50 (m, 9H), 6.61 (s, 1H), 4.36 (s, 2H), 3.48 (s, 3H), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$, δ) A peak at 208.9 ppm was observed in the ^{13}C NMR, but the allene decomposes during prolonged acquisitions.

4n. Prepared from ^{13}C-enriched **5a**•BPh_4 and **1g**. After workup of the reaction mixture, the crude material was passed through a pad of silica gel, eluting with CH_2Cl_2. Evaporation of the solvent gave a clear oil, showing a dominant ^{13}C NMR ($CDCl_3$) resonance at 208.4 ppm. For kinetics runs, this material was diluted in the appropriate solvent until the ^{13}C signal strength relative to internal standard was approximately equivalent to that observed for other samples at a starting allene concentraiton of 80 mM.

4o. Prepared from ^{13}C-enriched **5a**•BPh_4 and **1h**. A crude sample was isolated and used as described for **4n**;

the dominant ^{13}C NMR signal for the allene appeared at 208.8 ppm.

Cycloaromatization Product Isolation Studies

General Procedures

All cycloaromatization reactions were performed under dry nitrogen atmosphere; those conducted above the boiling point of the solvent were performed in heavy-walled glass pressure tubes with teflon screw caps and rubber seals (Ace Glass), which were loaded in the drybox and heated by nearly total immersion in an oil bath. Reactions were monitored when necessary by ^{13}C NMR of aliquots, following the disappearance of the resonance of the labeled allene central carbon. Upon completion of each reaction and removal of the solvent under vacuum, the products were isolated by column chromatography on silica gel (CH_2Cl_2/petroleum ether). Further purification was often performed by preparative thin layer chromatography on silica gel plates; multiple preparative TLC runs were occasionally required to obtain adequate separations of product constituents. Unless otherwise noted, cycloaromatization products were isolated as yellow oils. The expensive 1,4-cyclohexadiene was recovered from reaction mixtures by bulb-to-bulb vacuum transfer at low temperature prior to product isolation. Experimental details are summarized in Table 6; notes concerning specific reactions are included with characterization data.

Table 6. Experimental Details for Product Isolation Studies.

Allene	Amount (mmol)	Solvent	$[Allene]_{start}$	T (°C)	Reaction time
2b	50 mg (0.15)	MeOH	31 mM	40°	24 h
2b	86 mg (0.25)	1,4-CHD	5 mM	40°, then 23°	2 h, then 2 days
2c	19 mg (0.052)	MeOH	5 mM	23°	24 h
2a	185 mg (0.53)	MeOH	2.6 mM	60°	40 h
4g	68 mg (0.25)	MeOH	5 mM	40°	24 h
4h	18 mg (0.064)	MeOH	5 mM	45°	12 h
4a	59 mg (0.21)	MeOH	2.5 mM	85°	48 h
4b	8 mg (0.026)	MeOH	2.6 mM	85°	24 h
4c	17.5 mg (0.055)	MeOH	2.6 mM	85°	24 h
4d	20 mg (0.059)	MeOH	2.6 mM	85°	48 h
4e	50 mg (0.16)	MeOH	5 mM	105°	90 h
4g	68 mg (0.25)	1,4-CHD	5 mM	40°	40 h
4e	117 mg (0.37)	1,4-CHD	5.3 mM	105°	6 days
4f	75 mg (0.32)	1,4-CHD	5 mM	105°	6 days
4i	9 mg (0.03)	1,4-CHD	80 mM	60°	20 h
4f	88 mg (0.37)	MeOH	5 mM	110°	84 h
4i	83 mg (0.28)	MeOH	5 mM	60°	41 h
4j	44 mg (0.14)	MeOH	5 mM	60°	40 h
4f	38 mg (0.16)	4/1 THF/H_2O	5 mM	105°	6 days

Scheme 2.

7b (13 mg, 38 mmol, 24%): ^1H NMR ($CDCl_3$, δ) 8.04 (s, 1H), 7.85-7.87 (m, 1H), 7.78-7.81 (m, 1H), 7.40-7.49 (m, 4H), 7.17-7.23 (m, 1H), 7.10-7.15 (m, 1H), 6.22 (s, 1H), 3.53 (s, 3H), 3.20 (h, J = 6.6 Hz, 1H), 2.80 (h, J = 6.6 Hz, 1H), 1.37 (d, J = 6.6 Hz, 3H), 1.32 (d, J = 6.6 Hz, 3H), 1.31 (d, J = 6.9 Hz, 3H), 0.99 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, δ) 145.7, 142.6, 137.4, 133.5, 132.6, 132.1, 130.1, 128.5, 128.4, 127.9, 127.6,

126.1, 125.6, 124.6, 123.6, 100.8, 79.8, 78.5, 58.0, 30.2, 28.5, 25.3, 23.8, 23.6, 21.8; IR (CH_2Cl_2, cm^{-1}) 3045, 2968, 2930, 2227, 1776, 1599, 1464, 1321, 1060, 966; UV-Vis (CH_2Cl_2, nm) 234, 258, 278; HRMS: calcd for $C_{26}H_{28}O$, 356.2140; observed, 356.2132.

The H-trapped product **8b** was not isolated from the reaction of **2b** in methanol; the reported yield of 3% was calculated from ^1H NMR integration of the benzylic methylene of **8b** against the benzylic methine resonance of **7b** in crude reaction mixtures. The identity of **8b** was confirmed by comparison of NMR data with a sample obtained from the cycloaromatization of **2b** in 1,4-cyclohexadiene, as follows.

8b (28 mg, 86 mmol, 33%): ^1H NMR ($CDCl_3$, δ) 7.82 (d, J = 7.5 Hz, 1H), 7.74-7.78 (m, 2H), 7.57 (s, 1H), 7.47-7.50 (m, 1H), 7.40-7.45 (m, 2H), 7.12-7.20 (m, 2H), 6.91 (d, J = 6.6 Hz, 1H), 4.40 (s, 2H), 3.21 (h, J = 6.6 Hz, 1H), 2.84 (h, J = 6.6 Hz, 1H), 1.28 (d, J = 7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, δ) 146.7, 143.0, 137.3, 137.0, 133.2, 132.3, 129.3, 129.1, 128.1, 127.6, 126.3, 125.7, 125.5, 124.3, 123.9, 100.9, 78.5, 37.9, 29.5, 24.5, 23.6, 21.8; IR (CH_2Cl_2, cm^{-1}) 3051, 2968, 2930, 2870, 2227, 1597, 1465, 1363, 1321, 1103, 1043, 891; UV-Vis (CH_2Cl_2, nm) 234, 260, 278. When **8b** is made from 99% ^{13}C labeled **2b**, ^{13}C coupling is apparent in the peaks at 4.40 ppm in the ^1H NMR (d, $^2J_{CH}$ = 6.0 Hz) and 37.9 ppm in the ^{13}C NMR (d, $^1J_{CC}$ = 44.2 Hz); HRMS: calcd for $C_{25}H_{26}$, 326.2034; observed, 326.2019.

9b and 10b. These cyclohexadiene-trapped products are obtained as an inseparable mixture, and as is customary in the enediyne literature, are identified by mass spectroscopy and by the presence of a complex pattern in the olefinic region of the ^1H NMR. Note that the mixture is expected to contain both possible diastereomers of **10b**. Isolated as a yellow oil (20 mg, 49 mmol, 20%): ^1H NMR ($CDCl_3$, δ) 8.22 (s, 1H), 8.00-8.15 (m, 2H), 7.70-7.90 (m, 4H), 7.30-7.50 (m, 8H), 7.05-7.25 (m, 8H), 5.85-6.05 (m, 2H), 5.70-5.85 (m, 4H), 5.40-5.50 (m, 2H), 5.05-5.20 (m, 2H), 3.70-3.85 (m, 1H), 3.50-3.70 (m, 1H), 3.30-3.50 (m, 1H), 3.20-3.30 (m, 1H), 2.85-2.95 (m, 1H), 2.75-2.85 (m, 1H), 1.20-1.40 (m, 24H), 1.00-1.20 (m, 12H); ^{13}C NMR ($CDCl_3$, δ) 139.7, 139.4, 139.1, 137.0, 132.3, 129.3, 128.6, 128.4, 128.1, 128.0, 127.5, 126.1, 125.8, 125.5, 125.3, 124.5, 49.1, 40.0, 28.6, 27.2, 25.9, 23.6, 23.5, 21.8; IR (CH_2Cl_2, cm^{-1}) 3057, 2987, 2930, 2870, 2227, 1653, 1464, 1273, 950; UV-Vis (CH_2Cl_2, nm) 236, 284; CI-MS: m/z = 405.

7c (5.8 mg, 15 mmol, 28%) from **2c**•$^{13}C_1$: ^1H NMR ($CDCl_3$, δ) 7.92 (s, 1H), 7.80-7.83 (m, 1H), 7.73-7.77 (m, 1H), 7.61 (d, J = 7.5 Hz, 1H), 7.40-7.47 (m, 3H), 7.15-7.27 (m, 3H), 6.13 (d, $^2J_{CH}$ = 4.5 Hz, 1H), 3.50 (s, 3H), 1.50-1.61 (m, 4H), 1.39-1.47 (m, 4H), 1.20-1.34 (m, 4H), 0.83-0.96 (m, 6H); ^{13}C NMR ($CDCl_3$, δ) 137.1, 131.8, 131.3, 127.5, 127.4, 127.0, 126.5, 125.4, 125.2, 124.6, 123.9, 79.1 (d, $^1J_{CC}$ = 48.5 Hz), 57.2, 32.7, 31.7, 30.4, 29.2, 22.4, 21.6, 18.9, 13.6; IR (CH_2Cl_2, cm^{-1}) 3047, 2958, 2874, 2229, 1693, 1479, 1278, 1082, 966; UV-Vis (CH_2Cl_2, nm) 234, 258, 274.

Scheme 3.

7a (71 mg, 0.18 mmol, 37%): ^1H NMR ($CDCl_3$, δ) 8.42 (s, 1H), 7.89-7.97 (m, 3H), 7.52-7.57 (m, 3H), 7.20 (t, J = 7.5 Hz, 1H), 7.07 (t, J = 7.5 Hz, 1H), 6.86 (d, J = 7.8 Hz, 1H), 6.64 (s, 1H), 3.57 (s, 3H), 1.51 (s, 9H), 1.48 (s, 9H); ^{13}C NMR ($CDCl_3$, δ) 147.4, 143.7, 136.6, 133.4, 133.3, 132.0, 129.5, 128.4, 128.2, 128.0, 127.9, 126.5, 126.2, 125.5, 103.2, 80.4, 78.4, 58.3, 36.3, 32.5, 31.8, 28.7; IR (CH_2Cl_2, cm^{-1}) 2970, 2930, 2872, 2235, 1597, 1473, 1363, 1290, 1205, 1080, 910; UV-Vis (CH_2Cl_2, nm) 234, 260, 278; HRMS: calcd for $C_{28}H_{32}O$, 384.2453; observed, 384.2481.

11a (11 mg, 16 mmol, accounting for 6% of the allene): ^1H NMR ($CDCl_3$, δ) 7.55 (s, 1H), 7.30-7.33 (m, 1H), 7.17-7.23 (m, 2H), 6.79-7.01 (m, 6H), 5.60 (s, 1H), 1.46 (s, 9H), 1.42 (s, 9H); ^{13}C NMR ($CDCl_3$, δ) 145.9,

144.8, 143.6, 137.9, 137.0, 131.9, 128.5, 127.7, 127.0, 126.3, 125.9, 125.1, 123.2, 117.5, 104.0, 102.8, 78.5, 78.1, 52.0, 31.7, 31.6, 28.8, 28.7; IR (CH_2Cl_2, cm^{-1}) 3024, 2970, 2868, 2231, 1595, 1471, 1361, 1290, 1205, 910; UV-Vis (CH_2Cl_2, nm) 242, 258, 272, 284, 366; CI-MS: 706 m/z.

The H-trapped product **8a** was not isolated. The reported yield of 6% was obtained from ^1H NMR integration of the benzylic methylene signal (identified by comparison of its chemical shift with **8b**) with respect to a known amount of added *p*-dioxane.

Scheme 4.

12g (46 mg, 0.15 mmol, 61%) from **4g**•$^{13}C_1$: ^1H NMR ($CDCl_3$, δ) 8.00 (s, 1H), 7.81-7.88 (m, 3H), 7.49 (t, J = 3.6 Hz, 2H), 7.28 (d, J = 7.5 Hz, 2H), 7.19 (d, J = 7.2 Hz, 2H), 5.70 (d, $^2J_{CH}$ = 2.7 Hz, 1H), 3.53 (s, 3H), 3.32 (m, J = 3.3 Hz, 1H), 2.39 (s, 3H), 1.33 (d, J = 6.6 Hz, 3H), 1.20 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, δ) 145.1 (d, $^1J_{CC}$ = 54.7 Hz), 136.6, 132.8, 131.3, 128.6, 127.4, 127.2, 126.7, 126.4, 125.6, 125.4, 124.8, 124.1, 82.4 (d, $^1J_{CC}$ = 48.2 Hz), 56.8, 28.1, 24.2, 23.6, 20.7; IR (CH_2Cl_2, cm^{-1}) 3049, 2966, 2930, 2872, 2822, 1591, 1512, 1465, 1383, 1186, 1087, 893, 829; UV-Vis (CH_2Cl_2, nm) 234, 272.

12h (10 mg, 31 mmol, 49%) from **4h**•$^{13}C_1$: ^1H NMR ($CDCl_3$, δ) 7.95 (s, 1H), 7.78-7.85 (m, 2H), 7.75 (d, J = 7.8 Hz, 1H), 7.42-7.46 (m, 2H), 7.23 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 8.4 Hz, 2H), 5.61 (d, $^2J_{CH}$ = 3.6 Hz, 1H), 3.79 (s, 3H), 3.46 (s, 3H), 3.23 (m, J = 3.3 Hz, 1H), 1.26 (d, J = 6.6 Hz, 3H), 1.10 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, δ) 145.0 (d, $^1J_{CC}$ = 54.7 Hz), 136.6, 133.2, 132.7, 131.2, 128.6, 127.4, 126.7, 126.1, 125.3, 125.2, 124.8, 124.1, 82.1 (d, $^1J_{CC}$ = 48.3 Hz), 56.7, 54.8, 28.0, 24.2, 23.4; IR (CH_2Cl_2, cm^{-1}) 3061, 2964, 2931, 2822, 1610, 1510, 1248, 1174, 1084, 1033, 827; UV-Vis (CH_2Cl_2, nm) 234, 276.**12a** (26 mg, 82 mmol, 40%), from **4a**•$^{13}C_1$: ^1H NMR ($CDCl_3$, δ) 8.03 (s, 1H), 7.91 (d, J = 7.8 Hz, 1H), 7.84 (d, J = 8.1 Hz, 1H), 7.77 (d, J = 7.8 Hz, 1H), 7.40-7.49 (m, 2H), 7.16 (d, J = 8.4 Hz, 2H), 7.11 (d, J = 8.4 Hz, 2H), 6.21 (d, $^1J_{CH}$ = 3.0 Hz, 1H), 3.48 (s, 3H), 2.96 (s, 3H), 1.53 (s, 9H); ^{13}C NMR ($CDCl_3$, δ) 137.8, 136.5, 131.3, 129.7, 128.8, 128.3, 127.8, 127.1, 127.0, 126.7, 125.5, 125.1, 124.1, 80.7 (d, $^1J_{PC}$ = 46.4 Hz), 56.7, 35.4, 31.9, 20.6; IR (CH_2Cl_2, cm^{-1}) 3047, 2968, 2930, 2876, 2822, 1755, 1512, 1369, 1203, 1082, 1020, 891; UV-Vis (CH_2Cl_2, nm) 234, 272; CI-MS: 320 m/z. Inseparable mixtures of other minor products showed evidence of dimer formation by CI-MS (m/z = 575).

12b, **12c**, and **12d**. Mass spectrometry and ^{13}C NMR analysis of the crude reaction mixtures showed strong parent ions and single ^{13}C labeled peaks consistent with the proposed structures. For **12b**: m/z = 336, ^{13}C NMR ($CDCl_3$, δ) 138.2; for **12c**: m/z = 349, ^{13}C NMR ($CDCl_3$, δ) 138.6; for **12d**: m/z = 374, ^{13}C NMR ($CDCl_3$, δ) 137.9. In each case, the dominant product NMR peak was accompanied by the following minor resonances (<10% of the major peak intensity): for **12b**, 144.5; for **12c**, 144.6; for **12d**, 144.9 and 145.2 ppm, suggesting that dimers **13** may also be formed. However, signals of dimeric molecular weights were not detected by mass spectrometry.

Scheme 5.

14g (6.6 mg, 24 mmol, 10%) from **4g**•$^{13}C_1$: ^1H NMR ($CDCl_3$, δ) 7.80 (d, J = 7.5 Hz, 1H), 7.75 (d, J = 7.2 Hz, 2H), 7.57 (s, 1H), 7.39-7.42 (m, 2H), 7.10 (d, J = 7.2 Hz, 2H), 7.04 (d, J = 6.6 Hz, 2H), 4.20 (d, $^2J_{CH}$ = 6.0 Hz, 1H), 3.20-3.26 (m, J = 2.7 Hz, 1H), 2.34 (s, 3H), 1.254 (d, J = 6.6 Hz, 3H), 1.248 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, δ) 136.4, 135.5, 134.9, 132.4, 131.5, 128.8, 128.6, 128.1, 127.9, 127.2, 126.7, 124.8, 124.7, 123.5, 38.3 (d, $^1J_{PC}$ = 44.0 Hz), 28.6, 23.6, 20.6; IR (CH_2Cl_2, cm^{-1}) 3022, 2964, 2926, 2870, 1593, 1512, 1465, 1363, 1041, 891, 796; UV-Vis (CH_2Cl_2, nm) 234, 274; CI-MS: 277 m/z.

15g and 16g. Isolated from **4g•**$^{13}C_1$ as an inseparable mixture, which is expected to contain both possible diastereomers (9 mg, 26 mmol, 10%): ^{1}H NMR ($CDCl_3$, δ) 7.97 (s, 2H), 7.93 (s, 1H), 7.86 (s, 1H), 7.73-7.81 (m, 9H), 7.69 (d, J = 8.1 Hz, 4H), 7.38-7.41 (m, 8H), 7.19-7.26 (m, 12H), 7.05-7.12 (m, 12H), 5.90-6.00 (m, 2H), 5.53-5.80 (m, 12H), 4.39-4.47 (m, 1H), 4.27-4.32 (m, 2H), 3.63-3.80 (m, 3H), 3.35-3.50 (m, 4H), 3.17-3.28 (m, 2H), 2.70-2.73 (m, 4H), 2.28-2.30 (m, 10H), 1.30-1.34 (m, 10H), 1.10-1.18 (m, 10H); ^{13}C NMR ($CDCl_3$, δ) 142.4, 139.2, 138.8, 135.5, 131.8, 131.3, 129.9, 129.7, 128.5, 128.4, 128.3, 128.0, 127.8, 127.6, 127.0, 126.6, 126.3, 125.8, 125.5, 124.9, 124.8, 124.6, 124.5, 123.9, 123.8, 123.5, 86.0, 51.5 (d, $^1J_{CC}$ = 43.3 Hz), 47.44 (d, $^1J_{CC}$ = 43.9 Hz), 47.40 (d, $^1J_{CC}$ = 44.2 Hz), 39.4, 36.8, 36.7, 28.0, 27.2, 26.8, 26.1, 24.5, 24.3, 23.4, 23.3, 23.0, 20.5; IR (CH_2Cl_2, cm^{-1}) 3034, 2967, 2926, 2868, 1569, 1512, 1465, 1384, 891, 810; UV-Vis (CH_2Cl_2, nm) 236, 262; CI-MS: m/z = 354.

17g and 18g. Isolated from **4g•**$^{13}C_1$ as separate compounds after repeated preparative thin-layer chromatography (5 mg each, 9 mmol, 4%). For **17g** (*meso* diastereomer): ^{1}H NMR ($CDCl_3$, δ) 7.85 (s, 2H), 7.68-7.74 (m, 4H), 7.55 (d, J = 8.1 Hz, 2H), 7.33-7.37 (m, 4H), 6.89 (d, J = 8.1 Hz, 4H), 6.77 (d, J = 7.8 Hz, 4H), 5.36 (d, $^2J_{CH}$ = 3.3 Hz, 2H), 3.20-3.33 (m, 2H), 2.11 (s, 6H), 1.08 (d, J = 6.6 Hz, 6H), 1.03 (d, J = 6.6 Hz, 6H); ^{13}C NMR ($CDCl_3$, δ) 139.6, 138.4, 131.7, 131.1, 128.6, 128.1, 127.6, 127.0, 126.5, 124.6, 124.6, 124.2, 123.7, 123.4, 50.0 (d, $^1J_{CC}$ = 44.5 Hz), 29.2, 27.7, 24.5, 23.3, 20.3; IR (CH_2Cl_2, cm^{-1}) 3061, 2966, 2926, 2870, 1512, 1460, 1383, 1020, 889, 810; UV-Vis (CH_2Cl_2, nm) 236, 276; CI-MS: m/z = 549. For **18g** (*dl* diastereomer): ^{1}H NMR ($CDCl_3$, δ) 7.76 (d, J = 7.2 Hz, 2H), 7.53-7.60 (m, 6H), 7.22-7.27 (m, 4H), 6.80 (d, J = 7.5 Hz, 4H), 6.79 (d, J = 7.5 Hz, 4H), 5.25 (d, $^1J_{CH}$ = 3.6 Hz, 2H), 3.50-3.67 (m, 2H), 2.21 (s, 3H), 2.18 (s, 3H), 1.44-1.49 (m, 6H), 0.84-0.89 (m, 6H); ^{13}C NMR ($CDCl_3$, δ) 138.5, 137.2, 134.5, 131.7, 131.0, 128.9, 127.9, 126.9, 126.8, 126.4, 126.3, 125.5, 124.5, 124.3, 123.9, 51.4 (d, $^1J_{CC}$ = 43.7 Hz), 29.2, 27.7, 24.5, 23.7, 20.5; IR (CH_2Cl_2, cm^{-1}) 3063, 2991, 2926, 2868, 1512, 1456, 1039, 885; UV-Vis (CH_2Cl_2, nm) 236, 276; CI-MS: m/z = 549.

Scheme 6.

19e (40 mg, 0.13 mmol, 34%) from **4e•**$^{13}C_1$: ^{1}H NMR ($CDCl_3$, δ) 7.77-7.81 (m, 4H), 7.40-7.50 (m, 2H), 7.30-7.33 (m, 2H), 7.21-7.30 (m, 3H), 7.15 (d, J = 16.2 Hz, 1H), 6.01-6.08 (m, 2H), 2.90 (t, J = 7.2 Hz, 2H), 2.66 (q, J = 7.2 Hz, 2H), 1.49 (s, 9H); ^{13}C NMR ($CDCl_3$, δ) 145.7, 144.9, 141.3, 136.8, 135.2, 132.9, 131.1, 128.1, 128.0, 127.3, 127.2, 126.6, 125.5, 125.1, 123.7, 123.6, 55.2, 49.1, 35.5, 34.7, 30.9; IR (CH_2Cl_2, cm^{-1}) 3028, 2997, 2958, 2930, 2874, 1602, 1508, 1365, 1203, 1134, 970; UV-Vis (CH_2Cl_2, nm) 246, 288; CI-MS: m/z = 317. Evidence for trace amounts of dimers in the crude reaction mixture was provided by mass spectrometry (m/z = 628), but this species was not isolated.

19f (26 mg, 0.11 mmol, 35%) from **4f•**$^{13}C_1$: ^{1}H NMR ($CDCl_3$, δ) 7.77-7.79 (m, 4H), 7.39-7.44 (m, 2H), 7.12 (d, J = 14.1 Hz, 1H), 5.99-6.08 (m, 1H), 2.25-2.37 (m, 2H), 1.53 (s, 9H), 1.18 (t, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, δ) 145.3, 144.9, 137.0, 133.6, 131.2, 130.5, 127.9, 127.1, 126.5, 125.0, 123.5, 30.9, 29.3, 25.9, 13.1; IR (CH_2Cl_2, cm^{-1}) 3049, 2964, 2930, 2874, 1485, 1462, 1365, 1224, 1134, 970, 889; UV-Vis (CH_2Cl_2, nm) 246, 282; CI-MS: m/z = 240. A CI-MS of the crude product mixture also reveals the presence of trace amounts of dimer (m/z = 475) and a cyclohexadiene-trapped product (m/z = 318), but these were not isolated.

19i (6 mg, 21 mmol, 35%) from **4i•**$^{13}C_1$: ^{1}H NMR ($CDCl_3$, δ) 7.80 (s, 1H), 7.44-7.79 (m, 1H), 7.65 (d, J = 8.1 Hz, 1H), 7.38-7.41 (m, 3H), 7.19-7.32 (m, 5H), 6.80 (d, J = 15.3 Hz, 1H), 6.14-6.25 (m, 1H), 3.20-3.26 (m, 1H), 2.87 (t, J = 7.2 Hz, 2H), 2.62 (q, J = 7.2 Hz, 2H), 1.30 (d, J = 6.9 Hz, 6H); ^{13}C NMR ($CDCl_3$, δ) 135.4,

132.1, 128.6, 128.1, 127.9, 126.8, 125.4, 124.9, 124.8, 124.1, 122.7, 122.5, 40.5, 39.0, 36.1, 29.3, 23.0; IR (CH_2Cl_2, cm^{-1}) 3063, 3028, 2962, 2928, 2870, 1601, 1494, 1454, 1364, 968; UV-Vis (CH_2Cl_2, nm) 248, 284.

12f (44 mg, 0.16 mmol, 55%) from 80% of the reaction mixture of **4f**•$^{13}C_1$ in methanol, corresponding to a 68% total yield: ^1H NMR ($CDCl_3$, δ) 8.09 (s, 1H), 7.81-7.85 (m, 3H), 7.43-7.46 (m, 2H), 5.15 (dd, J = 5.1 Hz, $^2J_{CH}$ = 2.4 Hz, 1H), 3.39 (s, 3H), 1.58 (s, 9H), 1.34-1.40 (m, 1H), 0.44-0.60 (m, 4H); ^{13}C NMR ($CDCl_3$, δ) 141.7, 138.9, 132.3, 131.3, 127.5, 127.2, 126.9, 126.8, 126.6, 125.3, 125.1, 124.1, 78.6 (d, $^1J_{CC}$ = 46.1 Hz), 55.9, 35.6, 32.0, 16.6, 3.2, 0.5; IR (CH_2Cl_2, cm^{-1}) 3005, 2958, 2822, 1585, 1465, 1369, 1195, 1084, 1022, 889; UV-Vis (CH_2Cl_2, nm) 232, 276; HRMS: calcd for $C_{18}{}^{13}C_1H_{24}O$, 269.1860; observed, 269.1861.

Mass spectroscopy of mixed fractions containing numerous small bands revealed the presence of small amounts of dimeric products (m/z = 475), which were not further purified.

21i (45 mg, 0.14 mmol, 49%) from **4i**•$^{13}C_1$: ^1H NMR ($CDCl_3$, δ) 7.80 (s, 1H), 7.76-7.80 (m, 2H), 7.66 (d, J = 8.1 Hz, 1H), 7.31-7.46 (m, 7H), 6.81 (d, J = 15.3 Hz, 1H), 6.08-6.20 (m, 1H), 4.33 (t, J = 6.3 Hz, 1H), 3.31 (s, 3H), 3.16-3.29 (m, 1H), 2.80-2.89 (m, 1H), 2.64-2.73 (m, 1H), 1.32 (d, J = 6.9 Hz, 3H), 1.30 (d, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, δ) 136.2, 135.3, 131.5, 130.5, 129.7, 128.6, 128.0, 127.2, 126.9, 126.8, 126.4, 125.0, 124.8, 124.3, 122.5; IR (CH_2Cl_2, cm^{-1}) 3053, 3030, 2964, 2931, 2872, 2825, 1491, 1454, 1363, 1103, 968, 891; UV-Vis (CH_2Cl_2, nm) 234, 250, 286; CI-MS: m/z = 332.

21j (22 mg, 64 mmol, 45%) from **4j**•$^{13}C_1$: ^1H NMR ($CDCl_3$, δ) 7.83 (s, 1H), 7.72-7.79 (m, 3H), 7.56 (d, J = 7.5 Hz, 1H), 7.30-7.45 (m, 6H), 6.72 (d, J = 15.6 Hz, 1H), 6.12-6.24 (m, 1H), 4.31 (t, J = 6.6 Hz, 1H), 3.30 (s, 3H), 2.64-2.87 (m, 4H), 1.51-1.64 (m, 2H), 1.35-1.47 (m, 2H), 0.97 (t, J = 7.2 Hz, 3H); 13C NMR (CDCl3, _) 136.2, 135.2, 132.1, 129.4, 128.1, 128.0, 127.2, 127.0, 126.5, 126.3, 125.6, 125.0, 124.7, 123.7, 83.5, 56.3, 41.5, 32.9, 32.4, 22.2, 13.6; IR (CH2Cl2, cm-1) 3030, 2958, 2933, 2872, 2825, 1699, 1602, 1525, 1454, 1359, 1103, 966, 883; UV-Vis (CH2Cl2, nm) 234, 254, 288; CI-MS: m/z = 345.

22 (7 mg, 28 mmol, 18%) from **4f**•$^{13}C_1$, by extraction of the aqueous THF solution with diethyl ether and water, followed by drying and evaporation of the organic phase and chromatographic purification: ^1H NMR ($CDCl_3$, δ) 8.21 (s, 1H), 7.78-7.84 (m, 3H), 7.42-7.45 (m, 2H), 5.17 (dd, J = 6.0 Hz, $^2J_{CH}$ = 2.7 Hz, 1H), 1.54 (s, 9H), 1.40-1.50 (m, 1H), 0.55-0.70 (m, 2H), 0.40-0.50 (m, 2H); ^{13}C NMR ($CDCl_3$, δ) 141.6, 132.2, 131.4, 128.0, 127.2, 126.8, 126.7, 125.6, 125.2, 124.1, 71.5 (d, $^1J_{CC}$ = 2.7 Hz), 35.3, 32.0, 18.1, 3.3, 1.9; IR (CH_2Cl_2, cm^{-1}) 3599, 3059, 3005, 2972, 2877, 1489, 1365, 1290, 1205, 1134, 1024, 891; UV-Vis (CH_2Cl_2, nm) 232, 278; CI-MS: m/z = 256 (M+1 ion); m/z = 239 (loss of alcohol group).

Kinetics Studies

Representative HPLC Procedure. Allene diyne **2a** (4.5 mg, 13 mmol) was dissolved in nitrogen-purged anhydrous methanol (4.9 mL, 2.6 mM) inside an inert atmosphere glovebox. To this solution was added 1-methoxynaphthalene (8 mg, 50 mmol) as an internal standard. The solution was partitioned into 18 fractions, and each fraction (270 μL) was placed in a 2 mL screw top glass vial and closed inside the glovebox with a teflon lined heat resistant phenolic cap (Fisher). The vials were then removed from the drybox and submerged in a constant temperature bath at 60.0±0.1°C. Individual vials were removed from the bath at regular time intervals over 12 hours. To ensure that the cycloaromatization reaction was rapidly stopped, each sample was immediately dipped in liquid nitrogen for approximately 30 seconds and then stored in a freezer at -20°C. The relative amounts of **2a** vs. 1-methoxynaphthalene in each sample were measured by integration of their

respective areas on a reverse-phase HPLC trace (15 cm x 5 mm C_{18} reverse phase column, 95:5 MeOH:H_2O; retention times = 2.0 minutes for 1-methoxynaphthalene, 6.4 minutes for allene). The first order rate constant was obtained from the slope of the linear plot of ln[allene/standard] vs. time. Errors for each rate determination were obtained from standard least squares analysis.

Representative NMR Procedure. A 99% ^{13}C-labeled sample of allene diyne **2b** (11.4 mg, 35.2 mmol) was dissolved in nitrogen-purged anhydrous methanol (440 mL, 80 mM allene) and *p*-dioxane (25 mg, 305 mmol) was added as internal standard. The mixture was placed in a threaded 5 mm NMR tube (Wilmad) and closed inside the glovebox with a teflon lined phenolic cap. After wrapping the cap with parafilm, the tube was introduced into a preheated NMR probe. Fifteen decoupled ^{13}C NMR spectra were collected in unlocked mode, each comprised of 128 transients acquired over four minutes (sweep width 15000 Hz, pulse delay 1 sec), followed by an automated delay of six minutes before the following acquisition was started. The time of each data acquisition is defined as the time it begins. After careful phasing, the peak heights for the ^{13}C labeled allene central carbon (209 ppm) and the *p*-dioxane peak (67 ppm) were obtained from a computer generated peak listing for each spectrum. First order data analysis was performed in the same way as for **2a** above, substituting the ratio of NMR peak heights for the ratio of integrated HPLC peak areas. Integrating the NMR signals provides no better precision than measuring peak heights, and is significantly more laborious.

The temperature of the NMR probe was measured for each reaction using standard ethylene glycol or methanol samples by the method of Van Geet,[31] both before and after data acquisition, and were shown to vary by no more than 0.1°C over the course of each experiment.

Table 7 lists the results of all kinetics runs, organized by substrate type.

Table 7. Cycloaromatization kinetics data.

Allene-di(enynes)

entry	Compound	solvent	T (°C)	k (s^{-1})	$t_{1/2}$ (min)	# $t_{1/2}$s
1	**2a**	CH_3OH	60.0	$(2.29 \pm 0.03) \times 10^{-5}$	504	1.4
2	**2a**	CH_3OH	70.0	$(6.75 \pm 0.20) \times 10^{-5}$	174	1.4
3	**2a**	CH_3OH	85.0	$(2.36 \pm 0.08) \times 10^{-4}$	49	4.1
4	**2b**	CH_3OH	47.2	$(1.41 \pm 0.03) \times 10^{-3}$	8	1.8
5	**2b**	CH_3OH	39.1	$(5.34 \pm 0.39) \times 10^{-4}$	22	2.1
6	**2b**	CH_3OH	29.2	$(2.12 \pm 0.05) \times 10^{-4}$	54	2.8
7	**2b**	CH_3OH	29.2	$(1.86 \pm 0.04) \times 10^{-4}$	62	2.4
8	**2b**	CH_3OH	29.2	$(1.75 \pm 0.05) \times 10^{-4}$	66	2.3
9	**2b**	CH_3OH	28.6	$(2.03 \pm 0.06) \times 10^{-4}$	57	3.9
10	**2b**	CH_3OH	14.4	$(3.60 \pm 0.14) \times 10^{-5}$	321	1.0
11	**2b**	1,4-CHD	47.2	$(9.66 \pm 1.03) \times 10^{-4}$	12	2.5
12	**2b**	1,4-CHD	39.0	$(4.14 \pm 0.15) \times 10^{-4}$	28	2.9
13	**2b**	1,4-CHD	28.7	$(1.34 \pm 0.03) \times 10^{-4}$	86	2.9
14	**2b**	1,4-CHD	14.4	$(3.30 \pm 0.19) \times 10^{-5}$	350	0.9
15	**2c**	CH_3OH	29.2	$(3.37 \pm 0.10) \times 10^{-4}$	34	2.9

Allene enynes lacking t-butyl groups

16	**4g**	MeOH	27.9	$(4.83 \pm 0.20) \times 10^{-5}$	239	1.3
17	**4g**	MeOH	36.9	$(1.26 \pm 0.02) \times 10^{-4}$	**91**	2.1
18	**4g**	MeOH	46.1	$(3.32 \pm 0.12) \times 10^{-4}$	35	1.7
19	**4g**	MeOH	55.2	$(8.92 \pm 0.26) \times 10^{-4}$	13	1.9
20	**4h**	MeOH	34.1	$(9.11 \pm 0.11) \times 10^{-5}$	127	3.3
21	**4k**	MeOH	30.3	$(6.65 \pm 0.23) \times 10^{-5}$	173	1.4
22	**4l**	MeOH	27.9	$(2.83 \pm 0.05) \times 10^{-5}$	**408**	1.3
23	**4l**	MeOH	46.1	$(2.46 \pm 0.09) \times 10^{-4}$	**47**	2.3
24	**4n**	MeOH	27.0	$(4.15 \pm 0.16) \times 10^{-5}$	**278**	**0.5**
25	**4n**	MeOH	36.3	$(1.11 \pm 0.06) \times 10^{-4}$	**104**	**1.5**
26	**4n**	MeOH	42.6	$(2.05 \pm 0.07) \times 10^{-4}$	**56**	**2.0**
27	**4n**	MeOH	44.0	$(2.08 \pm 0.08) \times 10^{-4}$	**56**	**2.1**
28	**4n**	MeOH	47.7	$(3.78 \pm 0.08) \times 10^{-4}$	**31**	**2.0**
29	**4n**	MeOH	52.8	$(4.68 \pm 0.14) \times 10^{-4}$	**25**	**2.4**
30	**4n**	MeOH	57.9	$(7.92 \pm 0.42) \times 10^{-4}$	15	**2.4**
31	**4n**	MeOH	61.4	$(9.09 \pm 0.40) \times 10^{-4}$	15	**2.4**
32	**4o**	MeOH	28.9	$(4.38 \pm 0.40) \times 10^{-5}$	**264**	**0.4**
33	**4o**	MeOH	42.7	$(3.08 \pm 0.37) \times 10^{-4}$	**38**	**1.2**
34	**4g**	1,4-CHD	28.3	$(4.78 \pm 0.08) \times 10^{-5}$	242	2.5
35	**4g**	1,4-CHD	37.7	$(1.16 \pm 0.03) \times 10^{-4}$	99	3.0
36	**4g**	1,4-CHD	46.6	$(3.29 \pm 0.16) \times 10^{-4}$	35	2.6
37	**4g**	1,4-CHD	55.9	$(7.50 \pm 0.38) \times 10^{-4}$	15	2.9
38	**4k**	1,4-CHD	30.3	$(3.46 \pm 0.07) \times 10^{-5}$	336	1.4

Phenylcyclopropyl allene enynes

39	**4i**	CH_3OH	56.4	$(5.03 \pm 0.12) \times 10^{-5}$	230	2.4
40	**4i**	CH_3OH	57.2	$(5.23 \pm 0.09) \times 10^{-5}$	221	2..2
41	**4i**	CH_3OH	74.6	$(2.43 \pm 0.28) \times 10^{-4}$	47	2.1
42	**4i**	1,4-CHD	57.7	$(3.04 \pm 0.11) \times 10^{-5}$	379	1.4
43	**4i**	1,4-CHD	57.8	$(2.92 \pm 0.06) \times 10^{-5}$	396	1.8
44	**4j**	CH_3OH	56.0	$(6.69 \pm 0.22) \times 10^{-5}$	173	1.7
45	**4j**	CH_3OH	56.1	$(7.13 \pm 0.50) \times 10^{-5}$	162	1.9
46	**4e**	CH_3OH	95.2	$(3.99 \pm 0.11) \times 10^{-5}$	289	2.0
47	**4f**	CH_3OH	93.0	$(3.15 \pm 0.24) \times 10^{-5}$	365	1.8
48	**4f**	CH_3OH	108.6	$(7.33 \pm 0.62) \times 10^{-5}$	158	1.5

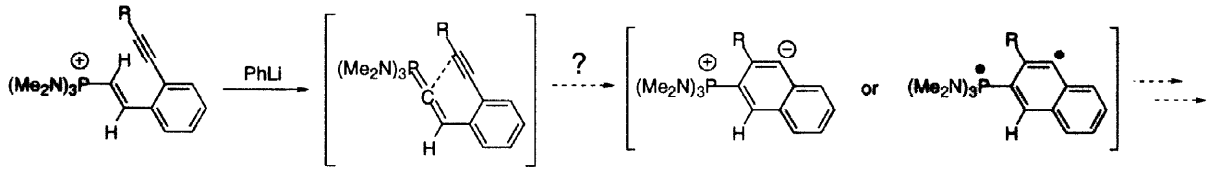
1,4-CHD = 1,4-cyclohexadiene; $t_{1/2}$ = half life; # $t_{1/2}$s = number of half lives followed in kinetics run

Acknowledgements. Acknowledgement is made to the donors of The Petroleum Research Fund, administered by the ACS, for partial support of this research (27397-AC1). Support from the National Science Foundation (CHE 93-13746) is gratefully acknowledged. We thank Cambridge Isotope Laboratories for a generous grant of $^{13}CH_3I$ through the CIL Research Grant Program. We are grateful to Dr. Yuesheng Wang for the synthesis of acetylenic aldehydes, to Ms. Kelly Reynolds and Mr. Marcus Brody for other synthetic contributions, and to Dr. Michal Sabat for x-ray crystallography.

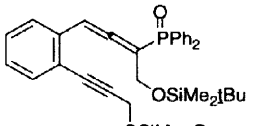
REFERENCES AND NOTES

1. Reviews: (a) Nicolaou, K. C.; Dai, W.-M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1387-1416. (b) Goldberg, I. H.*Acc. Chem. Res.* **1991**, *24*, 191-198. (c) Nicolaou, K. C.; Dai, W.-M.; Tsay, S.-C.; Estevez, V. A.; Wrasidlo, W. *Science* **1992**, *256*, 1172-1178. (d) Gleiter, R.; Kratz, D. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 842-845. (e) Grissom, J.W.; Gunawardena, G.U.; Klingberg, D.; Huang, D. *Tetrahedron* **1996**, *52*, 6453-6518.
2. (a) Myers, A. G.; Harrington, P. M.; Kwon, B.-M. *J. Am. Chem. Soc.* **1992**, *114*, 1086-1087. (b) Myers, A. G.; Dragovich, P. S. *J. Am. Chem. Soc.* **1993**, *115*, 7021-7022. (c) Myers, A. G.; Harrington, P. M.; Kuo, E. Y.*J. Am. Chem. Soc.* **1991**, *113*, 694-695. (d) Lamothe, M.; Fuchs, P. L. *J. Am. Chem. Soc.* **1993**, *115*, 4483-4496. (e) Kappen, L. S.; Goldberg, I. H.*Science* **1993**, *261*, 1319-1321. (f) Kappen, L. S.; Goldberg, I. H.; Frank, B. L.; Worth, L.,Jr.; Christner, D. F.; Kozarich, J. W.; Stubbe, J. *Biochemistry* **1991**, *30*, 2034-2042. (g) Dasgupta, D.; Goldberg, I. H. *Biochemistry* **1985**, *24*, 6913-6920. (h) Kappen, L. S.; Goldberg, I. H. *Proc. Natl. Acad. Sci. USA* **1992**, *89*, 6706-6710. (i) Dedon, P. C.; Goldberg, I. H. *J. Biol. Chem.* **1990**, *265*, 14713-14716. (j) Meschwitz, S. M.; Schultz, R. G.; Ashley, G. W.; Goldberg, I. H. *Biochemistry* **1992**, *31*, 9117-9121. (k) Chin, D. -H.; Goldberg, I. H. *J. Am. Chem. Soc.* **1992**, *114*, 1914-1915. (l) Frank, B. L.; Worth, L.,Jr.; Christner, D. F.; Kozarich, J. W.; Stubbe, J.; Kappen, L. S.; Goldberg, I. H. *J. Am. Chem. Soc.* **1991**, *113*, 2271-2275.
3. For allene enyne rearrangements, see reference 2b and: (a) Myers, A.G.; Dragovich, P. S.; Kuo, E. Y. *J. Am. Chem. Soc.* **1992**, *114*, 9369-9386. (b) Myers, A.G.; Kuo, E. Y.; Finney, N. S. *J. Am. Chem. Soc.* **1989**, *111*, 8057-8059. For cycloaromatization reactions of other NCSC analogues, see: (c) Nagata, R.; Yamanaka, H.; Murahashi, E.; Saito, I. *Tetrahedron Lett.* **1990**, *31*, 2907-2910. (d) Nagata, R.; Yamanaka, H.; Okazaki, E.; Saito, I. *Tetrahedron Lett.* **1989**, *30*, 4995-4998. (e) Fujiwara, K.; Kurisaki, A.; Hirama, M. *Tetrahedron Lett.* **1990**, *31*, 4329-4332. (f) Hirama, M.; Tokuda, M.; Fujiwara, K.*Synlett* **1991**, 651-653. (g) Mikami, K.; Matsueda, H.; Nakai, T. *Synlett* **1993**, *23*, 25.
4. See reference 1e, and: (a) Jones, R.R.; Bergman, R.G. *J. Am. Chem. Soc.* **1972**, *94*, 660-661. (b) Bergman, R.G. *Accounts Chem. Res.* **1973**, *6*, 25-31. (c) Lockhart, T.P.; Comita, P.B.; Bergman, R.G. *J. Am. Chem. Soc.* **1981**, *103*, 4082-4090. (d) Lockhart, T.P.; Bergman, R.G. *J. Am. Chem. Soc.* **1981**, *103*, 4091-4096. (e) Magnus, P.; Fortt, S.; Pitterna, T.; Snyder, J.P. *J. Am. Chem. Soc.* **1990**, *112*, 4986-4987. (f) Magnus, P.; Carter, P.; Elliott, J.; Lewis, R.; Harling, J.; Pitterna, T.; Bauta, W.E.; Fortt, S. *J. Am. Chem. Soc.* **1992**, *114*, 2544-2559. (g) Snyder, J.P. *J. Am. Chem. Soc.* **1990**, *112*, 5367-5369. (h) Semmelhack, M.F.; Neu, T.; Foubelo, F. *Tetrahedron Lett.* **1992**, *33*, 3277-3280. (i) Semmelhack, M.F.; Neu, T.; Foubelo, F. *J. Org. Chem.* **1994**, *59*, 5038-5047. (j) Nicolaou, K.C.; Zuccarello, G.; Riemer, C.; Estevez, V.A.; Dai, W.M. *J. Am. Chem. Soc.* **1992**, *114*, 7360-7371. (k) Nicolaou, K.C.; Dai, W.-M.; Hong, Y.P.; Baldridge, K.K.; Siegel, J.S.; Tsay, S.C. *J. Am. Chem. Soc.* **1993**, *115*, 7944-7953. (l) Maier, M.E.; Greiner, B. *Liebigs Ann. Chem.* **1992**, 855-861. (m) Bharucha, K.N.; Marsh, R.M.; Minto, R.E.; Bergman, R.G. *J. Am. Chem. Soc.* **1992**, *114*, 3120-3121. (n) Grissom, J.W.; Calkins, T.L. *J. Org. Chem.* **1993**, *58*, 5422-5427. (o) Boger, D.L.; Zhou, J. *J. Org. Chem.* **1993**, *58*, 3018-3024. (p) Yoshida, K.; Minami, Y.; Otani, T.; Tada, Y.; Hirama, M. *Tetrahedron Lett.* **1994**, *35*, 5253-5256. (q) See also: Warner, B.P.; Millar, S.P.; Broene, R.D.; Buchwald, S.L. *Science* **1995**, *269*, 814-816.
5. (a) Schmittel, M.; Strittmatter, M.; Kiau, S. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1843-1845. (b) Schmittel, M.; Strittmatter, M.; Kiau, S. *Tetrahedron Lett.* **1995**, *36*, 4979-4982. (c) Schmittel, M.; Strittmatter, M.; Vollmann, K.; Kiau, S. *Tetrahedron Lett.* **1996**, *37*, 999-1002.
6. (a) Reynolds, K.A.; Dopico, P.G.; Sundermann, M.J.; Hughes, K.A.; Finn, M.G. *J. Org. Chem.* **1993**, *58*, 1298-1299. (b) Hughes, K.A.; Dopico, P.G., Sabat, M.; M.G. Finn *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 554-555. (c) Reynolds, K.A.; Dopico, P.G.; Brody, M.S.; Finn, M.G. *J. Org. Chem.* **1997**, *62*, 2564-2573. (d) Reynolds, K.A.; Finn, M.G. *J. Org. Chem.* **1997**, *62*, 2574-2593.
7. Dieck, H. A.; Heck, R. F. *J. Organomet. Chem.* **1975**, *93*, 259.
8. It is possible that the decomposition process is an intramolecular cycloaromatization of the allenic phosphorane (shown below), which would account for the extreme sensitivity of the synthetic

methodology to the size of the alkyne substituent, in analogy to the all-carbon analogue described in the text.



9. Nagata, R.; Yamanaka, H.; Murahashi, E.; Saito, I. *Tetrahedron Lett.* **1990**, *31*, 2907-2910.
10. Geometry minimization was performed using the MM2 force field as implemented in Macromodel versions 4.0 and 4.5. For each compound, a Monte Carlo conformational search of enough starting structures (usually 1000) to generate ten or more duplicates of the first ten energy minima was performed.
11. The same molecular mechanics analysis of the Saito compound **6** (R=H) shows the *s-trans* conformation to be the more stable, but the calculated energy difference is much smaller (0.25 kcal/mol) than reported for the *ab intio* method.
12. (a) Pasto, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 37-46. (b) Pasto, D. J.; Yang, S. H. *J. Org. Chem.* **1986**, *51*, 1676-1680.
13. (a) Bowry, V. W.; Lusztyk, J.; Ingold, K. U. *J. Chem. Soc. Chem. Commun.* **1990**, 923-925. (b) Hollis, R.; Hughes, L.; Bowry, V. W.; Ingold, K. U. *J. Org. Chem.* **1992**, *57*, 4284-4287. (c) Beckwith, A. L. J.; Bowry, V. W. *J. Am. Chem. Soc.* **1994**, *116*, 2710-2716.
14. Espenson, J. H. *Chemical Kinetics and Reaction Mechanisms*, McGraw Hill: New York, 1981; pp 117-20.
15. Nicolaou, K.C.; Zuccarello, G.; Ogawa, Y.; Schweiger, E.J.; Kumazawa, T. *J. Am. Chem. Soc.* **1988**, *110*, 4866-4868.
16. (a) Snyder, J. P. *J. Am. Chem. Soc.* **1990**, *112*, 5367-5369. (b) Magnus, P.; Simon, F.; Pitterna, T.; Snyder, J. P. *J. Am. Chem. Soc.* **1990**, *112*, 4986-4987. (c) Houk, K.N.; Li, Y.; Evanseck, J.D. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 682-708. (d) Roth, W.R.; Hopf, H.; Horn, C. *Chem. Ber.* **1994**, *127*, 1765-1769. (e) Brandstetter, T.; Maier, M.E. *Tetrahedron* **1994**, *50*, 1435-1448.
17. For relevant *ab initio* calculations, see Kraka, E.; Cremer, D. *J. Am. Chem. Soc.* **1994**, *116*, 4929-4936.
18. A theoretical calculation of 3.491 Å as the upper bound of the "critical distance" (defined as the C1-C6 distance at which spontaneous cycloaromatization may occur) for the parent allene enyne **25** has been reported: Mitra, A.; Capitani, J.F. *Int. J. Quant. Chem.* **1994**, *49*, 363-369. For comparison, a molecular mechanics calculation on **25** done by our methods[10] shows a ground-state C1-C6 distance of 3.272 Å.
19. At 25°C, the difference in $\Delta H^{\ddagger}$ (-1.7 kcal/mol) alone would lead to an 18-fold rate acceleration for **2b**, and the difference in $\Delta S^{\ddagger}$ provides a 14-fold rate enhancement in the same direction.
20. We also observed no kinetic resolution of racemic allenes such as **4a** in cycloaromatization reactions conducted in enantiomerically pure chiral alcohol solvents (α-phenethyl alcohol, 2-butanol), even at high conversions.
21. Experimental measurements and calculations by Squires and coworkers have established that the parent α,3-dehydrotoluene diradical has a spin-coupled (singlet) ground state: Wenthold, P.G.; Wierschke, S.G.; Nash, J.J.; Squires, R.R. *J. Am. Chem. Soc.* **1993**, *115*, 12611-12612; Wenthold, P.G.; Wierschke, S.G.; Nash, J.J.; Squires, R.R. *J. Am. Chem. Soc.* **1994**, *116*, 7378-7392.
22. Koga, N.; Morokuma, K. *J. Am. Chem. Soc.* **1991**, *113*, 1907-1911.
23. In this context, it is interesting to note the rate difference between aromatic allene-ynes **4g** and **31**: at 37°C, the reported half life of **31** (23 h) (Nicolaou, K.C.; Maligres, P.; Shin, J.; de Leon, E.; Rideout, D. *J. Am. Chem. Soc.* **1990**, *112*, 7825-7826) is approximately 14 times that of **4g** at 37.7 °C in 1,4-cyclohexadiene (Table 6, entry 20). Thus, the phosphoryl residue of **31** proves to be severely destabilizing to the transition state relative to the *p*-tolyl group of **4g**.



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24. Creary, X.; Mehrsheikh-Mohammadi, M. E.; McDonald, S. *J. Org. Chem.* **1987**, *52*, 3254-3263.
25. Other processes include (a) pyrolysis of dibenzylmercurials: Dinctürk, S.; Jackson, R.A.; Townson, M. *J. Chem. Soc., Chem. Commun.* **1979**, 172-174; Dinctürk, S.; Jackson, R.A.; Townson, M.; Agirbas, H.; Billingham, N.C.; March, G. *J. Chem. Soc., Perkin Trans. 2.* **1981**, 1121-1126; Dinctürk, S.; Jackson, R.A. *J. Chem. Soc., Perkin Trans. 2* **1981**, 1127-1132; Agirbas, H.; Jackson, R.A. *J. Chem. Soc., Perkin Trans. 2.* **1983**, 739-742. (b) hyperfine coupling of benzylic radicals: Dust, J.M.; Arnold, D.R. *J. Am. Chem. Soc.* **1983**, *105*, 1221-1227 and 6531; Wayner, D.D.M.; Arnold, D.R. *Can. J. Chem.* **1984**, *62*, 1164-1168; Wayner, D.D.M.; Arnold, D.R. *Can. J. Chem.* **1985**, *63*, 2378-2383.
26. March, J. *Advanced Organic Chemistry*; John Wiley and Sons: New York, 1985; pp 242-244.
27. (a) Wells, P.R. "Linear Free Energy Relationships"; Academic Press: New York, 1976, p. 12. (b) Jaffé, H.H. *Chem. Rev.* **1953**, *53*, 191-261; Table 2, p. 205.
28. Toshima, K.; Ohta, K.; Ohtake, T.; Tatsuka, K. *Tetrahedron Lett.* **1991**, *32*, 391-394.
29. See also: (a) Nicolaou, K.C.; Skokotas, G.; Maligres, P.; Zuccarello, G.; Schweiger, E.J.; Toshima, K.; Wendeborn, S. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1272-1274. (b) Nicolaou, K.C.; Wendeborn, S.; Maligres, P.; Isshiki, K.; Zein, N.; Ellestad, G. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 418-420.
30 (a) Sonogashira, K.; Tohda,Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467-4470. (b) Takahashi, S.; Kuroyama, Y.; Sonogashira, K.; Hagihara, N. *Synthesis* **1980**, 627-631.
31. Gordon, A. J.; Ford, R. A. *The Chemist's Companion*, John Wiley and Sons: New York, 1972; p 303.