also restrained to some degree.

Various organized and confined structures such as crystals, organic hosts (cyclodextrin, deoxycholic acid, Dianin's compound), micelles, liquid crystals, and silica surfaces have been explored as media for photoreactions.[1] Each one of them possess unique features. Zeolites compare favorably with these as media for photoreactions. One of the disadvantages in using zeolites, like most other solid matrices, as the media can be the long duration (compared to solution) of irradiation required because of scattering problems. Also, one needs to continuously expose fresh surfaces to UV radiation through mechanical agitation. In spite of these drawbacks, zeolites should not be overlooked as a medium for photoreactions since we and others have successfully conducted photochemical and photophysical studies in this media.[2-4] Compared to most of the organic hosts, inclusion of a large variety of guests within zeolites is easily achieved. Zeolites are unique, stable, and photoinert host materials with well-defined pore structures that can offer predictable constraints on the motions of included guests which can be used to direct the probable course of the photoreactions within them.

Experimental Section

Materials. Benzoin alkyl ethers and alkyldeoxybenzoins were prepared by reported procedures[27] and were purified by column chromatography (silica gel/hexane). Spectral data for analytically pure materials were reported by us earlier.[17]

Zeolites 13X (NaX) and LZ-Y52 (NaY) were obtained from Linde. The cation of interest was exchanged into these powders by contacting the material with the appropriate nitrate solution at 90 °C. For each gram of zeolite, 10 mL of a 10% nitrate solution was used. This was repeated a number of times. The samples were then thoroughly washed with water and dried. Exchange loadings were typically between 37 and 84%. Exchange levels for individual zeolites were as follows: LiX, 46%; KX, 64%; RbX, 49%; CsX, 37%; LiY, 64%; KY, 84%; RbY, 68%; CsY, 62%. Prior to use these samples were heated in a furnace at 500 °C in air for about 10 h. Activated zeolites were used immediately.

Inclusion of Ketones within Zeolites. Known amounts of benzoin ethers/alkyldeoxybenzoins and the activated zeolites were stirred together in 20 mL of hexane for about 10 h. In a typical preparation 250 mg of the zeolite and 5 mg of the ketone were taken in 20 mL of the solvent. White powder collected by filtration of the solvent was washed with ether twice and dried under nitrogen. Samples were taken in Pyrex cells fitted with Teflon-brand stopcocks, degassed thoroughly (10^{-4} mm), and sealed. These samples were generally dry and contained less than 1% of water.

Photolysis and Isolation of Products. Samples containing 125 mg of the complex were degassed in Pyrex cells and irradiated with 450-W mercury lamps. Irradiation cells were rotated periodically to provide uniform exposure. Generally about 15% conversion was obtained in about 2 h of irradiation. After photolysis products were extracted by stirring the samples in ether (20 mL) for about 6 h. In some cases the zeolite was dissolved with concentrated HCl and extracted with ether. Control experiments established that the products are stable to the acid extraction conditions. Products were analyzed by GC (Hewlett Packard Model 5890; SE-30 capillary column), using *trans*-stilbene as the internal standard. Structures of all products have been established earlier and the spectral data are consistent with the literature reports.[17]

Acknowledgment. We thank A. Pittman and P. Hollins for valuable technical assistance and N. J. Turro for useful discussions.

(27) Fisher, E. *Chem. Ber.* **1893**, *26*, 2412.

Synthetic and Kinetic Studies of the Intramolecular Diels-Alder Reactions of Cycloalkenylallenylphosphine Oxides

Michael L. Curtin and William H. Okamura*

Department of Chemistry, University of California, Riverside, California 92521

Received March 28, 1990

Kinetic investigations reveal that diphenylphosphinoyl (diphenylphosphine oxide) substituted cycloalkenylallenes **13b-d** undergo intramolecular Diels-Alder (IMDA) cyclizations at room temperature to afford adducts with *gem*-dialkyl effect accelerations of 4.6 (*gem*-dimethyl), 21.1 (*gem*-diethyl), and 27.8 (*gem*-dipropyl), respectively, relative to **13a**. Arrhenius data reveals $\Delta G^{\ddagger}$'s of between 22.1 and 23.9 kcal/mol for vinylallenes **13a-c**. Vinylallenes **24** and **25** revealed mono-*tert*-butyl acceleration effects of 70.5 and 205, respectively, relative to the parent **13a**. Cycloalkenyl ring size studies showed that vinylallenes **13b** and **33a-c** had cyclization rates within a factor of 10 of one another. Tether length studies revealed that the three carbon tethered allene **43b** exhibits an 850-fold decrease in cyclization rate versus the two carbon tethered allene **13b**. A comparison of the rate of IMDA cyclization of the three carbon tethered **43a** and **43b** revealed a *gem*-dimethyl effect of 2.6, quite similar in magnitude to the 4.6 value observed for the two carbon tethered derivatives **13a** and **13b**. An X-ray crystallographic analysis of **34a** firmly established the stereochemical course of the reaction, including the anti relationship of the bridgehead hydrogens in the resulting polycycles.

Introduction

For the vinylallenic variant of the intramolecular Diels-Alder (IMDA) reaction[1-3] in which the vinylallene serves as the diene component of the reaction, there are five ways in which diene and dienophile can be tethered (Chart I).[1,4,5] As depicted in Scheme I, because of the rigidity of vinylallenyl system 1, the type I IMDA cyclization was anticipated to lead to polycycle **2** in a completely regio-, enantio-, and diastereoselective manner. Indeed, the complete facial selectivity of this reaction was

(1) Okamura, W. H.; Curtin, M. L. *Synlett* **1990**, 1.

(2) For reviews of the chemistry of vinylallenes, see: (a) Egenburg, I. Z. *Russ. Chem. Rev.* **1978**, *47*, 470. (b) Okamura, W. H. *Acc. Chem. Res.* **1983**, *16*, 81.

(3) For reviews of the IMDA reaction, see: (a) Craig, D. *Chem. Soc. Rev.* **1987**, *16*, 187. (b) Fallis, A. G. *Can. J. Chem.* **1984**, *62*, 183. (c) Ciganek, E. *Org. React.* **1984**, *32*, 1.

(4) Type I IMDA reactions: (a) Deutsch, E. A.; Snider, B. B. *J. Org. Chem.* **1982**, *47*, 2682. (b) Deutsch, E. A.; Snider, B. B. *Tetrahedron Lett.* **1983**, *24*, 3701. (c) Snider, B. B.; Burbaum, B. W. *J. Org. Chem.* **1983**, *48*, 4370. (d) Keck, G. E.; Kachensky, D. F. *J. Org. Chem.* **1986**, *51*, 2487.

(5) Type V_E IMDA reactions: (a) Reich, H. J.; Eisenhart, E. K. *J. Org. Chem.* **1984**, *49*, 5282. (b) Reich, H. J.; Eisenhart, E. K.; Olson, R. E.; Kelly, M. J. *J. Am. Chem. Soc.* **1986**, *108*, 7791.

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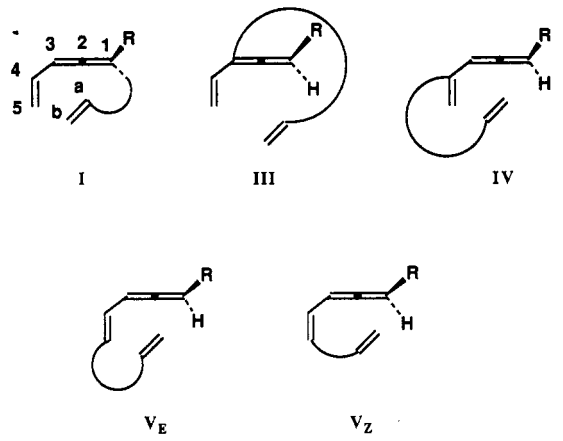
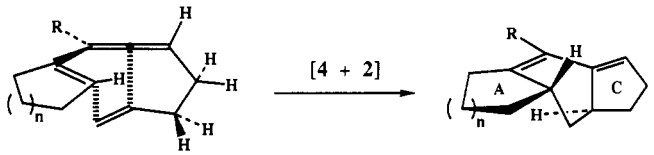
Chart I



I III IV

V_E V_Z

Scheme I



1 2

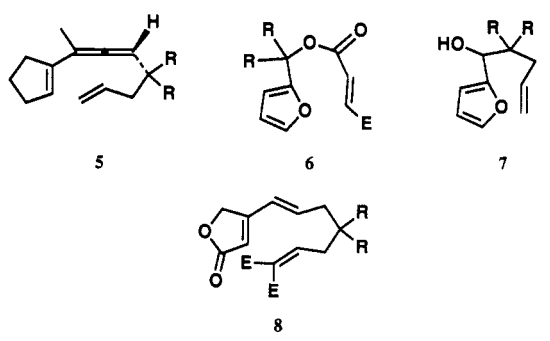
3 4

established in this laboratory and used in a key step in a concise synthesis of (+)-sterpurene.[6] In order to further develop the type I IMDA process, we were prompted to investigate more closely the effects of various structural changes on the rates of cyclization of cycloalkenylallenes of general type **3** to linearly fused polycycles of type **4**. It was believed that the presence of the ring fused to the vinyl portion of the vinylallene would allow us to maximize the stereochemical information available from the study. Also, since the cyclization was expected to be completely regioselective, facial selective, and exo/endo selective, a more quantitative assessment of substituent effects in this Diels–Alder process would be simplified. Of the many possible structural variations which could be studied, those of the allenyl substituents (**3**, X), tether substituents (**3**, R), cycloalkenyl ring size (**3**, *n*), and tether length (**3**, *z*) were selected for study.

Results and Discussion

Tether *gem*-Dialkyl Substituents. We have previously shown[6b] that a modest 2.4-fold rate acceleration is observed due to the tether *gem*-dimethyl group during the IMDA reaction of cycloalkenylallene **5** (R = Me vs H) (Chart II). The observation of only a modest acceleration was surprising, because Jung and Gervay recently reported a 2000-fold acceleration in rate caused by *gem*-dimethyl substitution in furan **6** (R = CH_3 vs H).[7] A similar study has also been carried out for furan **7** (R = CH_3 vs *n*-Pr) by Sternbach although the reactivity profile was not

Chart II[a]

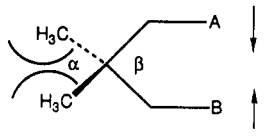


5 6 7 8

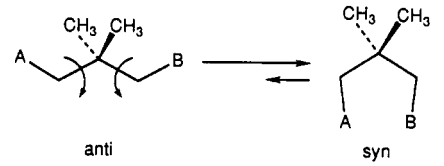
[a] E = COOMe or COOEt.

Scheme II

Thorpe-Ingold effect



Reactive Rotamer effect



anti syn

quantitated.[8] The data for **5** resembles that of **8** (R = CH_3 vs H) studied by Boeckman which showed a modest cyclization rate acceleration of about 4.[9]

The "*gem*-dimethyl effect" is well known and was reported as early as 1915.[10] It is currently believed that the "*gem*-dimethyl" effect is a combination of the "Thorpe–Ingold effect", a decrease in the internal bond angle (β) at the *gem*-dialkyl center which places the reactive centers (A and B in Scheme II) in closer proximity, and the "reactive rotamer effect", an overall increase in the population of the more reactive syn rotamer, with the "reactive rotamer effect" predominating.[7a,11]

However, a quantitative reactivity profile for the progression from an unsubstituted bridging alkyl chain to one containing *gem*-dimethyl, -diethyl, and -di-*n*-propyl substituents appears not to have been reported for the IMDA process. Furthermore, changes in activation parameters involved in such a progression have not been determined.

As an initial paradigm for studies of the vinylallene variant of the IMDA process, we selected the diphenylphosphinoyl-substituted system **3** (X = $P(O)Ph_2$, $n = z = 1$) because of its ease of preparation and analysis along with the convenient rate at which it cyclizes. It is well known that propargylic alcohols react with chlorodiphenylphosphine (CDP) to initially afford phosphinite esters which undergo [2,3]-sigmatropic shifts to give allenyl-

(6) (a) Gibbs, R. A.; Okamura, W. H. *J. Am. Chem. Soc.* **1988**, *110*, 4062. (b) Gibbs, R. A.; Bartels, K.; Lee, R. W. K.; Okamura, W. H. *J. Am. Chem. Soc.* **1989**, *111*, 3717.

(7) (a) Jung, M. E.; Gervay, J. *Tetrahedron Lett.* **1988**, *29*, 2429. (b) Jung, M. E.; Gervay, J. *J. Am. Chem. Soc.* **1989**, *111*, 5469. (c) Jung, M. E. *Synlett* **1990**, 186.

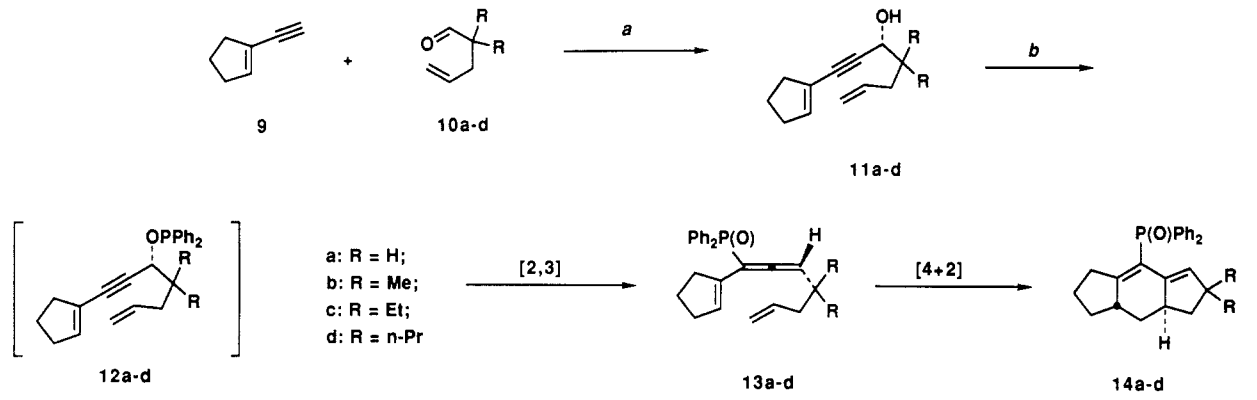
(8) Sternbach, D. D.; Rossana, D. M.; Onan, K. D. *Tetrahedron Lett.* **1985**, *26*, 591.

(9) Boeckman, R. K., Jr.; Ko, S. S. *J. Am. Chem. Soc.* **1982**, *104*, 1033.

(10) Beesley, R. M.; Ingold, C. K.; Thorpe, J. F. *J. Chem. Soc.* **1915**, *107*, 1080.

(11) For a general discussion of *gem*-dialkyl effects in other systems, see: (a) Allinger, N. L.; Zalkow, V. *J. Org. Chem.* **1960**, *25*, 701. (b) Dale, J. *J. Chem. Soc.* **1963**, 93. (c) DeTar, D.-L. F.; Luthra, N. P. *J. Am. Chem. Soc.* **1980**, *102*, 4505. (d) Schleyer, P. v. R. *J. Am. Chem. Soc.* **1961**, *83*, 1368. (e) Eberson, L.; Welinder, *J. Am. Chem. Soc.* **1971**, *93*, 5821. (f) Harfenist, M.; Thom, E. *J. Org. Chem.* **1972**, *37*, 841.

Scheme III[a]



[a] (a) 9, *n*-BuLi, Et_2O, 0 °C, 30 min; **10a–d**, 0 °C to room temperature, 2 h (**11a**, 65%; **11b**, 53%; **11c**, 72%; **11d**, 69%); (b) Ph_2PCl, DMAP, Et_2O, room temperature, 3–18 h (**14a**, 69%; **14b**,71%; **14c**, 70%; **14d**, 63%).

Table I. Relative Rates of Cyclization of Allenylphosphine Oxides 13a–d

substrate	R	rel rate	half-life, min, at 25.0 °C
13a	H	1.0	656
13b	Me	4.6	143
13c	Et	21.2	30.9
13d	*n*-Pr	27.8	23.6

phosphine oxides.[12] Racemic alcohols **11a–d** were readily prepared in good yields from 1-ethynyl-1-cyclopentene (**9**)[13] and the corresponding 4-pentenals (**10a–d**)[14] (Scheme III). Treatment of alcohols **11a–d** with CDP in the presence of 4-(*N*,*N*-dimethylamino)pyridine (DMAP) gave phosphinite esters **12a–d** which spontaneously rearranged to vinylallenes **13a–d** and subsequently cyclized at room temperature to afford phosphine oxides **14a–d** as single diastereomers (by ^1H and ^{13}C NMR analyses as well as HPLC analysis).

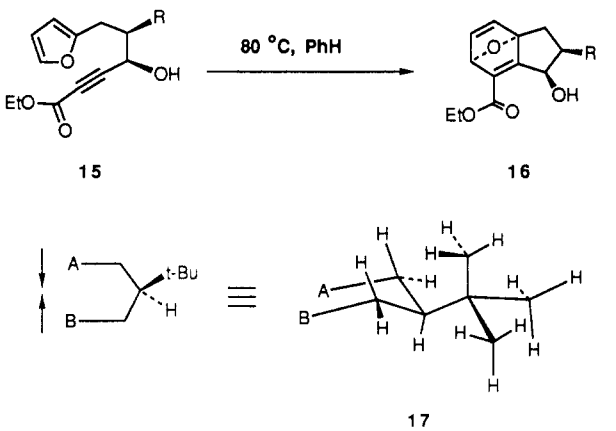
Conditions were found, however, by which allenylphosphine oxides **13a–d** (already contaminated by cyclized vinylphosphine oxides **14a–d**) could be obtained for rate studies (see the Experimental Section). The kinetic results at 25.0 ± 0.1 °C are summarized in Table I. As expected, the larger *gem*-dialkyl groups gave larger rate enhancements. Compared to the tether unsubstituted system **13a**, the *gem*-dimethyl derivative **13b** cyclized 4.6 times faster, similar to the results obtained for IMDA cyclization of both **5**[6b] and **8**[9] (Chart II). It was found that the *gem*-diethyl system **13c** afforded a rate enhancement of 21.2 compared to the parent system. Thus, the acceleration induced by changing from dimethyl (**13b**) to diethyl (**13c**) is as large (4.6-fold) as going from dihydrogen (**13a**) to dimethyl (**13b**) (4.6-fold). Finally, the *gem*-dipropyl derivative **13d** exhibited a smaller incremental rate enhancement (1.3-fold) compared to the *gem*-diethyl derivative **13c** (an overall

Table II. Activation Parameters at 25 °C for the Cyclization of Allenylphosphine Oxides 13a–c[a]

compd	E_a	log A	$\Delta H^\ddagger$	$\Delta S^\ddagger$	$\Delta G^\ddagger$
13a	21.3 (0.2)[b]	10.8 (0.3)	20.7 (0.2)	−11.1 (0.7)	23.9 (0.8)
13b	18.3 (0.1)	9.3 (0.4)	17.7 (0.1)	−18.0 (0.4)	23.1 (0.9)
13c	19.5 (0.2)	10.9 (0.5)	18.9 (0.2)	−10.7 (0.8)	22.1 (1.0)

[a] Units: E_a, $\Delta H^\ddagger$, $\Delta G^\ddagger$ = kcal/mol; $\Delta S^\ddagger$ = cal/mol K; A = s^{-1}. [b] Standard deviations are given in parentheses.

Scheme IV

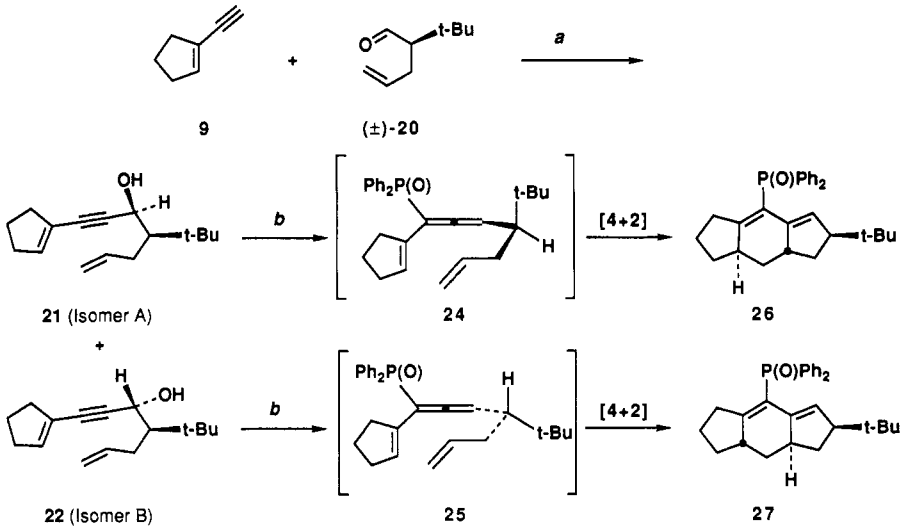


27.8-fold increase compared to **13a**). Thus, the *n*-propyl group resembles the ethyl group, and no special effect can be attributed to *n*-propyl groups as suggested in an earlier case.[8] It is not clear, however, why the ethyl case is so different from the methyl case considering that their relative steric bulk is not very different, as reflected, for example, by their respective A values.[15] Of course alkyl group effects in the context of cyclohexane conformational analysis may differ considerably from their effects in the IMDA process.

Activation parameters (25.0 °C) for the cyclization of **13a–c** observed over a 14–24 °C temperature range are summarized in Table II. Most significantly, while there is a trend in overall reactivity ($\Delta G^\ddagger$ in Table II) no trends exist in either the enthalpy or entropy of activation terms. This data implies that the origin of the observed rate

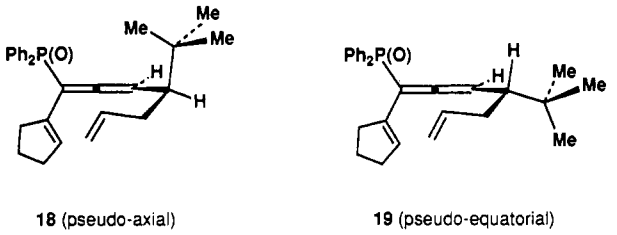
(12) Mark, V. *Mechanisms of Molecular Migrations*; Thyagarajan, B. S., Ed.; Wiley Interscience: New York, 1971; Vol. 2, pp 319–437.
(13) Brandsma, L. *Preparative Acetylenic Chemistry*; Elsevier: Amsterdam, 1971; p 137.
(14) (a) 4-Pentenal (**10a**): Montgomery, L. K.; Matt, J. W. *J. Am. Chem. Soc.* **1967**, *89*, 6556. (b) 2,2-Dimethyl-4-pentenal (**10b**): Salomon, R. G.; Ghosh, S. *Org. Synth.* **1984**, *62*, 125. (c) 2,2-Diethyl-4-pentenal (**10c**): Barbot, F.; Miginiac, P. *Helv. Chim. Acta* **1979**, *62*, 1451. (d) 2,2-Dipropyl-4-pentenal (**10d**): Martin, S. F.; Gompper, R. *J. Org. Chem.* **1974**, *39*, 2814.
(15) Hirsch, J. A. *Top. Stereochem.* **1967**, *1*, 199.

Scheme V[a]



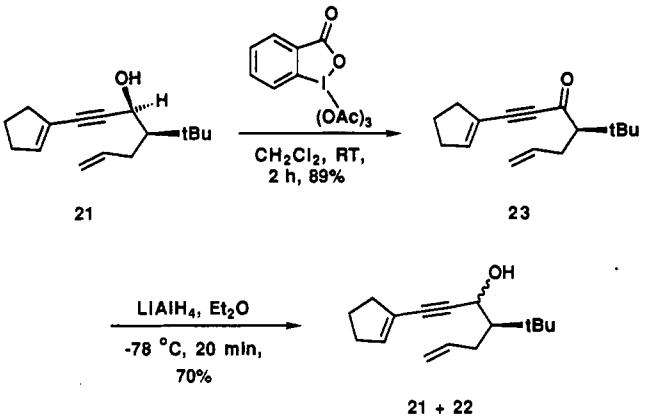
[a] (a) **9**, *n*-BuLi, Et_2O, 0 °C, 30 min; (±)-**20**, 0 °C to room temperature, 2 h (8:1 **21**/**22**, 87%); (b) Ph_2PCl, DMAP, Et_2O, room temperature, 4 h (**26**, 58%; **27**, 82%).

Chart III



18 (pseudo-axial) **19** (pseudo-equatorial)

Scheme VI



enhancements lies in a complex contribution of a variety of small effects not easily dissected into more specific effects (e.g., nonbonded interactions, reactive rotamer effects, etc.).

Tether *tert*-Butyl Substituents. Recently, De Clercq[16] reported that a single *tert*-butyl group on the bridging chain of furan **15** (R = *t*-Bu vs H) exerted a 240-fold rate acceleration in the cyclization to diene **16**. It was proposed that the *tert*-butyl substituent "anchors" the side chain in a conformation in which the bulky group occupies a pseudoequatorial position anti to the reactive termini (A and B in **17**, Scheme IV). It is the resulting parallel orientation of the reactive termini which was thought to be responsible for the observed rate acceleration. Since further data on the *tert*-butyl effect was lacking, an examination of this effect on the cyclization of allene **3** (R = *tert*-butyl, H; $n = z = 1$) was of interest. Due to the complete facial selectivity of the vinylallene IMDA reaction it was believed that use of diastereomeric propargylic alcohols would allow for the unique examination of dual systems in which the *tert*-butyl group was forced to alternatively occupy a pseudoaxial or pseudoequatorial position in the reactive rotamers (**18** and **19** in Chart III).

Accordingly, treatment of racemic 2-*tert*-butyl-4-pentenal (**20**) with the lithium salt of enyne **9** afforded an 8:1 diastereomeric mixture of propargylic alcohols **21** (isomer A) and **22** (isomer B) in good yield (Scheme V). This result is somewhat in contrast to De Clercq's work in which it was found that the addition of lithium ethyl propiolate to 2-*tert*-butyl-3-(2-furyl)propionaldehyde afforded a single diastereomer. Our stereochemical assignment of the isomeric alcohols is primarily based on the Felkin–Anh or Cram rule[17] and by analogy to the assignments of De Clercq.[16] In an attempt to further substantiate these assignments, propargylic alcohol **21** was oxidized to ketone **23** with the Dess–Martin periodinane reagent[18] and reduced back to a mixture of alcohols **21** and **22**. It was found that while neither sodium borohydride nor lithium tri-*tert*-butoxyaluminohydride could affect reduction of **23** under normal conditions, lithium aluminum hydride reduction was complete in 20 min even at −78 °C. However, this procedure afforded a 1:1 mixture of isomeric alcohols. In additional attempts to affect a Felkin–Anh or Cram directed reduction, ketone **23** was treated with Darvon alcohol–$LiAlH_4$ complex[19] which unexpectedly gave

Table III. Relative Rates of Cyclization of Allenylphosphine Oxides 13a, 24, and 25

substrate	rel rate	half-life, min, at 25.0 °C
13a	1.0	656
24 (isomer A)	70.5	9.3
25 (isomer B)	205	3.2

(16) Cauwberghs, S.; De Clercq, P. J.; Tinant, B.; Declercq, J. P. *Tetrahedron Lett.* **1988**, *29*, 2493.

(17) (a) Cherest, M.; Felkin, H.; Prudent, N. *Tetrahedron Lett.* **1968**, 2199. (b) Anh, N. T.; Eisenstein, O. *Nouv. J. Chim.* **1977**, *1*, 61.

(18) (a) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155. (b) de Lera, A. R.; Okamura, W. H. *Tetrahedron Lett.* **1987**, *28*, 2921.

(19) (a) Brinkmeyer, R. S.; Kapoor, V. M. *J. Am. Chem. Soc.* **1977**, *99*, 8339. (b) Cohen, N.; Lopresti, R. J.; Neukom, C.; Saucy, G. *J. Org. Chem.* **1980**, *45*, 582. (c) Wender, P. A.; Ihle, N. C.; Correia, C. R. D. *J. Am. Chem. Soc.* **1988**, *110*, 5904.

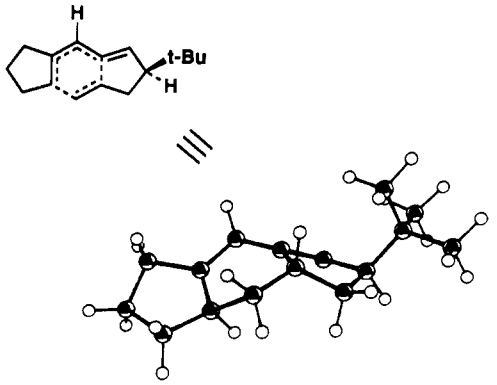


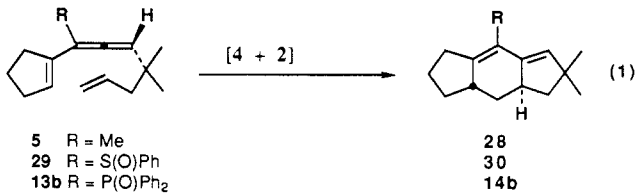
Figure 1. Model transition state for cyclization of allenylphosphine oxide **24**.

a 28:1 diastereomeric mixture with alcohol **21** still predominating (Scheme VI).

Separation of the isomeric alcohols by preparative HPLC and treatment with CDP and DMAP as above afforded isomeric vinylphosphine oxides **26** (isomer A) and **27** (isomer B) (Scheme V). Rate studies on the cyclization of allenylphosphine oxide **24** (isomer A), in which the *tert*-butyl group apparently occupies a pseudoaxial positon (Chart III), revealed a half-life of 9.3 min, indicating a ~70-fold rate enhancement versus the unsubstituted allene **13a** (Table III). It was also determined that allene **25** (isomer B), bearing a pseudoequatorial *tert*-butyl group cyclized rather quickly at room temperature. Quantitative experiments of the last 15% of cyclization indicated a reaction half-life of 3.2 min. This half-life constitutes a 2.9-fold acceleration over the diastereomeric allene **24** and an overall acceleration of ~200 versus the parent allene **13a**.

These results agree with the accelerating effect observed by De Clercq and seem to indicate that the "mono-*tert*-butyl effect" is general. It is interesing to note that the *tert*-butyl isomer **25**, which rearranges faster than the diastereomer **24**, cyclizes about 10 times faster than the *gem*-dipropyl-substituted vinylallene **13d**. The origin of the "anchoring" effect of the *tert*-butyl group in relationship to the tether *gem*-dialkyl effect is not clear. However, in line with De Clercq's work, a *tert*-butyl group which is forced to occupy a pseudoaxial orientation in the transition state (**24**) leads to a modestly slower cyclization rate when compared to its diastereomer (**25**). This unexpectedly small difference can be understood by considering molecular mechanics calculations[20] of a model transition state of the cyclization of **24** which indicate that the incipient five-membered ring is nearly flat, thus placing the *tert*-butyl group in a position with very little axial character (Figure 1).

Allenyl Substituents. Previous studies[6b] determined that vinylallene **5** cyclized to polycycle **28** with a half-life of ~91 h at 23 °C in $CDCl_3$, while allenyl sulfoxide **29** cyclized to vinyl sulfoxide **30** with a half-life of ~39 min under the same conditions. These results can be con-



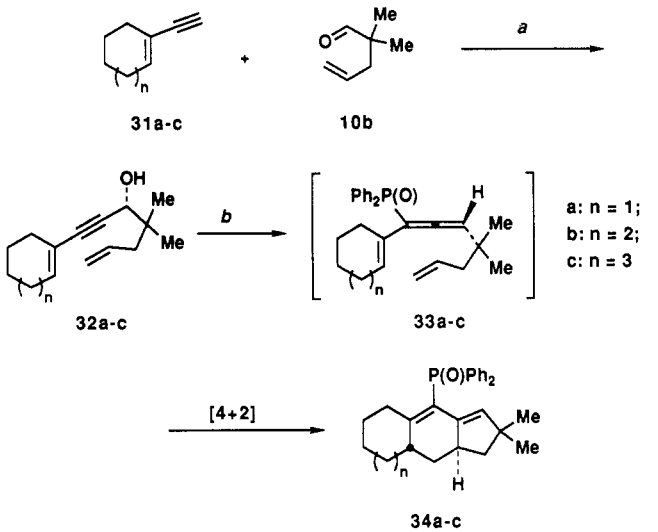
(1)

5 R = Me
29 R = S(O)Ph
13b R = P(O)Ph$_2$

28
30
14b

(20) These calculations were performed using the PCMODEL program available from Serena Software, Bloomington, IN. We thank Professor M. Mark Midland for valuable assistance with these calculations.

Scheme VII[a]



[a] (a) **31a–c**, *n*-BuLi, Et_2O, 0 °C, 30 min; **10b**, 0 °C to room temperature, 2 h (**32a**, 81%; **32b**, 83%; **32c**, 76%); (b) Ph_2PCl, DMAP, Et_2O, room temperature, 3–18 h (**34a**, 56%; **34b**, 82%; **34c**, 85%).

Table IV. Relative Rates of Cyclization of Allenylphosphine Oxides 13b and 33a–c

substrate	rel rate	half-life, min, at 40.0 °C
13b	3.9	33.6
33a	1.1	115
33b	6.8	19.2
33c	1.0	130

trasted with this study, which has established that allenylphosphine oxide **13b** undergoes cyclization at 23 °C in $CDCl_3$ with a half-life of 184 min (extrapolated from Arrhenius data). While changing the allenyl substituent from methyl to phenylsulfinyl (**5** to **29**) afforded a rate acceleration of ~140, the progression from a methyl to diphenylphosphinoyl moiety (**5** to **13b**) gives a somewhat smaller acceleration of ~30.[21] Despite the 4-fold difference between the phenylsulfinyl and diphenylphosphinoyl groups, both acceleration effects can be attributed to these electron-withdrawing groups acting to induce an inverse electron demand IMDA reaction.[22-24]

Ring Size Effects. An additional structural change which was explored was that of the size of the ring annulated to the vinyl portion of the vinylallene. Synthesis of the desired allenes began with the coupling of 2,2-dimethyl-4-pentenal (**10b**) with 1-ethynyl-1-cycloalkenes **31a–c**[13] to afford propargylic alcohols **32a–c** (Scheme VII). Treatment of these alcohols in the usual fashion afforded allenyl phosphine oxides **33a–c** which spontaneously cyclized at room temperature to give vinylphosphine oxides **34a–c**, again as single diastereomers (by ^1H and ^{13}C NMR analyses and HPLC analysis) in acceptable yields.

(21) This trend in acceleration agrees with the relative electronegativities of the sulfoxide and phosphine oxide moieties as exemplified by their respective σ_m values: S(O)Me (0.52) and P(O)Me_2 (0.42). Hansch, C.; Leo, A.; Unger, S. H.; Kim, K.-H.; Nikaitani, D.; Lien, E. J. *J. Med. Chem.* **1973**, *16*, 1207.

(22) For an example of this effect used in synthesis, see: Posner, G. H.; Haces, A.; Harrison, W.; Kinter, C. M. *J. Org. Chem.* **1987**, *52*, 4836 and the references therein.

(23) For the accelerating effect of a sulfoxide on a [1,5]-sigmatropic shift, see: (a) Okamura, W. H.; Shen, G.-Y.; Tapia, R. *J. Am. Chem. Soc.* **1986**, *108*, 5018. (b) Shen, G. Y.; Tapia, R.; Okamura, W. H. *J. Am. Chem. Soc.* **1987**, *109*, 7499.

(24) For a discussion of inverse electron demand Diels–Alder reactions, see: Boger, D. L.; Weinreb, S. M. *Hetero Diels–Alder Methodology in Organic Synthesis*; Academic Press: Orlando, FL, 1987.

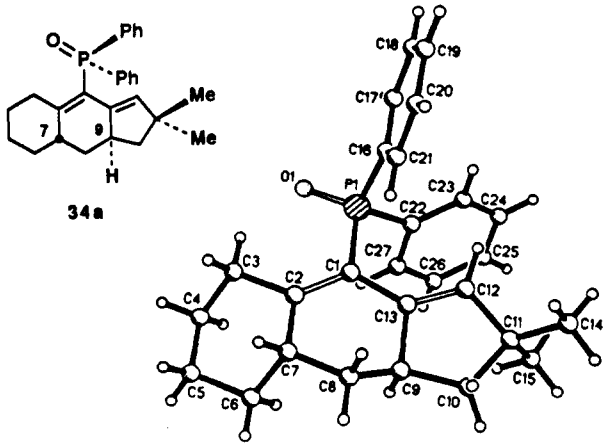
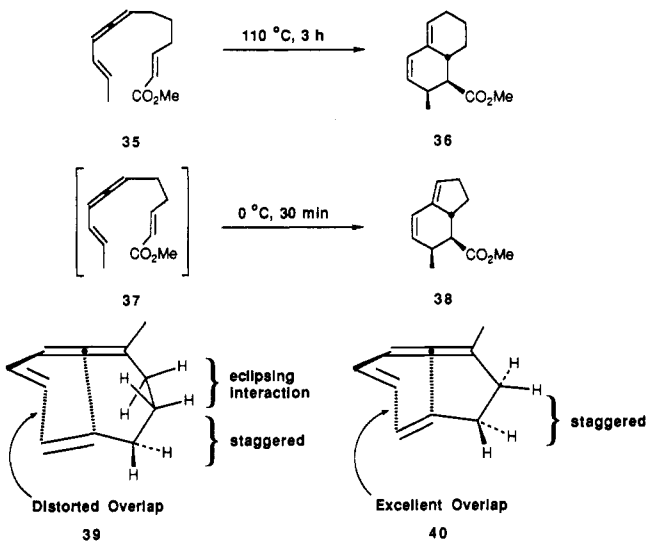


Figure 2.

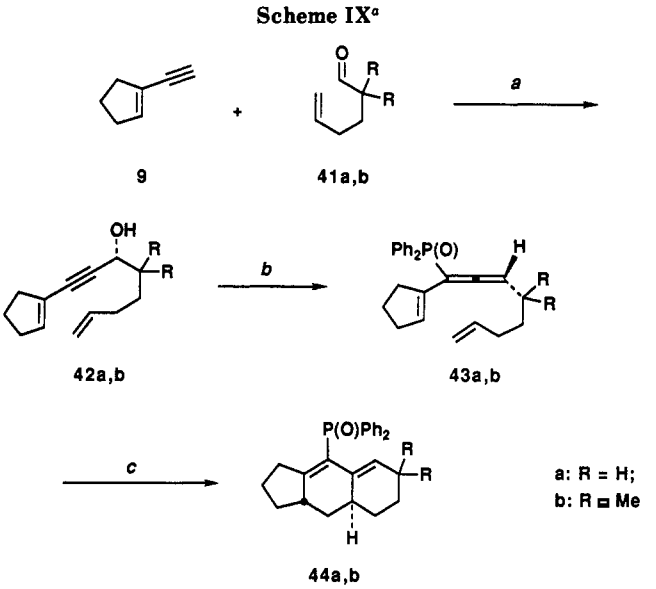
Scheme VIII



The rates of cyclization could be conveniently studied at 40.0 °C, and the data is summarized in Table IV. While it can be seen that the seven-membered ring system cyclizes the fastest, the rate constants all fall within a factor of 10 of one another.[25] As no trend in rate with increasing ring size can be seen, we believe that the differences in observed rates are a result of a combination of small effects which cannot be easily discerned. An important consequence of this study was that recrystallization of phosphine oxide **34a** afforded crystals of sufficient quality for X-ray crystallographic analysis.[26] The most salient feature of the crystal structure was the definitive establishment of the anti relationship between the bridgehead hydrogens (H_7 and H_9 in Figure 2). This data along with the complete facial selectivity of the cyclization firmly supports the proposed transition state model (**1** in Scheme I) and the view that the allenyl system is too rigid to cyclize in any other fashion.

Tether Length Effect. It has been shown by Snider[4c] that the length of the tether linking diene and dienophile in the IMDA reaction of vinylallenes seems to significantly affect their reactivity toward cycloaddition. It was found that while cyclization of vinylallene **35**, which possesses

Scheme IX[a]

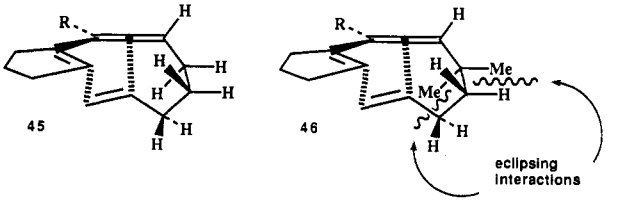


[a] (a) **9**, *n*-BuLi, Et_2O, 0 °C, 30 min; **41a,b**, 0 °C to room temperature, 2 h (**42a**, 78%; **42b**, 79%); (b) Ph_2PCl, DMAP, Et_2O, room temperature, 3–12 h (**43a**, 80%; **43b**, 70%); (c) C_6D_6, 98 °C, 12–17 h (**44a**, 89%; **44b**, 56%).

Table V. Relative Rates of Cyclization of Allenylphosphine Oxides 43a,b

substrate	rel rate	half-life, min, at 98.0 °C
43a	1.0	710
43b	2.6	272

Chart IV



a three carbon tether to decalin **36** required elevated temperatures, the two carbon tethered analogue **37** spontaneously cyclized to hydrindane **38** (Scheme VIII). This can be explained by considering molecular models. While the three carbon tethered system **39** has distorted orbital overlap and eclipsing interactions between the tether hydrogens, the analogous two carbon tethered system **40** has excellent orbital overlap between the reacting centers and a staggered arrangement on the tether.

In order to quantitate this effect, a three carbon tethered allenylphosphine oxide was synthesized. Treatment of 2,2-dimethyl-5-hexenal (**41b**)[27] with the lithium acetylide anion of enyne **9** gave properglylic alcohol **42b**, which upon treatment with CDP and DMAP afforded allenylphosphine oxide **43b** uncontaminated by cyclization product **44b** (Scheme IX). Initial experiments determined that cyclization did not occur even at 55 °C! However, on a preparative scale allene **43b** could be cyclized to vinylphosphine **44b** in a sealed tube at 98 °C. Only a single diastereomer was detected by ^1H and ^{13}C NMR analyses. Quantitative experiments showed that the half-life for cyclization at 98 °C was 272 min (Table V), which corresponds to an 850-fold decrease in rate versus the corresponding two carbon tethered allene **13b**.

(25) For a ring size effect on the [1,5]-hydrogen shift of a series of vinylallenones, see ref 2b.

(26) We thank Dr. Joseph W. Ziller at the University of California, Irvine, for the X-ray analysis. Full details are given in the supplementary material.

(27) House, H. O., Liang, W. C.; Weeks, P. D. *J. Org. Chem.* **1974**, *39*, 3102.

While this result confirmed our expectations, the role of the tether *gem*-dimethyl group came into question. Dreiding models seemed to indicate that, whereas the tether unsubstituted allene transition-state model **45** possesses a hydrogen–hydrogen and a hydrogen–methylene eclipsing interaction, the analogous dimethyl-substituted derivative transition-state model **46** possesses more severe methyl–hydrogen and methyl–methylene eclipsing interactions (Chart IV). It was therefore possible that the *gem*-dimethyl group may actually cause a retardation in the cyclization rate of **43b**, just the opposite of what is more typically observed.[28] To determine if this was the case, 5-hexenal (**41a**)[29] was coupled with enyne **9** as above to give alcohol **42a**. Treatment of the latter with CDP and DMAP afforded the stable allenylphosphine oxide **43a**. Heating **43a** at 98 °C gave cyclized phosphine oxide **44a** in high yield, again as a single diastereomer. Kinetic experiments revealed a half-life of 710 min for cyclization, indicating a 2.6-fold decrease in rate versus **43b**. This *gem*-dimethyl effect is close to that seen for **13a** versus **13b** above (4.6) and seems to indicate that the transition state tether interactions depicted in Chart IV may be exaggerated by molecular models.

Summary. Rate studies have explored the effects of tether *gem*-dialkyl groups, allenyl substituents, fused ring size, and tether length on the intramolecular Diels–Alder reaction of vinylallenes. Additional new data on the "*tert*-butyl effect" has been provided. Mechanistic insight into the reaction has been developed which we hope will extend beyond the specific processes described herein. Finally, it has been further demonstrated that the IMDA reaction of vinylallenes is a versatile and convenient method to construct a wide range of polycycles.

Experimental Section[30]

1-(Cyclopent-1′-en-1′-yl)-4,4-diethyl-6-hepten-1-yn-3-ol (11c). Enyne **9** (2.14 g, 23 mmol) in dry ether (100 mL) under nitrogen was cooled to 0 °C, and *n*-BuLi (15.4 mL, 1.51 M in hexanes, 23 mmol) was added dropwise to give a clear yellow solution of the acetylide anion. After 30 min, aldehyde **10c** (3.27 g, 23 mmol) was added via syringe to the reaction mixture. After an additional 5 min, the cooling bath was removed and the reaction mixture was stirred at room temperature for 2 h. After water (4 mL) was added to quench the reaction, K_2CO_3 was added to the mixture until a paste formed. The reaction mixture was diluted with additional ether, and the ether layer was then dried and filtered. The solvent was removed, and the crude propargyl alcohol was purified by chromatography (8 × 18 cm column; 95:5 hexanes/ethyl acetate) to yield after vacuum drying 3.92 g (72%) of **11c** as a viscous, yellow oil. An analytical sample was prepared by HPLC purification (95:5 hexanes/ethyl acetate; 8 mL/min; Rainin Dynamax 60A).

1-(Cyclopent-1′-en-1′-yl)-4,4-dipropyl-6-hepten-1-yn-3-ol (11d). As in the preceding procedure, enyne **9** (0.87 g, 9.4 mmol) in ether (20 mL) was converted to its acetylide anion, which was reacted with aldehyde **10d** (1.59 g, 9.4 mmol) to afford after workup and purification 1.70 g (69%) of **11d** (viscous, yellow oil).

(7*R,9*S**)-2-(Diphenylphosphinoyl)tricyclo[7.3.0.0^{3,7}]-dodeca-1,3-diene (14a) and 1-(1′-Cyclopenten-1′-yl)-1-(diphenylphosphinoyl)-1,2,6-heptatriene (13a).** To a stirred solution of propargyl alcohol **11a** (504 mg, 2.86 mmol) and 4-(*N*,*N*-dimethylamino)pyridine (DMAP, 419 mg, 3.43 mmol) in ether (10 mL, freshly distilled from Na/benzophenone ketyl) under nitrogen at room temperature was added chlorodiphenylphosphine (CDP, 501 μL, 3.43 mmol) dropwise via syringe. After the mixture was stirred at room temperature for 32 h, water (10 mL) was added to quench the reaction. The organic layer was separated, and the aqueous layer was extracted with ether. The combined organic layers were dried, filtered, and concentrated. Purification of the crude phosphine oxide by flash chromatography (4.0 × 16 cm, 20:80 hexanes/ethyl acetate) yielded after vacuum drying 711 mg (69.0%) of phosphine oxide **41a** as a clear viscous oil. A sample for characterization was prepared by HPLC purification (ethyl acetate; 4 mL/min; Rainin Dynamax 60A).

For the kinetic studies, a sample enriched in allene **13a** was prepared in the following manner. The above procedure was followed [497 mg (2.82 mmol) of propargylic alcohol **11a**, 517 mg (4.23 mmol) of DMAP, ether (10 mL) and 617 μL (4.23 mmol) of CDP] except that the reaction mixture was allowed to stand for only 1 h at 25 °C before workup. At this time the reaction was quenched with water (2 mL); after removal of the aqueous phase by pipette the organic phase was dried, filtered, and concentrated as quickly as possible (first by concentration on a rotary evaporator under water aspirator pressure and then final drying on a vacuum pump). The crude material was redissolved in $CDCl_3$, divided among a number of NMR tubes, and cooled to −78 °C. A sample was removed and placed in the NMR probe, which was calibrated to a specific temperature. After equilibration to the desired temperature, ^{1}H NMR spectra (300 MHz) were recorded at regular intervals. The spectra typically revealed the presence of both allene **13a** and cyclized product **14a** together with a small amount of residual solvent (ether). The rate of reaction was monitored by following the disappearance of the δ 6.0 signal ($H_{2'}$) of allene **13a** versus the appearance of the δ 5.02 signal (H_4) of cyclized product **14a**. Another signal of the allene **13a** [δ 5.6 (H_6)] was also monitored versus the H_4 signal of cyclized product **14a** to calculate the irreversible first-order rate constant. Good agreement (±3%) was obtained. Further details of the kinetic investigation are presented below and in the supplementary material section.

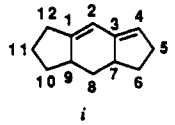
(7*R,9*S**)-2-(Diphenylphosphinoyl)-5,5-dimethyltricyclo[7.3.0.0^{3,7}]dodeca-1,3-diene (14b) and 1-(1′-Cyclopenten-1′-yl)-1-(diphenylphosphinoyl)-4,4-dimethyl-1,2,6-heptatriene (13b).** The general procedure described for the preparation of **14a** was followed, using the following materials: propargyl alcohol **11b** (149 mg, 0.73 mmol), 4-(*N*,*N*-dimethylamino)pyridine (DMAP, 269 mg, 2.19 mmol), ether (10 mL), and chlorodiphenylphosphine (CDP, 393 μL, 2.19 mmol). Purification of the crude tricyclic phosphine oxide by flash chromatography (silica gel, 3.0 × 16 cm, 1:1 hexanes/ethyl acetate) yielded 202 mg (71.3%) of phosphine oxide **14b** as a colorless oil.

For the kinetic studies, the above procedure described for **13a** was followed [152 mg (0.75 mmol) of propargylic alcohol **11b**, 137 mg (1.12 mmol) of DMAP, ether (10 mL), and 201 μL (1.12 mmol) of CDP] except that the reaction mixture was allowed to stand for only 0.5 h at 25 °C before workup. The rate of reaction was monitored by following the disappearance of the δ 6.0 signal ($H_{2'}$) of allene **13b** versus the appearance of the δ 4.73 signal (H_4) of cyclized product **14b**. Another signal of the allene **13b** [δ 5.5 (H_6)]

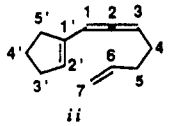
(28) For an example of rate retardation by a *gem*-dimethyl group, see: Blagoeva, I. B.; Tashev, D. T.; Kirby, A. J. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1157. We are grateful to Dr. Bruce E. Maryanoff for informing us of this reference.

(29) Ikeda, T.; Yue, S.; Hutchinson, C. R. *J. Org. Chem.* **1985**, *50*, 5193.

(30) (a) All chiral substances reported in this study are racemic. The tricyclic IMDA adducts (except that shown in the ORTEP structure in Figure 2) and the allenes are numbered systematically (IUPAC) as exemplified by structures i and ii shown below.



i



ii

(b) Spectral and other analytical data, along with a detailed description of the kinetic studies, are presented in the supplementary material. All experiments involving air- and/or moisture-sensitive materials were carried out under a nitrogen or argon atmosphere, which was dried prior to use by passage through a column of KOH layered with $CaSO_4$. Tetrahydrofuran, ether and benzene were distilled from sodium benzophenone ketyl immediately prior to use. Hexanes was distilled from CaH_2. Unless otherwise indicated for workup procedures, organic solutions were dried over $MgSO_4$, filtered, and then finally concentrated on a rotary evaporator at reduced pressure. The purity of all new compounds were judged by a combination of HPLC and ^{1}H and ^{13}C NMR analyses before mass spectral determination. Satisfactory combustion analyses were also obtained for selected compounds. For other new compounds, the level of purity is indicated by the inclusion of copies of NMR spectra presented in the supplementary material.

was also monitored versus the H_4 signal of cyclized product **14b** to calculate the irreversible first-order rate constant.

(7*R,9*S**)-2-(Diphenylphosphinoyl)-5,5-diethyltricyclo[7.3.0.0^{3,7}]dodeca-1,3-diene (14c) and 1-(1′-Cyclopenten-1′-yl)-1-(diphenylphosphinoyl)-4,4-diethyl-1,2,6-heptatriene (13c).** As for the preparation of **14a**, propargyl alcohol **11c** (304 mg, 1.31 mmol), 4-(*N*,*N*-dimethylamino)pyridine (DMAP, 240 mg, 1.96 mmol), ether (10 mL), and chlorodiphenylphosphine (CDP, 352 μL, 1.96 mmol) yielded after workup and purification 382 mg (70.1%) of phosphine oxide **14c** as a clear, viscous oil.

For the kinetic studies, a sample enriched in allene **13c** was prepared as described for **13a** using 268 mg (1.15 mmol) of propargylic alcohol **11c**, 211 mg (1.73 mmol) of DMAP, $CDCl_3$ (5 mL), and 311 μL (1.73 mmol) of CDP except that the reaction mixture was allowed to stand for only 10 min at 25 °C before workup. The rate of reaction was monitored by following the disappearance of the δ 6.0 signal ($H_{2'}$) of allene **13c** versus the appearance of the δ 4.81 signal (H_4) of cyclized product **14c**. Another signal of the allene **13c** [δ 5.2 (H_3)] was also monitored versus the H_4 signal of cyclized product **14c** to calculate the irreversible first-order rate constant.

(7*R,9*S**)-2-(Diphenylphosphinoyl)-5,5-dipropyltricyclo[7.3.0.0^{3,7}]dodeca-1,3-diene (14d) and 1-(1′-Cyclopenten-1′-yl)-1-(diphenylphosphinoyl)-4,4-dipropyl-1,2,6-heptatriene (13d).** As given for the preparation of **14a**, **14d** was prepared from propargyl alcohol **11d** (317 mg, 1.22 mmol), 4-(*N*,*N*-dimethylamino)pyridine (DMAP, 179 mg, 1.46 mmol), ether (10 mL), and chlorodiphenylphosphine (CDP, 262 μL, 1.46 mmol). Workup and then purification afforded 342 mg (63.2%) of phosphine oxide **14d** as a clear, viscous oil.

For the kinetic studies, the procedure for preparing **13a** was followed using 110 mg (0.42 mmol) of propargylic alcohol **11d**, 62 mg (0.51 mmol) of DMAP, $CDCl_3$ (5 mL), and 91 μL (0.51 mmol) of CDP, but the reaction mixture was allowed to stand for only 10 min at 25 °C before workup. The rate of reaction was monitored by following the disappearance of the δ 6.0 signal ($H_{2'}$) of allene **13d** versus the appearance of the δ 4.86 signal (H_4) of cyclized product **14d**. Another signal of the allene **13d** [δ 5.22 (H_3)] was also monitored versus the H_4 signal of cyclized product **14d** to calculate the irreversible first-order rate constant.

2-*tert*-Butyl-4-pentenal (20). A solution of 3,3-dimethylbutanal (9.57 g, 95.6 mmol), allyl alcohol (11.1 g, 191 mmol), *p*-toluenesulfonic acid (25 mg), and benzene (30 mL) in diphenyl ether (70 mL) was refluxed under a 50-cm Vigreux column topped with a Dean–Stark trap and condenser. After 44 and 64 h, additional equivalents of allyl alcohol were added to the mixture (22.2 g total; 382 mmol). At 70 h, NMR analysis indicated that the reaction was complete. The product was distilled from the solvent under vacuum (~40 mm) and purified by flash chromatography (silica gel, 5 × 18 cm column; 5% ethyl ether/hexanes) to afford 4.45 g (33.2%) of aldehyde **20** as a clear, colorless liquid which was used without further purification. A sample for characterization was prepared by HPLC purification (4 mL/min; 3% ethyl acetate/hexanes; Rainin Dynamax 60A).

1-(Cyclopent-1′-en-1′-yl)-4-*tert*-butyl-6-hepten-1-yn-3-ol (Major, Less Polar Isomer A, and Minor, More Polar Isomer B) (21 and 22). A mixture of enyne **9** (1.39 g, 15 mmol) in ether (40 mL) under nitrogen was cooled to 0 °C, and *n*-BuLi (9.4 mL, 1.51 M in hexanes, 15 mmol) was added dropwise to give a clear yellow solution of the acetylide anion. After 30 min, aldehyde **20** (2.11 g, 15 mmol) was added and after an additional 5 min, the cooling bath was removed and the reaction mixture was stirred at room temperature for 2 h. Water (4 mL) was added to quench the reaction, and K_2CO_3 was added to the mixture until a paste formed. The reaction mixture was diluted with additional ether, and the ether layer was dried and filtered. The solvent was removed, and the crude propargyl alcohol was purified by chromatography (silica gel, 8 × 18 cm column; 93:7 hexanes/ethyl acetate) to yield 3.04 g (86.8%) of a mixture of alcohols **21** (isomer A) and **22** (isomer B). Separation of the isomers (~8:1, A:B mixture) was achieved by HPLC purification (95:5 hexanes/ethyl acetate; 8 mL/min; Rainin Dynamax 60A).

In a separate procedure, propargylic ketone **23** (55 mg, 0.24 mmol) in ether (10 mL) was added via syringe to a stirred, cooled (−78 °C) suspension of lithium aluminum hydride (LAH, 23 mg, 0.58 mmol) in ether (15 mL) under argon. The mixture was stirred at −78 °C for 20 min at which time the ^1H NMR spectrum of an aliquot indicated that the reaction was complete. The reaction was quenched with saturated NH_4Cl (10 mL), and the aqueous layer was extracted with ether. The combined organic layers were washed with water (20 mL), dried, filtered, and concentrated. The crude product was passed through a silica gel plug with hexanes. Concentration of the filtrate afforded a residue which was purified by HPLC (3% ethyl acetate/hexanes; 4 mL/min; Rainin Dynamax 60A) to afford a mixture of propargylic alcohols **21** (isomer A, 15.9 mg) and **22** (isomer B, 15.4 mg; 31.3 mg total, 70%).

In an alternative reduction procedure, a solution of (2*S*,3*R*)-(+)-4-(dimethylamino)-1,2-diphenyl-3-methyl-2-butanol (Chirald, 101 mg, 0.36 mmol) in ether (7 mL) was added dropwise to a stirred, cooled (0 °C) suspension of $LiAlH_4$ (6.8 mg, 0.17 mmol) in ether (15 mL). The resulting mixture was stirred for 2 min and then cooled to −78 °C at which time propargylic ketone **23** (36 mg, 0.16 mmol) in ether (5 mL) was added dropwise via syringe over 40 min. The reaction mixture was stirred at −78 °C for 4 h and at 25 °C for 15 min, at which time the reaction was quenched with water (5 mL). The organic layer was washed with 1 M HCl to remove the Chirald, dried, filtered, and concentrated. The crude product was passed through a silica gel plug with hexanes, the filtrate was concentrated, and the resulting residue was purified by HPLC (3% ethyl acetate/hexanes; 4 mL/min; Rainin Dynamax 60A) to afford a mixture of propargylic alcohols **21** (isomer A, 20.6 mg) and **22** (isomer B, 1.1 mg; 21.7 mg total, 60%) along with starting material **23** (6 mg).

1-(Cyclopent-1′-en-1′-yl)-4-*tert*-butyl-6-hepten-1-yn-3-one (23). A solution of propargyl alcohol **21** (isomer A, 813 mg, 3.50 mmol) in dry CH_2Cl_2 (6 mL) was added via syringe to a stirred suspension of Dess–Martin periodinane reagent (3.70 g, 8.72 mmol) and CH_2Cl_2 (60 mL) at room temperature. After 2 h the reaction was shown to be complete (by TLC), and the mixture was poured into a stirred solution of $Na_2S_2O_3 \cdot 5H_2O$ (6 g) in saturated aqueous $NaHCO_3$ (100 mL). The layers were separated, the aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were washed with saturated aqueous $Na_2S_2O_3 \cdot 5H_2O$ (40 mL), saturated aqueous $NaHCO_3$ (30 mL), and water (30 mL), dried, filtered, and concentrated. The crude ketone was chromatographed (silica gel, 3 × 18 cm; 3% ethyl acetate/hexanes) to afford 718 mg (89%) of propargylic ketone **23** as a clear, spectrally homogeneous liquid.

In a separate procedure, pyridinium chlorochromate (PCC, 1.91 g, 8.70 mmol) was ground with silica gel (70–230 mesh, 2 g) using a mortar and pestle. The resulting free-running light orange solid was suspended in CH_2Cl_2 (25 mL) at 25 °C, and then propargylic alcohol **21** (Isomer A, 1.01 g, 4.35 mmol) in CH_2Cl_2 (5 mL) was added via cannula in one portion. The mixture was stirred at 25 °C for 5 h at which time it was filtered through a column of Florisil (3 × 2 in.) with ether (150 mL). Concentration of the filtrate gave a yellow oil, which was chromatographed (silica gel, 3 × 18 cm; 3% ethyl acetate/hexanes) to afford 667 mg (67%) of propargylic ketone **23** as a clear liquid which was spectrally homogeneous.

(5*R,7*S**,9*R**)-2-(Diphenylphosphinoyl)-5-*tert*-butyltricyclo[7.3.0.0^{3,7}]dodeca-1,3-diene (26, Isomer A) and 1-(1′-Cyclopenten-1′-yl)-1-(diphenylphosphinoyl)-4-*tert*-butyl-1,2,6-heptatriene (24, Isomer A).** As for the preparation of **14a**, propargyl alcohol **21** (isomer A, 226 mg, 0.97 mmol), DMAP (142 mg, 1.16 mmol), ether (10 mL), and chlorodiphenylphosphine (CDP, 209 μL, 1.16 mmol) were reacted and worked up. Purification of the product afforded 233 mg (58%) of phosphine oxide **26** (clear, viscous oil). A sample for characterization was prepared by HPLC purification (10% isopropyl alcohol/hexanes; 4 mL/min; Rainin Dynamax 60A).

For kinetic studies, the above procedure was followed [54 mg (0.23 mmol) propargylic alcohol **21**, 34 mg (0.28 mmol) of DMAP, $CDCl_3$ (3 mL), and 50 μL (0.28 mmol) of CDP] except that the reaction mixture was allowed to stand for only 12 min at 25 °C before workup. The rate of reaction was monitored by following the disappearance of the δ 0.75 signal ($H_{t\text{-}Bu}$) of allene **24** versus the appearance of the δ 0.49 signal ($H_{t\text{-}Bu}$) of cyclized product **26**.

(5*R,7*R**,9*S**)-2-(Diphenylphosphinoyl)-5-*tert*-butyltricyclo[7.3.0.0^{3,7}]dodeca-1,3-diene (27, Isomer B) and 1-(1′-Cyclopenten-1′-yl)-1-(diphenylphosphinoyl)-4-*tert*-butyl-1,2,6-heptatriene (25, Isomer B).** As for the preparation of **14a**, **27** was prepared by reacting propargyl alcohol **22** (isomer B, 194

mg, 0.83 mmol), DMAP (122 mg, 1.00 mmol), ether (10 mL), and chlorodiphenylphosphine (CDP, 180 μL, 1.00 mmol). Workup and flash chromatography (silica gel, 1:1 hexanes/ethyl acetate) yielded 282 mg (81%) of phosphine oxide **27** as a clear, viscous oil.

For the kinetic studies, the above procedure was followed [57 mg (0.25 mmol) propargylic alcohol **22**, 70 mg (0.57 mmol) of DMAP, $CDCl_3$ (3 mL), and 50 μL (0.28 mmol) of CDP] except that the reaction mixture was allowed to stand for only 2.5 min at 25 °C before workup. The rate of reaction was monitored by following the disappearance of the δ 0.52 signal ($H_{t\text{-}Bu}$) of allene **25** versus the appearance of the δ 0.65 signal ($H_{t\text{-}Bu}$) of cyclized product **27**.

1-Ethynyl-1-cyclooctene (31c). A mixture of 1-ethynylcyclooctanol (8.35 g, 54.9 mmol) and pyridine (30 mL, distilled from KOH) under nitrogen was preheated to 100 °C. A solution of $POCl_3$ (3.7 mL, 38 mmol) in pyridine (10 mL) was added in several portions over a 15-min period in a manner such that the temperature of the reaction mixture was maintained between 100 and 110 °C. The reaction mixture was heated at 100 °C for 10 min, allowed to cool to only 75 °C (in order to prevent solidification of the mixture), and then poured slowly and carefully into a beaker containing 200 mL of ice chips in water. The resulting mixture was extracted with ether, and the combined ether layers were washed with 1 M HCl, saturated aqueous $CuSO_4$, and water, dried ($MgSO_4$), and filtered. The ether was removed by distillation, and the remaining residue was distilled via a Kugelrohr apparatus under aspirator vacuum (bp 75 °C, 30 mm) to afford 4.54 g (62%) of enyne **31c** as a clear, spectrally homogeneous liquid.

1-(Cyclohex-1′-en-1′-yl)-4,4-dimethyl-6-hepten-1-yn-3-ol (32a). A mixture of enyne **31a** (5.00 g, 47.1 mmol) in ether (100 mL) under nitrogen was cooled to 0 °C, and *n*-BuLi (31.2 mL, 1.51 M in hexanes, 47.1 mmol) was added dropwise via syringe to give a clear yellow solution of the acetylide anion. After 30 min, aldehyde **10b** (5.28 g, 47.1 mmol) was added via syringe to the reaction mixture and after an additional 5 min the cooling bath was removed and the mixture was stirred at room temperature for 2 h. After a standard workup (water, ether), the resulting crude propargyl alcohol was purified by chromatography (silica gel, 8 × 18 cm column; 95:5 hexanes/ethyl acetate) to yield 8.31 g (81%) of propargyl alcohol **32a** as a clear, spectrally homogeneous liquid.

1-(Cyclohept-1′-en-1′-yl)-4,4-dimethyl-6-hepten-1-yn-3-ol (32b). Via the procedure outlined above for the preparation of **32a**, propargyl alcohol **32b** was prepared from enyne **31b** (1.00 g, 8.33 mmol), ether (50 mL), *n*-BuLi (5.52 mL, 1.51 M in hexanes, 8.33 mmol), and aldehyde **10b** (0.93 g, 12.8 mmol). The crude propargyl alcohol was purified by chromatography (silica gel, 90:10 hexanes/ethyl acetate) to yield 1.60 g (83%) of propargyl alcohol **32b** as a clear, spectrally homogeneous liquid.

1-(Cyclooct-1′-en-1′-yl)-4,4-dimethyl-6-hepten-1-yn-3-ol (32c). Via the procedure outlined above for the preparation of **32a**, propargylic alcohol **32c** was prepared using enyne **31c** (2.09 g, 15.6 mmol), ether (100 mL), *n*-BuLi (9.75 mL, 1.6 M in hexanes, 15.6 mmol), and aldehyde **10b** (1.75 g, 15.6 mmol). There was obtained 2.94 g (76%) of propargyl alcohol **32c** as a clear, spectrally homogeneous liquid.

(7*R,9*S**)-2-(Diphenylphosphinoyl)-5,5-dimethyltricyclo[7.4.0.0^{3,7}]trideca-1,3-diene (34a) and 1-(1′-Cyclohexen-1′-yl)-1-(diphenylphosphinoyl)-4,4-dimethyl-1,2,6-heptatriene (33a).** As for the preparation of **14a**, propargyl alcohol **32a** (384 mg, 1.76 mmol), 4-(*N*,*N*-dimethylamino)pyridine (DMAP, 322 mg, 2.64 mmol), ether (10 mL), and chlorodiphenylphosphine (CDP, 473 μL, 2.64 mmol) yielded after workup and purification 399 mg (56%) of phosphine oxide **34a** as a clear, viscous oil. Recrystallization with ethyl acetate afforded a crystalline solid (mp 159–160 °C) which was spectrally and HPLC homogeneous. The X-ray crystallographic structure determination results of the material are presented in the supplementary material.

For the kinetic studies, the procedure for preparing **13a** was followed using 339 mg (1.55 mmol) of propargylic alcohol **32a**, 285 mg (2.53 mmol) of DMAP, ether (10 mL), and 419 μL (2.33 mmol) of CDP. However, the reaction mixture was allowed to stand for only 1 h at 25 °C before workup. The rate of reaction was monitored by following the disappearance of the δ 6.3 signal ($H_{2'}$) of allene **33a** versus the appearance of the δ 4.33 signal (H_4) of cyclized product **34a**. Another signal of the allene **33a** [δ 5.5 (H_6)] was also monitored versus the H_4 signal of cyclized product **34a** to calculate the irreversible first-order rate constant.

(7*R,9*S**)-2-(Diphenylphosphinoyl)-5,5-dimethyltricyclo[7.5.0.0^{3,7}]tetradeca-1,3-diene (34b) 1-(1′-Cyclohepten-1′-yl)-1-(diphenylphosphinoyl)-4,4-dimethyl-1,2,6-heptatriene (33b).** As for the preparation of **14a**, propargyl alcohol **32b** (432 mg, 1.86 mmol), 4-(*N*,*N*-dimethylamino)pyridine (DMAP, 273 mg, 2.23 mmol), ether (10 mL), and chlorodiphenylphosphine (CDP, 401 μL, 2.23 mmol) yielded after workup and purification 364 mg (82%) of phosphine oxide **34b** as a clear, viscous oil which was spectrally homogeneous.

For the kinetic studies, the procedure for preparing **13a** was followed using 249 mg (1.07 mmol) of propargylic alcohol **32b**, 196 mg (1.61 mmol) of DMAP, ether (10 mL), and 289 μL (1.61 mmol) of CDP, wherein the reaction mixture was allowed to stand for only 1 h at 25 °C before workup. The rate of reaction was monitored by following the disappearance of the δ 6.50 signal ($H_{2'}$) of allene **33b** versus the appearance of the δ 4.45 signal (H_4) of cyclized product **34b**. Another signal of the allene **33b** [δ 5.5 (H_6)] was also monitored versus the H_4 signal of cyclized product **34b** to calculate the irreversible first-order rate constant.

(7*R,9*S**)-2-(Diphenylphosphinoyl)-5,5-dimethyltricyclo[7.6.0.0^{3,7}]pentadeca-1,3-diene (34c) and 1-(1′-Cycloocten-1′-yl)-1-(diphenylphosphinoyl)-4,4-dimethyl-1,2,6-heptatriene (33c).** As for the preparation of **14a**, propargyl alcohol **32c** (199 mg, 0.81 mmol), 4-(*N*,*N*-dimethylamino)pyridine (DMAP, 148 mg, 1.21 mmol), ether (10 mL), and chlorodiphenylphosphine (CDP, 218 μL, 1.21 mmol) yielded after workup and purification 294 mg (85%) of phosphine oxide **34c** as a clear, viscous oil.

For the kinetic studies, the procedure for preparing **13a** was followed using 287 mg (1.16 mmol) of propargylic alcohol **32c**, 213 mg (1.75 mmol) of DMAP, ether (10 mL), and 314 μL (1.75 mmol) of CDP, but the reaction mixture was allowed to stand for only 1 h at 25 °C before workup. The rate of reaction was monitored by following the disappearance of the δ 6.28 signal ($H_{2'}$) of allene **33c** versus the appearance of the δ 4.56 signal (H_4) of cyclized product **34c**. Another signal of the allene **33c** [δ 5.14 (H_3)] was also monitored versus the H_4 signal of cyclized product **34c** to calculate the irreversible first-order rate constant.

1-(Cyclopent-1′-en-1′yl)-7-octen-1-yn-3-ol (42a). A mixture of enyne **9** (1.18 g, 12.8 mol) in ether (100 mL) under nitrogen was cooled to 0 °C, and *n*-BuLi (8.03 mL, 1.51 M in hexanes, 12.8 mmol) was added dropwise via syringe to give a clear yellow solution of the acetylide anion. After 30 min, aldehyde **41a** (1.26 g, 12.8 mmol) was added via syringe to the reaction mixture, and after an additional 5 min the cooling bath was removed and the mixture was stirred at room temperature for 2 h. After a standard workup (water, ether) the resulting crude propargyl alcohol was purified by chromatography (silica gel, 8 × 18 cm column; 90:10 hexanes/ethyl acetate) to yield 1.90 g (78.0%) of **42a** as a clear liquid. A sample for characterization was prepared by HPLC purification (8 mL/min; 10% ethyl acetate/hexanes; Rainin Dynamax 60A).

1-(Cyclopent-1′-en-1′-yl)-4,4-dimethyl-7-octen-1-yn-3-ol (42b). Via the above procedure, propargylic alcohol **42b** was prepared by the preceding procedure using enyne **9** (1.09 g, 11.9 mmol), ether (50 mL), *n*-BuLi (7.42 mL, 1.6 M in hexanes, 11.9 mmol), and aldehyde **41b** (1.50 g, 11.9 mmol). The crude alcohol was purified by chromatography (silica gel, 90:10 hexanes/ethyl acetate) to yield 2.05 g (79%) of propargyl alcohol **42b** as a clear liquid, which was spectrally homogeneous and used without further purification.

1-(1′-Cyclopenten-1′-yl)-1-(diphenylphosphinoyl)-1,2,7-octatriene (43a). As for the preparation of **14a**, propargyl alcohol **42a** (2.04 g, 10.7 mmol), 4-(*N*,*N*-dimethylamino)pyridine (1.57 g, 12.8 mmol), ether (50 mL) and chlorodiphenylphosphine (2.30 mL, 12.8 mmol) yielded after workup and purification 3.21 g (80%) of allenylphosphine oxide **43a** as a clear viscous oil which was spectrally homogeneous. This material was of adequate purity for conversion (including kinetic studies) to the Diels–Alder product as described separately.

1-(1′-Cyclopenten-1′-yl)-1-(diphenylphosphinoyl)-4,4-dimethyl-1,2,7-octatriene (43b). As for the preparation of **14a**

propargyl alcohol **42b** (255 mg, 1.17 mmol), 4-(*N*,*N*-dimethylamino)pyridine (171 mg, 1.40 mmol), ether (10 mL), and chlorodiphenylphosphine (252 μL, 1.40 mmol) yielded after workup and purification 315 mg (70%) of allenyl phosphine oxide **43b** as a clear viscous oil which was homogeneous by HPLC (10% isopropyl alcohol/hexanes; 4 mL/min; Rainin Dynamax 60A) but contaminated by minor impurities which were apparent in the ^{1}H NMR and mass spectra. This material was of adequate purity for conversion (including kinetic studies) to the Diels–Alder product as described separately.

(8*R,10*S**)-2-(Diphenylphosphinoyl)tricyclo[8.3.0.0^{3,8}]-trideca-1,3-diene (44a).** A solution of allenylphosphine oxide **43a** (1.11 g, 2.96 mmol) in 20 mL of benzene (freshly distilled from Na/benzophenone) was placed in an ampoule with a screw-cap seal. The sealed, argon-flushed ampoule was placed in an oil bath and heated at 120 °C for 17 h. After cooling the ampoule, the product was rinsed into a round-bottom flask with ether, and then the ether solution was concentrated. The resulting residue was chromatographed (silica gel, 5 × 16 cm, 1:1 ethyl acetate/hexanes) to afford after vacuum drying, 987 mg (89%) of phosphine oxide **44a** as a white solid (mp 196–198 °C) which was spectrally homogeneous.

For the kinetic studies, a solution of allenylphosphine oxide **43a** (20 mg, 0.05 mmol) in C_6D_6 (1 mL) was placed in a 7-in. 5-mm NMR tube and put through three freeze–thaw cycles under vacuum. The tube was then sealed under vacuum and placed in a thermostated constant temperature bath set at 98.5 °C. At regular intervals the tube was removed from the bath and cooled and the ^{1}H NMR spectrum was taken. The spectra typically revealed the presence of both allene **43a** and cyclized product **44a**. The rate of reaction was monitored by following the disappearance of the δ 6.6 signal ($H_{2'}$) of allene **43a** versus the appearance of the δ 5.8 signal (H_4) of cyclized product **44a**.

(8*R,10*S**)-2-(Diphenylphosphinoyl)-5,5-dimethyltricyclo[8.3.0.0^{3,8}]trideca-1,3-diene (44b).** As for the preparation of **44a**, allenylphosphine oxide **43b** (287 mg, 0.71 mmol) in dry benzene (50 mL) was heated at 125 °C for 12 h. Workup and purification as above afforded 162 mg (56%) of phosphine oxide **44b** as a white solid, which was spectrally homogeneous. Recrystallization with ethyl acetate gave white needles (mp 145–147 °C).

For the kinetic studies, a solution of allenylphosphine oxide **43b** (19 mg, 0.05 mmol) in $CDCl_3$ (1 mL; freshly passed through a short column of alumina), prepared as described above for the solution of **43a**, was placed in a thermostated constant temperature bath set at 98.5 °C. As above, the rate of reaction was monitored by following the disappearance of the δ 6.0 signal ($H_{2'}$) of allene **43b** versus the appearance of the δ 5.02 signal (H_4) of cyclized product **44b**. An identical procedure was followed to measure the irreversible first-order rate constant in C_6D_6. In this case the disappearance of the δ 6.6 signal ($H_{2'}$) of allene **43b** was monitored versus the disappearance of the δ 5.4 signal (H_4) of cyclized product **44b**.

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Supplementary Material Available: Spectral data for all new compounds and general experimental details (59 pages). Ordering information is given on any current masthead page.

An Efficient and Selective Method for the Preparation of Iodophenols

Kevin J. Edgar* and Stephen N. Falling

Eastman Chemical Company, Research Laboratories, Eastman Kodak Company, P.O. Box 1972, Kingsport, Tennessee 37662

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Direct iodination of a wide range of phenols may be achieved with unprecedented selectivity in aqueous alcohol solvents by the action of a reagent preparated in situ from sodium hypochlorite and sodium iodide. Para-substituted phenols (or ortho-substituted, when the para-position is already occupied) are obtained in fair to excellent yields by simple isolation techniques. The extent of iodination is easily controlled by stoichiometry. The technique is also useful with some anilines.

In recent years, iodophenols have assumed increasing importance in chemistry and pharmacology. This renewed interest can be ascribed to two developments. First, the weak carbon–iodine bond facilitates the oxidative addition of aryl iodides to low-valent transition metals (for instance, Pd and Rh). The chemistry of the resulting Ar–M–I intermediates has been a popular and fruitful area of investigation,[1] leading to valuable new syntheses of arenecarboxylic acids and esters, aryl olefins, and other useful classes of compounds. While aryl bromides (and occasionally aryl chlorides) often can also be used in these reactions, there are many published cases in which use of the reactive aryl iodides has special value,[2a] and this is particularly true in the case of aryl halides substituted by electron-donating groups such as hydroxyl.[2b]

Secondly, polyiodinated phenols have been used as imaging agents in noninvasive medical diagnostic techniques.[3] The ability to iodinate selectively and efficiently will become increasingly important as more specific imaging agents are developed.[4] In addition, the ability to gain rapid access to specific radioiodinated species is of importance to their use as therapeutic and diagnostic agents.[5]

Despite the importance of iodophenols, and the long history of electrophilic aromatic halogenation, there are

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