(1 mL) at 0 °C under H_2. Approximately 2.5 mL of hydrogen was absorbed over 110 min. The reaction mixture was passed through a short plug of silica gel. The crude product was shown by VPC to consist of a mixture of lactone **11** (95.4%) and starting material (4.6%). Chromatography on silica gel (1:1 hexane–ether) gave pure lactone **11**, 18 mg (75%): IR (neat film) 1726, 1716, 1175, 1025 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.38 (br s, 1 H, HCO bridgehead), 4.17 (q, 3 H, J = 7.1 Hz, OCH_2CH_3), 2.81 (apparent t, 2 H), 2.56 (m, 2 H), 2.35–1.52 (m, 7 H), 1.26 (t, 3 H, J = 7.1 Hz, CH_2CH_3), 1.05 (d, 3 H, J = 6.1 Hz, CH_3CH); ^{13}C NMR ($CDCl_3$) δ 174.0, 173.5, 78.5, 66.3, 44.9, 34.7, 33.5, 29.2, 28.3, 26.5, 25.9, 18.3, 14.3.

The hydrogenation was found to be a sensitive reaction, often giving two as yet unidentified side products at times as the major product. The temperature of the reduction was found to be important in minimizing these side reactions; optimum yields were obtained at or below room temperature.

Cyclohexanol 12. A solution of bicyclic lactone **11** (11 mg, 0.046 mmol) in ethanol (2 mL) was added to a solution of NaOEt (50 mg Na) in ethanol (10 mL) at 0 °C under an atmosphere of N_2. The reaction mixture was stirred at 0 °C for 30 min, treated with saturated NH_4Cl, and concentrated. The residue was extracted with ether, washed (H_2O), and dried ($MgSO_4$). Concentration gave an oil, 14 mg (100%): IR (film) 3450 (OH), 1726 (C=O), 1265, 1170, 1150, 1090, 1030 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 4.12 (two partially superimposed q, 4 H, J = 7.1 Hz, OCH_2), 3.97 (d, t, 1 H, J = 11.3, 4.4 Hz, HOC*H*), 2.5–1.35 (m, 12 H), 1.24 (two partially superimposed t, 6 H, J = 7.1 Hz, CH_2CH_3), 0.95 (d, 3 H, J = 7.1 Hz, CH_3CH).

Oxidation of Cyclohexanol 12. Cyclohexanol **12** (12.5 mg, 0.04 mmol) in CH_2Cl_2 (2 mL) was added to a stirred suspension of pyridinium chlorochromate (56 mg, 0.26 mmol) in CH_2Cl_2 (2 mL). After stirring for 20 min, the reaction mixture was filtered through silica gel and concentrated to give 14 mg of crude product. VPC analysis indicated a mixture of starting material (64%) and ketone product (34%). Further oxidation with pyridinium chlorochromate (200 mg, 6 mmol) for 1 h in CH_2Cl_2 at room temperature followed by washing gave 9.5 mg of an oil (76%) that was shown by VPC to be a mixture of starting material (13%) and ketone (87%). The ketone product had an identical VPC retention time (two columns) and spectral properties (^1H and ^{13}C NMR), with the *minor* product (**10b**) resulting from acid or base cleavage of bridgehead enol lactone **7**.

Stereochemical Studies of the Hydrolysis of Bridgehead Enol Lactone 7. Pure samples of bridgehead enol lactone **7** were subjected to the indicated reaction conditions. After the specified amount of time, the reaction mixtures were quenched with water, neutralized and extracted with ether, filtered through a short plug of silica gel, and concentrated. The product mixture was analyzed by VPC with a 50-m SE-30 capillary column; retention times: **7**, 14.91 min, **10b**, 16.01 min, **10a**, 16.15 min. The results are summarized below. The stability of keto diesters **10a** and **10b** under a variety of reaction conditions is also given below.

The following ethanolysis experiments of enol lactone **7** are averages of at least two runs. The reagents, temperature, time, and final product distribution [**7**:(**10a** + **10b**) (ratio)] are specified as follows:

Base Cleavage. NaOEt/EtOH (0.15 M), −6 °C, 30 min, 0:100 (85:15); NaOEt/EtOH (0.02 M), −2 °C, 30 min, 0:100 (84.9:15.1); Na_2CO_3/EtOH (0.1 M), 20 °C, 44 h, 1.8:95.6 (90.5:9.5).

Acid Cleavage. HCl/EtOH (0.05 M), 20 °C, 9 H, 0:96.8 (81:19); HCl/EtOH (0.1 M), 20 °C, 10 h, 3.1:94.7 (83.5:16.5); HCl/EtOH (0.1 M), −40 °C, 8 h, 65.4:32.6 (82.8:17.2); H_2SO_4/EtOH (0.1 M), 20 °C, 5 min, 81.5:17.0 (73:27).

Epimerization of Keto Diesters 10a and 10b. The epimerization experiments are average of at least two runs. The *initial* isomer ratio (**10a**:**10b**), reagents, temperature, time, and *final* isomer ratio (**10a**:**10b**) are specified as follows:

Base Epimerization. 5:95, NaOEt/EtOH (0.08 M), −2 °C 30 min, 86:14; 0:100, $NaCO_3$/EtOH (0.1 M), 20 °C, 44 h, 53:47; 90:10, Et_3N (neat), 100 °C, 24 h, 87.4:12.6.

Acid Epimerization. 0:100, HCl/EtOH (0.1 M), 20 °C, 36.9:63.1; 5:95, H_2SO_4/EtOH (0.1 M), 20 °C, 5 min, 5:95.

Acknowledgment. We thank the National Science Foundation for their generous support of our research. NMR and mass spectra were determined with spectrometers purchased with the assistance of NSF instrumentation grants. High-field NMR were obtained at the Southern California Regional NMR Facility (NSF Grant 7916324A1).

Registry No. 3, 4388-56-1; **4**, 692-29-5; **5**, 82979-04-2; **6**, 82979-05-3; *exo*-**7**, 82979-06-4; **10a**, 82979-08-6; **10b**, 82979-07-5; **11**, 82979-09-7; **12**, 82979-10-0; 3-bromopropionaldehyde ethylene acetal, 18742-02-4; 2-methyl-1-buten-3-yne, 78-80-8.

Chiral and Stereochemical Control via Intramolecular Diels–Alder Reaction of *Z* Dienes[1]

Stephen G. Pyne,[2a] Mark J. Hensel,[2b] and P. L. Fuchs*

Contribution from the Department of Chemistry, Purdue University, West Lafayette, Indiana 47907. *Received November 24, 1981*

Abstract: Chiral *Z* dienes undergo intramolecular Diels–Alder reaction with enones to afford cis-fused products with complete stereo- and enantiospecificity.

The intramolecular Diels–Alder reaction of *E* dienes is a valuable and often-used strategy in organic synthesis.[3] A limitation associated with this expedient is that an *E* diene (**1**) has two relatively easily accessible transition states (endo, exo) which, in many instances, afford mixtures of cis- and trans-fused products (**2**, **3**). This problem is further exacerbated by the introduction of an additional asymmetric center at the pentadienylic position of the diene (**1**, X ≠ H). In this latter instance, it is possible for a mixture of four products (**2**α, **2**β, **3**α, **3**β) to result from the intramolecular Diels–Alder reaction (Scheme I). There have been a number of recent notable examples utilizing just such strategy; however, in many of these cases, a mixture of products was observed.[4-7]

(1) Cytochalasin Support Studies. 4. For paper 3, see A. K. Musser and P. L. Fuchs, *J. Org. Chem.*, submitted for publication. Syntheses via Vinyl Sulfones. 8. For paper 7, see J. C. Saddler and P. L. Fuchs, *J. Am. Chem. Soc.*, **103**, 2112 (1981).

(2) (a) Postdoctoral Research Associate; (b) Graduate Research Associate.

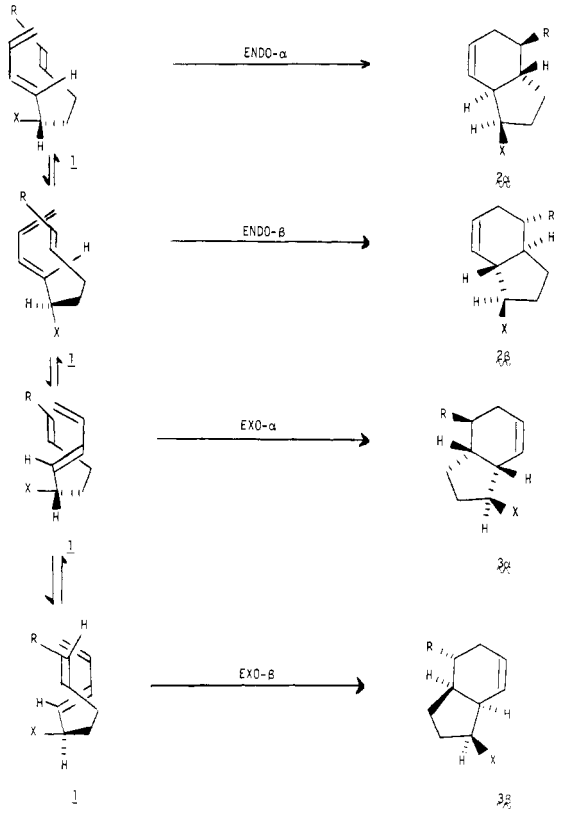
(3) Recent Reviews: (a) R. G. Carlson, *Annu. Rep. Med. Chem.*, **9**, 270 (1974); (b) W. Oppolzer, *Angew. Chem., Int. Ed. Engl.*, **16**, 10 (1977); (c) G. Brieger and J. N. Bennett, *Chem. Rev.*, **80**, 63 (1980).

(4) (a) W. R. Roush and S. E. Hall, *J. Am. Chem. Soc.*, **103**, 5200 (1981); (b) K. C. Nicolaou and R. L. Magolda, *J. Org. Chem.*, **46**, 1506 (1981); (c) W. R. Roush and A. G. Myers, *ibid.*, **46**, 1509 (1981); (d) M. P. Edwards, S. V. Ley, and S. G. Lister, *Tetrahedron Lett.*, **22**, 361 (1981); (e) B. M. Trost, D. O'Krongly, and J. L. Belletire, *J. Am. Chem. Soc.*, **102**, 7595 (1980); (f) B. Nader, R. W. Frank, and S. M. Weinreb, *ibid.*, **102**, 1153 (1980); (g) W. R. Roush, *ibid.*, **102**, 1390 (1980); (h) W. R. Roush, *J. Org. Chem.*, **44**, 4008 (1979); (i) D. F. Taber and B. P. Gunn, *J. Am. Chem. Soc.*, **101**, 3992 (1979).

(5) Often the product (**2**) derived from the "endo" transition state is highly favored; however, there are numerous cases[6,7] where mixtures of products or products (**3**) derived only from the "exo" transition state are formed.

0002-7863/82/1504-5719$01.25/0

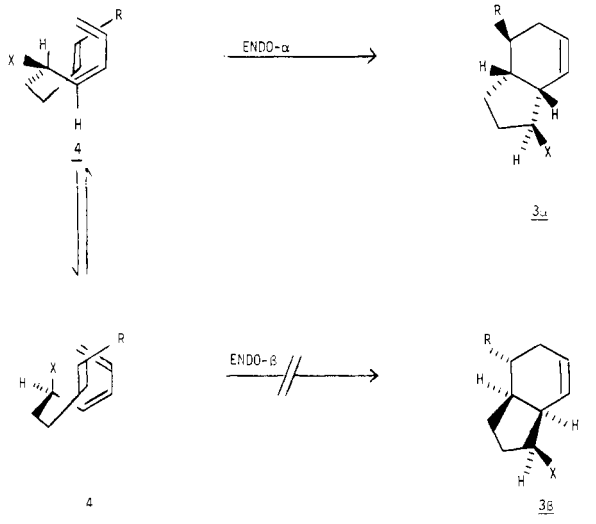
Scheme I



Dienes of the *Z* configuration lend themselves much more readily to predictions about product stereochemistry. Because of its geometry, a *Z* diene can only attain a single transition state in the intramolecular Diels–Alder reaction; moreover, the stereochemical constraints of the reaction are very strongly transmitted to the carbon which is allylic to the diene moiety. Specifically, in the requisite planar s-cis conformation, substituents at the pentadienylic center experience substantial nonbonded interactions with the *Z* hydrogen at the diene terminus.[8] In the case of an unsymmetrically substituted diene such as **4**, it can be seen that the steric interactions in the transition state endo-α are substantially less destabilizing than those in endo-β (assuming that X is more sterically demanding than H). It seems apparent that the reaction will follow the pathway (endo-α) which best minimizes this destabilizing interaction. *For chiral dienes, this effect translates into asymmetric induction by the reaction occurring from a single diastereotopic face of the dienophile* (Scheme II). The ability of a chiral center to influence diastereoface selection has been previously observed by David in intermolecular Diels–Alder reactions of *Z* dienes.[40]

Confidence in the viability of the strategy outlined in Scheme II was considerably enhanced by the important observation of House and Cronin that a pair of triene esters **1**, **4** (R = $CO_2C_2H_5$, X = H) cyclize at 180 °C *at competitive rates* to afford bicyclic adducts **2**α and **3** (R = $CO_2C_2H_5$, X = H), respectively.[9] This finding indicates that for the *Z* diene **4** the presence of both the diene and dienophile within the same molecule minimizes the consequences of steric destabilization of the requisite s-cis conformation which is so pronounced in intermolecular Diels–Alder reactions of *Z* dienes.[8] That is, whenever the diene attains the s-cis conformation in the intramolecular reaction, it already has the dienophile in close proximity ready to undergo unimolecular cyclization. This must be compared to the intermolecular case where a second-order reaction must be superimposed upon the s-cis ⇄ s-trans conformational equilibrium.[10]

Scheme II



A useful illustration of this strategy would be cyclization of *Z* amide **6** to lactam **7**. Lactam **7** is a potential substrate for an enolate-promoted fragmentation approach to cytochalasin C (Scheme III).[11] Prior to construction of the fully functionalized cytochalasin C substrate **6**, it was deemed prudent to first investigate the basic intramolecular Diels–Alder concept with the simpler systems **30** and **31**.[12] Synthesis of the chiral amino dienes **16-*Z*, 26-*ZE*** was envisaged to arise via a pair of organophosphorus reactions on an aldehyde derived from L-phenylalanine (**5**), and thus bearing the requisite 3-(*S*) chirality necessary for the natural product (Scheme III).

Synthesis of Chiral Amino Dienes

Treatment of the *N*-tosyl derivative of L(−)-phenylalanine (**8**)[13] with borane–dimethyl sulfide complex[14] in tetrahydrofuran affords a near-quantitative yield of alcohol **9**. Reaction of **9** with sodium hydride to effect deprotonation of the sulfonamide moiety of **9** followed by N-benzylation yields the nicely crystalline bis-protected amine **11** (78%). A more efficient synthesis of **11** can be accomplished by inversion of the benzylation and reduction steps. In this alternative procedure sulfonamide acid **8** is allowed to react with excess benzyl bromide to produce the bis-benzylated ester **10**. Subsequent lithium aluminum hydride reduction of ester **10** then smoothly affords alcohol **11**. Oxidation of **11** with pyridinium

(6) (a) E. Wenkert, K. Naemura, *Synth. Commun.*, **3**, 45 (1973); (b) J. J. S. Bajorek and J. K. Sutherland, *J. Chem. Soc., Chem. Commun.*, 1559 (1975); (c) G. Frater, *Tetrahedron Lett.*, 4517 (1976); (d) W. Oppolzer, R. Achini, E. Pfenniger, and H. P. Wever, *Helv. Chim. Acta*, **59**, 1186 (1976); (e) W. Oppolzer and W. Frostle, *ibid.*, **58**, 590 (1975).

(7) (a) H. W. Gschwend, A. O. Lee, and H. P. Meier, *J. Org. Chem.*, **38**, 2169 (1973); (b) H. W. Gschwend and H. P. Meier, *Angew. Chem., Int. Ed. Engl.*, **11**, 294 (1972); (c) H. W. Gschwend, *Helv. Chim. Acta*, **56**, 1763 (1973).

(8) It is this interaction that is responsible for the 10^5 times reactivity difference between *trans*- and *cis*-pentadiene in the *intermolecular* Diels–Alder reaction: (a) A. S. Onishchenko in "Diene Synthesis", S. Monson, Ed., Israel Program for Scientific Translation, LTD, Jerusalem, 1964, pp 11–18; (b) J. Sauer, *Angew. Chem., Int. Ed. Engl.*, **5**, 211 (1966); (c) *ibid.*, **6**, 16 (1967).

(9) H. O. House and T. H. Cronin, *J. Org. Chem.*, **30**, 1061 (1965).

(10) Other examples involving intramolecular Diels–Alder reactions of *Z* dienes include: (a) biomimetic synthesis of alkaloids of the Vincadifformine type [M. E. Kuehne, C. L. Kirkemo, T. H. Matsko, and J. C. Bohnert, *J. Org. Chem.*, **45**, 3259 (1980), and references contained therein]; (b) cyclization of a racemic (*Z*)-diene bearing a substituent at the pentadienylic center (stereochemistry resulting from the pentadienylic center unspecified) [W. Oppolzer, C. Fehr, and J. Warneke, *Helv. Chim. Acta*, **60**, 48 (1977)]; and (c) *Z* → *E* isomerization of an unreactive *Z*-diene in preference to Diels–Alder cyclization [R. F. Borch, A. J. Evans, and J. J. Wade, *J. Am. Chem. Soc.*, **99**, 1612 (1977)].

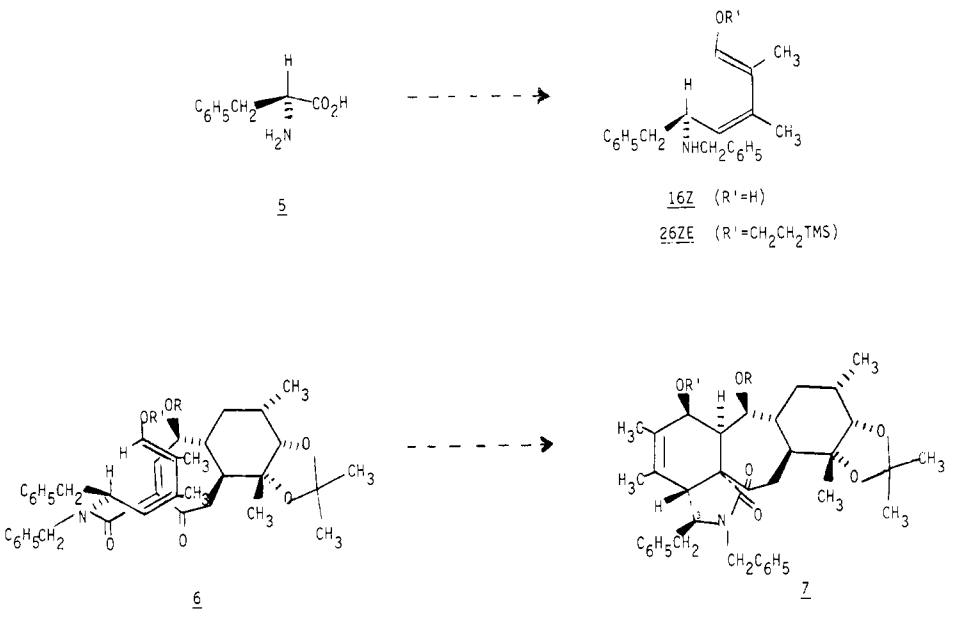
(11) For discussion of enolate-promated fragmentations, see D. A. Clark and P. L. Fuchs, *J. Am. Chem. Soc.*, **101**, 3567 (1979).

(12) A preliminary communication of a portion of this work (model **33**) has already been published: S. G. Pyne, M. J. Hensel, S. R. Byrn, A. T. McKenzie, and P. L. Fuchs, *J. Am. Chem. Soc.*, **102**, 5962 (1980).

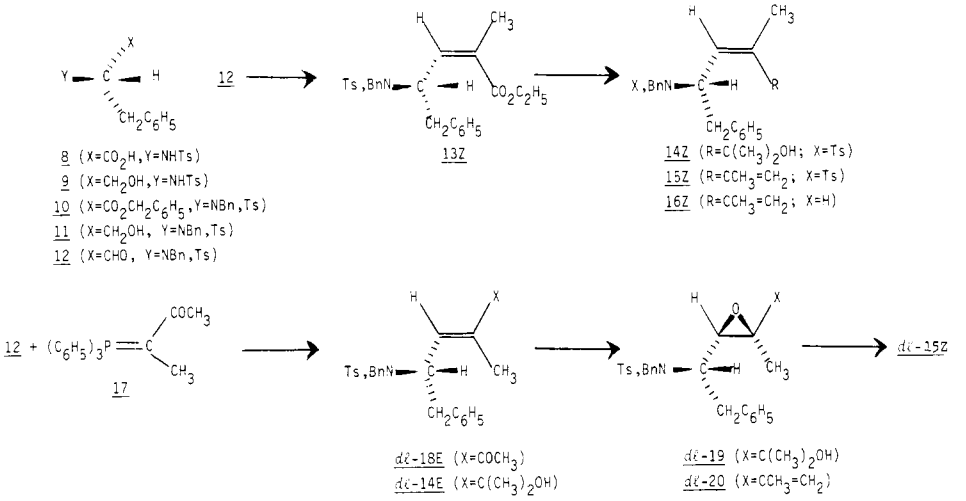
(13) E. W. McChesney and W. K. Swann, *J. Am. Chem. Soc.*, **59**, 116 (1937).

(14) Review on $BH_3(CH_3)_2S$: C. F. Lane, *Aldrichimica Acta*, **8**, 20 (1975).

Scheme III



Scheme IV



chlorochromate[15] in methylene chloride yields the requisite chiral aldehyde **12**. Sodium borohydride reduction of aldehyde **12** returns alcohol **11** with no loss of optical activity (Scheme IV).

Treatment of aldehyde **12** with the sodium salt of 2-methylphosphonoacetate affords a 1:1 mixture of trisubstituted esters **13-*Z*/13-*E*** in near-quantitative yield.[16] Separation of these esters is readily effected on a preparative scale via medium-pressure liquid chromatography. Reaction of the chiral vinyl ester **13-*Z*** with excess methyl Grignard in ether at −78 °C produces tertiary allylic alcohol **14-*Z*** in 90% yield. Dehydration of **14-*Z*** via reaction with methanesulfonyl chloride and triethylamine in methylene chloride[17] yields amino diene **15-*Z***, presumably via the intermediate tertiary allylic mesylate. Reductive cleavage of the sulfonamide moiety of **15-*Z*** via the method of Trost[18] smoothly affords secondary amine **16-*Z*** (83% overall from **12**). Repetition of the above three reaction sequence with the isomeric vinyl ester **13-*E*** affords the isomeric series **14-*E***, **15-*E***, **16-*E*** for the purposes of spectral assignment (see Tables I and II, supplementary material, for ^{13}C NMR of amino dienes). The undesired vinyl ester **13-*E*** could be "recycled" via photoequilibration[19] to a 1:2 mixture of vinyl esters **13-*Z*/13-*E*** (Scheme IV).

A stereospecific synthesis of diene **16-*Z*** was also achieved. Reaction of chiral aldehyde **12** with keto ylide **17** proceeded very slowly at room temperature (5 days, 65%); attempts to conduct the reaction at higher temperatures (THF, reflux) afforded complex product mixtures. Moreover, it was subsequently found that enone ***dl*-18-*E*** was essentially racemic. This reaction apparently represents a rare example of aldehyde epimerization catalyzed by the very weakly basic stable ylide **17**. Presumably the hindered nature of both aldehyde **12** and ketophosphorane **17** contribute to sufficiently retard the progress of the Wittig reaction such that the rate of the epimerization reaction becomes highly competitive, thus producing racemic **12** as substrate for the sluggish Wittig reaction.

Treatment of enone ***dl*-18-*E*** with excess methylmagnesium bromide produces racemic alcohol ***dl*-14-*E***, thus confirming the racemic nature of ***dl*-18-*E***. Reaction of this racemic alcohol with

(15) E. J. Corey and W. J. Suggs, *Tetrahedron Lett.*, 2647 (1975).

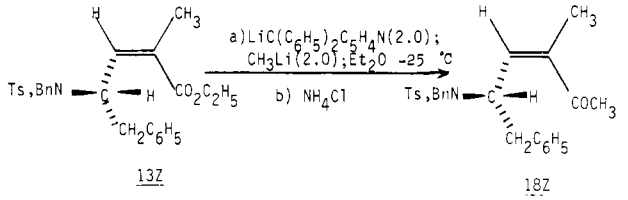
(16) (a) G. Schmid, T. Fukuyama, K. A. Kasaka, and Y. Kishi, *J. Am. Chem. Soc.*, **101**, 259 (1979); (b) T. H. Kinstle and B. Y. Mandawas, *Chem. Commun.*, 1699 (1968). Attempts to effect a more favorable **13-*Z*/13-*E*** ratio by reaction of **12** with methyl trimethylphosphonoacetate reagent under the Kishi conditions (ref 16a) have thus far produced no stereochemical improvement.

(17) R. K. Crossland and K. L. Servis, *J. Org. Chem.*, **35**, 3195 (1970).

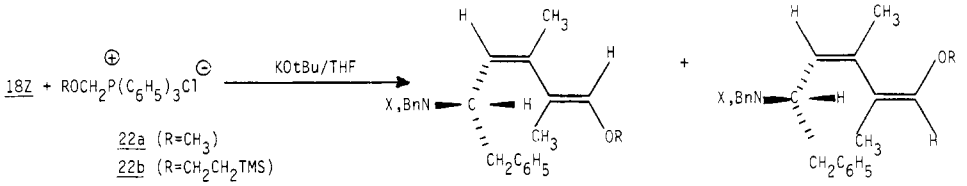
(18) (a) B. M. Trost, H. C. Arndt, P. E. Strege, and T. R. Verhoeven, *Tetrahedron Lett.*, 3477 (1976). (b) For general methods of reductive cleavage of sulfonamides, see: K. S. Quaal, S. Ji, Y. Mi Kim, W. D. Closson, and A. Zubieta, *J. Org. Chem.*, **43**, 1311 (1978), and references contained therein.

(19) J. D. Coyle and H. A. J. Carless, *Chem. Soc. Rev.*, **1**, 465 (1972), and references contained therein.

Scheme V



13Z 18Z

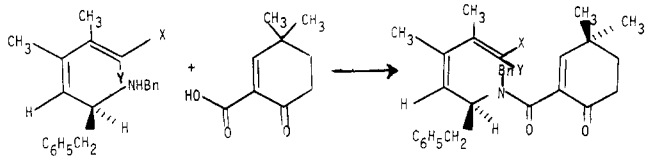


22a (R=CH3)
22b (R=CH2CH2TMS)

23ZE (R=CH3,X=Ts), [7:1]
24ZE (R=CH2CH2TMS,X=Ts) [7:1]
25ZE (R=CH3,X=H)
26ZE (R=CH2CH2TMS, X=H)

23ZZ (R=CH3,X=Ts)
24ZZ (R=CH2CH2TMS, X=Ts)
25ZZ (R=CH3,X=H)
26ZZ (R=CH2CH2TMS, X=H)

Scheme VI



16Z (X=Y=H) 29 30 (X=Y=H); 85%
26ZE (X=OCH2CH2TMS,Y=H) 31 (X=OCH2CH2TMS, Y=H); 56%
26ZZ (X=H,Y=OCH2CH2TMS) 32 (X=H, Y=OCH2CH2TMS); 85%

m-chloroperoxybenzoic acid in methylene chloride affords a *single* diastereomeric epoxy alcohol *dl*-**19** whose relative configuration was not determined.[20] Dehydration of epoxy alcohol *dl*-**19** with phosphorus oxychloride in pyridine at 60 °C smoothly yields allylic epoxide *dl*-**20**.[21] Deoxygenation of epoxide *dl*-**20** via the betaine method[22] affords "inverted" diene *dl*-**15**-*Z* (60%) uncontaminated by any trace of isomeric olefin *dl*-**15**-*E*[23] (Scheme IV).

The fully functionalized alkoxy diene **26**-*ZE* required for the synthesis of cytochalasin C was also prepared from chiral vinyl ester **13**-*Z*. Slow addition of ester **13**-*Z* to a solution of lithium diphenyl-2-pyridylmethide[24] and methyllithium followed by a quench with ammonium chloride affords enone **18**-*Z* in 81% yield. The function of the dipyridylmethide is to effect deprotonation of the initially formed enone **18**-*Z*, thus preventing subsequent addition of methyllithium to the enone carbonyl.[25,26] Use of other companion bases such as LDA or lithium hexamethyldisilazide was far less effective at preventing over-reaction of the methyllithium. Treatment of enone **18**-*Z* with either the α-alkoxyphosphorane generated in situ via the reaction of potassium *tert*-butoxide and α-methoxyphosphonium chloride[27] **22a** or its β-silylethyl analogue **22b** (prepared in 94% yield from the known α-halo ether **21**[28] by reaction with triphenylphosphine in benzene at reflux) affords a 7:1 mixture of alkoxy dienes **23**-*ZE*/**23**-*ZZ* (64%) and **24**-*ZE*/**24**-*ZZ* (84%), respectively. Reductive cleavage of the sulfonamide moiety was again smoothly accomplished using the Trost reagent[18] yielding the secondary amino dienes **25**-*ZE*/**25**-*ZZ*; **26**-*ZE*/**26**-*ZZ*. Isomer separation of sulfonamides **23**-*ZE*/**23**-*ZZ* and **24**-*ZE*/**24**-*ZZ* proved impractical; furthermore, the *methoxy* desulfonylated secondary amino dienes **25**-*ZE*/**25**-*ZZ* also could not be easily separated. Fortunately, the desulfonylated β-silylethyl alkoxy dienes **26**-*ZE*/**26**-*ZZ* could be readily isolated and purified by routine chromatographic procedures (Scheme V).

For the purpose of spectral comparison as an adjunct to structure assignment, the isomeric β-silylethyl alkoxy dienes *dl*-**28**-*EE*/*dl*-**28**-*EZ* were also prepared. Treatment of racemic enone *dl*-**18**-*E* with the alkoxy phosphorane derived from phosphonium salt **22b** affords an inseparable 2:1 mixture of *dl*-**27**-*EZ*/*dl*-**27**-*EE* in 75% yield. Desulfonylation of this mixture by the sodium amalgam procedure affords diene mixture *dl*-**28**-*EE*/*dl*-**28**-*EZ* (90%). Samples of *dl*-**28**-*EZ* and *dl*-**28**-*EE* of purity sufficient for spectral assignment were separated only with great difficulty. (See Supplementary Material.)

Stereochemistry of Amino Dienes

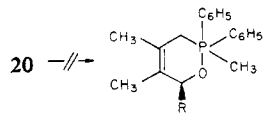
The principal criterion for assignment of the configuration of trisubstituted olefins and dienes prepared in the previous section was the ^{13}C NMR chemical shift. It has been amply established for an isomeric pair of olefins,[29] 1,3 dienes,[29] or enol ethers[30] that steric compression results in an upfield shift of γ carbons which

(20) The stereocontrol (if sulfonamide-directed) in this reaction may be similar to that observed in analogous acyclic trisubstituted homoallylic ethers: Y. Kishi, *Aldrichimia Acta*, **13**, 23 (1980).

(21) This sequence was established prior to the development of the chemistry in Scheme VII and has not been repeated with chiral alcohol **14**-*E*.

(22) (a) E. Vedejs and P. L. Fuchs, *J. Am. Chem. Soc.*, **93**, 4070 (1971); (b) *ibid.*, **95**, 822 (1973); (c) E. Vedejs, K. A. J. Snoble, and P. L. Fuchs, *J. Org. Chem.*, **38**, 1178 (1973).

(23) One source of the diminished yield in this reaction might be SN2′ 1,4-addition of the phosphide anion to allyl epoxide **20**. If such a reaction is indeed occurring, it must not be subsequently affording diene products via intermediate i, since a **15**-*E*/**15**-*Z* product mixture would be expected to result.



i

(24) D. A. Clark, C. A. Bunnell, and P. L. Fuchs, *J. Am. Chem. Soc.*, **100**, 777 (1978).

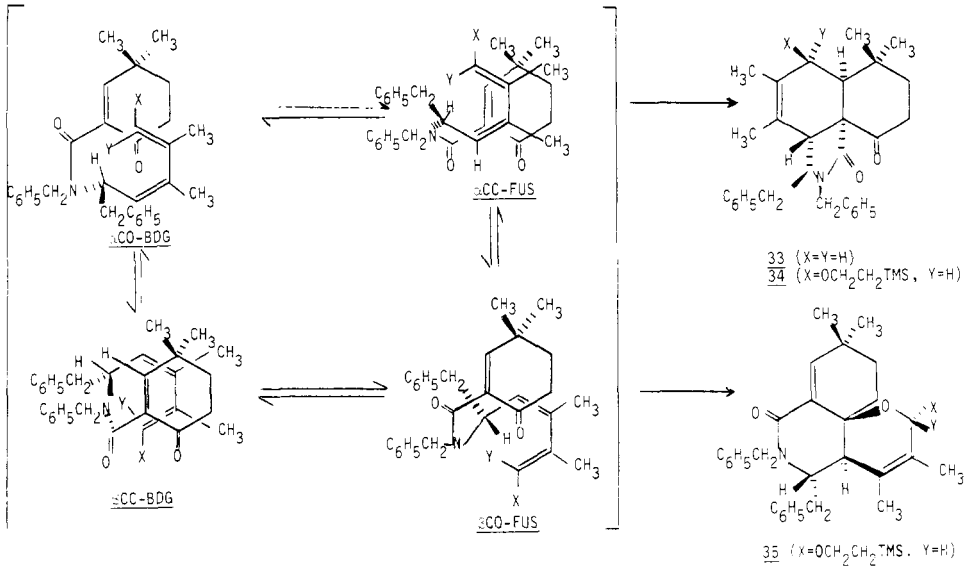
(25) For other examples of ester → ketone transformations see: G. Majetich, P. A. Grieco, and S. Bongers, *J. Org. Chem.*, **46**, 209 (1981), and references contained therein.

(26) Similar treatment of vinyl ester **13**-*E* also smoothly affords enone **18**-*E*.

(27) Y. Ohfune, P. A. Grieco, C. L. J. Wang, and G. Majetich, *J. Am. Chem. Soc.*, **100**, 5946 (1978), and references contained therein.

(28) B. H. Lipschutz and J. J. Pegram, *Tetrahedron Lett.*, 3343 (1980).

Scheme VII



REACTANT	TEMP. (°C)	TIME (h)	Product (s) (YIELD)	RECOV. SM
30 (X=Y=H)	110°	40	33 (95%)	<1
31 (X=OCH$_2$CH$_2$TMS, Y=H)	110°	15	34 (79%); 35 (15%)	1
32 (X=H, Y=OCH$_2$CH$_2$TMS)	110°	48	-	95
32 (X=H, Y=OCH$_2$CH$_2$TMS)	168°	48	-	90

are in a cisoid relationship. Application of this diagnostic to the vinyl methyl resonance of enones **18-*Z*** and ***dl*-18-*E*** and vinyl esters **13-*Z*** and **13-*E*** shows the expected higher field resonance for the *E* isomers where the methyl group is in a cis relationship with the chiral alkyl side chain. Additional confidence in the accuracy of the above assignments can be obtained from the proton NMR. In this instance, comparison of the chemical shift of the β vinyl hydrogens demonstrates the well-known effect[31] of enhanced deshielding when the β hydrogen is cisoid to the carbonyl group (see Tables I and II, supplementary material). A final piece of evidence is the internal consistency of the chemistry which ensues from ester **13-*Z***, namely, conversion of **13-*Z*** to **18-*Z*** followed by its subsequent transformations to adduct **33**, which has been verified by an X-ray structure.[12]

Establishment of the stereochemistry of the requisite chiral alkoxy dienes **16-*Z*** and **26-*ZE*** was also accomplished using carbon NMR. The chemical shift data of the two vinyl methyl groups for the various configurational isomers shows a superposition of both electronic and steric compression effects. The simple dienes (**16-*Z***, **16-*E***) show their "CH_{3b}" resonance at lower field than do the dienyl ethers (**26-*ZE***, **26-*ZZ***, **28-*EE***, **28-*EZ***) presumably due to the mesomeric (electron-donating) effect of the alkoxy group.[30] Furthermore, and of greatest importance for the structure assignment, the alkoxy group provides additional shielding (via the steric compression mechanism)[30] when arranged in a cisoid relationship to CH_{3b} (see Table II, supplementary material).

The enantiomeric purity of dienes **16-*Z*** and **26-*ZE*** as well as the racemized enone ***dl*-18-*E*** was determined by ozonolysis followed by a borohydride workup to produce alcohol **11**. Degradation of the dienes(**16-*Z***, **26-*ZE***) prepared via the phosphonate routes (Scheme IV) yielded alcohol **11** without appreciable loss of enantiomeric integrity (>95% from $[\alpha]_D^{25}$ and ^{1}H NMR chiral shift reagent comparisons). By comparison, application of the above analysis to the enone prepared via the ketophosphorane route (Scheme IV) afforded alcohol **11** which was shown to be essentially racemic.

Cyclization of Model Amides

Treatment of each of the chiral amino dienes (**16-*Z***, **26-*ZE***, **26-*ZZ***) with 3,3-dimethyl-6-oxocyclohex-1-enecarboxylic acid (**29**)[32] in the presence of the Mukaiyama halopyridium coupling reagent[33] afforded model amides **30–32** (Scheme VI).

Heating a 0.01 M solution of amide **30** in toluene for 40 h affords the chiral tricyclic lactam **33** in >95% yield.[12,34] Verification of the structural assignment of lactam **33** has been accomplished by X-ray analysis.[12] Cyclization of the oxygen-substituted amide **31** occurred somewhat more readily to produce a mixture of the analogous tricyclic **34** (79%) and a minor adduct **35** (15%) resulting from the intramolecular Diels–Alder addition of the diene moiety to the carbonyl group of amide **31**.[35,36] The highly encumbered isomeric *ZZ* amide **32** is recovered unchanged under conditions where *ZE* isomer **31** has undergone complete cyclization. Several aspects of these reactions merit further discussion. As can be seen by inspection of Scheme VII, there are four possible transition states that maintain the smaller, *hydrogen substituent* as the interacting group at the pentadienylic position of the diene (cf. Scheme II). Literature precedent on intramolecular Diels–Alder reactions[3,4,6,10] suggested that the transition states [αCO-BDG, βCC-BDG] leading to bridged adducts would be noncompetitive with those [αCC-FUS, βCO-FUS] leading to fused adducts **33–35**. Although this expectation was indeed realized, the recent finding by Martin[37] that bridged bicyclic adducts are the exclusive products of the intramolecular Diels–Alder reaction of an acyclic acyl enamine as well as an

(29) (a) M. J. Curry and I. D. R. Stevens, *J. Chem. Soc.*, Perkin *Trans. 1*, 1756 (1980), and references therein; (b) N. K. Wilson and J. B. Stothers, *Top. Stereochem.*, **8**, 1 (1974); (c) D. E. Dorman, M. Jautelat, and J. D. Roberts, *J. Org. Chem.*, **36**, 2757 (1971).

(30) (a) E. Taskinen, *J. Org. Chem.*, **43**, 2773 (1978); (b) *ibid.*, **43**, 2776 (1978); (c) J. K. Crandall and A. C. Rojas, *ibid.*, **40**, 2225 (1975).

(31) H. B. Kagan, "Stereochemistry Fundamentals and Methods", Georg Thieme, Stuttgart, 1977, pp 48–55, and references contained therein.

(32) Prepared from 4,4-dimethylcyclohexanone by sequential reaction with dimethyl carbonate, phenyl selenyl chloride, hydrogen peroxide, and sodium hydroxide: D. A. Clark and P. L. Fuchs, unpublished results.

(33) E. Bald, K. Saigo, and T. Mukaiyama, *Chem. Lett.*, 1163 (1975).

(34) The isomeric *E* diene prepared from diene **16-*E*** and vinyl carboxylic acid **29** is recovered largely unchanged under comparable conditions.

(35) For Diels–Alder reactions between 1-alkoxydienes and carbonyl groups see: (a) J. F. Keana and P. E. Eckler, *J. Org. Chem.*, **41**, 2850 (1976); (b) J. Jurczak and M. Tkacz, *ibid.*, **44**, 3347 (1979).

(36) The synthetic potential of this reaction is under development and will be further reported at a later date.

acyclic enamine with an unactivated diene serves to indicate the potential viability of this competitive pathway.

The appearance of a minor product (**35**) in the cyclization of substrate **31** is probably a consequence of the dipolar contribution afforded by the diene moiety. The alkoxy substituent should serve to promote the formation of **35** (relative to the analogous X = H case) since the [βCO-FUS] transition state is enhanced by the resonance effect of the alkoxy group, whereas the [αCC-FUS] transition state would be expected to be somewhat retarded by the same effect. Nevertheless, even in this instance, the ketone carbonyl serves only to provide minor competition for the enone double bond [**31** → **34** (79%)]. Finally, it can be seen that the *ZZ* diene **32** can be recovered unchanged even after 48 h at 168 °C. At 190 °C, **32** is slowly consumed to produce a myriad of products that were not further characterized.[38]

Thus it has been established that the intramolecular Diels–Alder reaction of chiral *Z* dienes is a viable method for the enantiospecific construction of functionalized lactams.[39]

Experimental Section

General Procedures. Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 137 spectrophotometer in chloroform solution, unless otherwise stated. ^{1}H NMR spectra were recorded on either a Perkin-Elmer R-32, a Nicolet 360, or a Nicolet 470 instrument at 90, 360, and 470 MHz, respectively. The spectra were measured in deuteriochloroform, unless otherwise stated, relative to tetramethylsilane (δ 0.00 ppm). Each signal is described in terms of chemical shift in parts per million from tetramethylsilane, multiplicity, intensity, and coupling constant (Hz) in that order with the use of the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; and $W_{1/2}$, width of peak at half-height. ^{13}C NMR spectra were recorded on a Varian CFT-20 instrument operating at 20 MHz or on a Varian XL200 MHz operating at 50 MHz. The spectra were measured in deuteriochloroform solution, unless otherwise stated, relative to tetramethylsilane (δ 0.00 ppm). Both ^{1}H-decoupled and off-resonance spectra were recorded. Mass spectra were recorded on a CEC-21-110-B high-resolution mass spectrometer at an ionizing voltage of 70 eV and an ionizing current of 100 A. Exact mass determinations were obtained on the CEC-21-110-B instrument. Microanalyses were performed by C. S. Yeh and M. Lam, Department of Chemistry, Purdue University.

Optical rotations were measured with a Rudolph Research Autopol III automatic polarimeter in chloroform solution (unless otherwise specified) at the sodium D line in a 10-cm long cell at the designated concentration in g/100 mL.

All reactions were run under a positive pressure of nitrogen. All organic extracts were dried over anhydrous sodium sulfate, filtered, and then evaporated on a Büchi Rotavapor. Tetrahydrofuran (THF) and ether were distilled under nitrogen from sodium benzophenone ketyl. Methylene chloride, toluene, triethylamine, and pyridine were distilled from calcium hydride. Thin-layer chromatography (TLC) was performed on 0.25-mm E. Merck precoated silica gel plates (60 F-254). Preparative thick-layer chromatography (preparative TLC) was performed on 2 mm × 20 × 20 cm E. Merck precoated silica gel plates (60 F-254). Column chromatography was performed on silica gel 60–200 mesh obtained from Sargent–Welch.

(2*S*)-2-*p*-Toluenesulfonamido-3-phenylpropionic Acid (8). To a mechanically stirred solution of L(−)-phenylalanine (25.0 g, 151 mmol) dissolved in 250 mL of 1.5 N NaOH at 25 °C was added *p*-toluenesulfonyl chloride (34.6 g, 182 mmol) in ether (150 mL). After 6 h of stirring, concentrated HCl was added to the viscous white solution until it was homogeneous and acidic to congo red indicator paper. The ether layer was separated and the aqueous layer extracted twice with ether. The combined extracts were dried and concentrated. The crude product was recrystallized from ether giving pure **8**[13] (41.1 g, 85%) as white crystals: mp 165.5–167 °C, $[\alpha]^{25}_D$ −1.34° (*c* 10.0, acetone). Shift reagent studies showed no enantiomeric impurity. ^{1}H NMR (acetone-d_6) δ 8.01 (bs, 1 H), 7.61 (d, 2 H, J = 8 Hz), 7.40–7.15 (m, 7 H), 6.55 (d, 1 H, J = 9 Hz), 4.30–3.98 (m, 1 H, H_M of ABM), 3.00 (m, 2 H, H_A, H_B of ABM, J_{AB} = 14 Hz, J_{AM} = 7.5 Hz, J_{BM} = 6 Hz), 2.37 (s, 3 H); ^{13}C NMR (acetone-d_6) δ 172.48 (s), 143.61 (s), 138.86 (s), 137.13 (s), 130.12 (d), 128.96 (d), 127.56 (d), 127.38 (d), 57.75 (d), 39.33 (t), 21.32 (q); mass spectrum *m/e* 319 (3%, M^+).

(2*S*)-2-*p*-Toluenesulfonamido-3-phenylpropanol (9). To a mechanically stirred solution of **8** (58.5 g, 0.183 mol) in dry THF (600 mL) at 0 °C was added dropwise borane–methyl sulfide complex[14] (Aldrich, 10.2 M, 0.403 mol, 39.6 mL) over a period of 1 h, in which time a heavy white precipitate formed. After 48 h at 25 °C water was carefully added to destroy excess reagent and the reaction mixture was poured into saturated NaCl solution and extracted twice with ether. The combined extracts were dried and concentrated. Pure alcohol **9** (54.9 g, 98% yield) was obtained after crystallization from ether–hexane: mp 73–74 °C; $[\alpha]^{25}_D$ −38.8° (*c* 1.93, EtOH); ^{1}H NMR ($CDCl_3$/CF_3CO_2H) δ 7.46 (d, 2 H, J = 8 Hz), 7.3–6.8 (m, 7 H), 4.05–3.40 (m, 3 H), 2.68 (m, 2 H), 2.39 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 143.27 (s), 137.19 (s), 137.07 (s), 129.66 (d), 129.21 (d), 128.56 (d), 127.01 (d), 126.54 (d), 63.94 (t), 56.86 (d), 37.75 (t), 21.48 (q); mass spectrum *m/e* 274 (16%, $M^+ - CH_2OH$), 214 (39%, $M^+ - C_7H_7$), 155 (100); exact mass: calcd for $C_{15}H_{16}NO_2S$ ($M^+ - CH_2OH$) 274.090, found 274.095.

(2*S*)-2-(*N*-Benzyl-*p*-toluenesulfonamido)-3-phenylpropionic Acid Benzyl Ester (10). A mixture of **8** (20.0 g, 62.6 mmol), potassium carbonate (26.0 g, 188 mmol), and benzyl bromide (22.3 mL, 188 mmol) was stirred at 25 °C until the reaction was complete by TLC (26 h). Triethylamine (17.5 mL, 126 mmol) was added and stirring continued for 2 h; 600 mL of water was added and the aqueous phase was separated and extracted twice with ether. The combined ether portions were washed four times with water (60 mL), dried, and concentrated giving the crude product as a yellow oil. This was purified by plug filtration through silica gel (300 g), with methylene chloride–hexane (1:1) as eluent giving **10** as a gray oil (30.7 g, 98%); $[\alpha]^{25}_D$ −18.0° (*c* 1.93, $CHCl_3$).

10: IR ($CHCl_3$) 1725 (C=O), 1330, 1140 (SO_2NR_2); ^{1}H NMR ($CDCl_3$) δ 7.64 (d, 2 H, J = 8.5 Hz), 7.50–6.80 (m, 17 H), 4.95–4.55 (m, 1 H, H_M of ABM), 4.74 (d, 2 H, J = 2 Hz), 4.43 (dd, 2 H, J = 15 Hz), 3.14 (m, 1 H, H_B of ABM, J_{AB} = 14 Hz, J_{BM} = 29 Hz), 2.88 (m, 1 H, H_A of A_{BM}, J_{AB} = 14 Hz, J_{AM} = 6 Hz), 2.33 (s, 3 H); ^{13}C NMR ($CDCl_3$) 169.79 (s), 143.30 (s), 137.06 (s), 136.85 (s), 135.00 (s), 129.37 (d), 129.24 (d), 128.36 (d), 128.28 (d), 127.57 (d), 126.64 (d), 66.79 (t), 61.25 (d), 49.61 (t), 37.40 (t), 21.40 (q); mass spectrum *m/e* 408 (53%, $M^+ - C_7H_7$).

(2*S*)-2-(*N*-Benzyl-*p*-toluenesulfonamido)-3-phenylpropanol (11). (i) From Sulfonamide 9. To a stirred suspension of "oil-free" sodium hydride (1.02 g, 42.3 mmol) in dry THF (125 mL) at 25 °C was added, over a period of 15 min, a solution of the alcohol **9** (12.3 g, 40.3 mmol) in THF (25 mL). After 30 min, benzyl bromide (7.92 g, 46.34 mmol) was added and the solution was heated to reflux for 36 h. The reaction mixture was then cooled, poured into saturated NaCl solution, and extracted twice with ether. The extracts were dried and concentrated and the crude product was purified by column chromatography on silica gel (300 g). Elution with hexane–methylene chloride (3:2) afforded alcohol **11** (12.35 g, 78%) as a white solid: mp 92–93 °C; $[\alpha]^{25}_D$ −53.5° (*c* 1.96); ^{1}H NMR ($CDCl_3$) δ 7.64 (d, 2 H, J = 8 Hz), 7.54–6.75 (m, 12 H), 4.47 (dd, 2 H, J = 15 Hz), 4.04 (m, 1 H), 3.40 (m, 2 H), 2.62 (d, 2 H, J = 7.5 Hz), 2.29 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 143.38 (s), 137.85 (s), 129.71 (d), 128.89 (d), 128.71 (d), 128.51 (d), 128.21 (d), 127.84 (d), 127.23 (d), 126.50 (d), 62.62 (t), 62.62 (d), 48.86 (t), 36.48 (t), 21.49 (q); exact mass: calcd for $C_{22}H_{21}NO_2S$ ($M^+ - CH_3OH$) 363.129, found 363.129.

(ii) From Dibenzyl Ester 10. At 25 °C, ester **10** (30.9 g, 61.9 mmol) in dry ether (150 mL) was added dropwise to a stirred solution of lithium aluminum hydride (1.49 g, 39.1 mmol) in dry ether (300 mL). This was then heated at reflux (2 h) and cooled to 25 °C. Water was carefully added dropwise to destroy excess $LiAlH_4$, and the reaction mixture was poured into ice–water. After acidification with 10% HCl to pH 3, the ether was separated, dried, and concentrated. Crystallization from ether–hexane gave 20.3 g of pure product. The remaining oil was chromatographed on silica gel (300 g) using gradient elution (25% CH_2Cl_2–hexane, then 50% CH_2Cl_2–hexane, then CH_2Cl_2, then 25% ethyl acetate–hexane) giving an additional 3.69 g. The combined yield of **11** was 24.0 g (98%).

(2*S*)-2-(*N*-Benzyl-*p*-toluenesulfonamido)-3-phenylpropanal (12). To a mechanically stirred suspension of pyridinium chlorochromate[15] (18.6 g, 86.2 mmol) in methylene chloride (800 mL) at 25 °C was added alcohol **11** (11.35 g, 28.7 mmol) in methylene chloride (50 mL) over 10 min. After 3.5 h, ether (1 L) was added, and stirring was continued for 15 min. The ether was decanted and the above process was repeated twice more. The combined ether solution was washed with saturated NaCl solution (4×), dried, concentrated, and then filtered through a small plug of silica gel. Pure aldehyde **12** (13.88 g, 75%) was obtained after recrystallization from ether–hexane: mp 91–92 °C; $[\alpha]^{25}_D$ −117.6° (*c* 2.03); ^{1}H NMR ($CDCl_3$) δ 9.42 (s, 1 H), 7.68 (d, 2 H, J = 8 Hz), 7.4–6.8 (m, 12 H), 4.27 (dd, 2 H, J = 15 Hz), 4.19 (dd, 1 H, J = 6, 8

(37) S. F. Martin, T. Chou, and C. Tu, *J. Am. Chem. Soc.*, **102**, 5274 (1980). See also a study by the same authors using cyclic acyl enamines as well as enamines which give fused adducts: S. F. Martin, *ibid.*, **102**, 3294 (1980).

(38) A. D. Barone and P. L. Fuchs, unpublished results.

(39) For application of this reaction to the synthesis of chiral cytochalasin C substrate (part 7), see S. G. Pyne, S. Chen, D. C. Spelmeyer, and P. L. Fuchs, *J. Am. Chem. Soc.*, following paper.

(40) S. David, et al., *J. Chem. Soc. Perkin Trans. 1*, 1795, 2330, 2521 (1979), and references contained therein.

Hz), 3.33 (dd, 1 H, J = 6, 15 Hz), 2.78 (dd, J = 8, 15 Hz), 2.43 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 197.62 (d), 143.79 (s), 137.50 (s), 137.24 (s), 135.53 (s), 129.83 (d), 128.92 (d), 128.57 (d), 127.46 (d), 126.61 (d), 67.42 (d), 50.50 (t), 33.18 (t), 21.48 (q); mass spectrum m/e 363 (100%, $M^+ - CH_2O$), 302 (33%, $M^+ - C_7H_7$); exact mass: calcd for $C_{22}H_{21}NO_2S$ ($M^+ - CH_2O$) 363.129, found 363.129.

Ethyl (4*S*)-(*Z*)-4-(*N*-Benzyl-*p*-toluenesulfonamido)-2-methyl-5-phenylpent-2-enoate (13-*Z*) and Ethyl (4*S*)-(*E*)-4-(*N*-Benzyl-*p*-toluenesulfonamido)-2-methyl-5-phenylpent-2-enoate (13*E*). To a stirred suspension of "oil-free" sodium hydride (506 mg, 21.0 mmol) in dry THF (30 mL) at 0 °C was added triethyl-2-methylphosphonoacetate (5.0 g, 21.0 mmol) in THF (20 mL) dropwise, over a period of 15 min. Aldehyde **12** (4.50 g, 11.4 mmol) was added in one portion to the above solution at 0 °C. After 30 min at 0 °C and 2 h at 25 °C the reaction mixture was poured into water and extracted twice with ether. The combined extracts were washed with water and saturated NaCl solution and dried (TLC (ether–hexane 1:1): **13-*Z***, R_f 0.5; **13-*E***, R_f 0.4). Separation of **13-*Z*** from **13-*E*** by medium-pressure liquid chromatography (ethyl acetate–hexane, 1:5) afforded **13-*Z*** (2.53 g, 46%) and **13-*E*** (2.92 g, 53%) as pale yellow oils.

13-*Z*: $[\alpha]^{25}_D$ +34.7° (c 2.53); ^{1}H NMR ($CDCl_3$) δ 7.60 (d, 2 H, J = 8 Hz), 7.35–7.0 (m, 10 H), 6.91 (d, 1 H, J = 8 Hz), 6.88 (d, 1 H, J = 8 Hz), 5.87 (qd, 1 H, J = 1.5, 10 Hz), 5.45 (H_M of CH_AH_BC(NTs, Bn)H_MCH_X=, 1 H, J_{MA} = 7 Hz, J_{MB} = 8 Hz, J_{MX} = 10 Hz), 4.38 (AB quartet, J_{AB} = 15 Hz), 3.98 (q, 2 H, J = 7 Hz), 2.85 (AB of ABX, 2 H, J_{AB} = 13 Hz, J_{AX} = 7 Hz, J_{BX} = 8 Hz), 2.37 (s, 3 H), 1.67 (d, 3 H, J = 1.5 Hz), 1.14 (t, 3 H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 164.03 (s), 142.89 (s), 138.31 (s), 137.84 (d), 137.54 (s), 129.64 (d), 129.29 (d), 128.42 (d), 128.06 (d), 127.55 (d), 127.35 (d), 126.17 (d), 60.39 (t), 57.93 (d), 50.22 (t), 40.84 (t), 21.41 (q), 20.47 (q), 14.06 (q); mass spectrum m/e 432 (4%, $M^+ - C_2H_5O$), 386 (100%, $M^+ - C_7H_7$); exact mass: calcd for $C_{26}H_{26}NO_3S$ ($M^+ - C_2H_5O$) 432.163, found 432.166.

13-*E*: $[\alpha]^{25}_D$ +38.3° (c 2.92); ^{1}H NMR ($CDCl_3$) δ 7.68 (d, 2 H, J = 8 Hz), 7.45–7.05 (m, 10 H), 6.95 (d, 1 H, J = 8 Hz), 6.90 (d, 1 H, J = 8 Hz), 6.55 (qd, 1 H, J = 1.5, 10 Hz), 4.72 (H_M of CH_AH_BC-(NTs,Bn)H_MCH_X, 1 H, J_{MA} = 10 Hz, J_{MB} = 5 Hz, J_{MX} = 10 Hz), 4.43 (AB quartet, 2 H, J_{AB} = 16 Hz), 4.07 (q, 2 H, J = 7 Hz), 2.95 (dd, 1 H, J = 5, 13 Hz), 2.59 (dd, 1 H, J = 10, 13 Hz), 2.38 (s, 3 H), 1.22 (d, 3 H, J = 1.5 Hz), 1.20 (t, 3 H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 167.23 (s), 143.30 (s), 137.93 (s), 137.64 (s), 137.07 (s), 136.29 (d), 130.99 (d), 130.25 (d), 130.00 (d), 129.57 (d), 129.24 (d), 128.54 (d), 128.32 (d), 127.70 (d), 127.31 (d), 126.84 (d), 126.54 (d), 60.58 (t), 57.97 (d), 49.26 (t), 41.01 (t), 21.42 (q), 14.18 (q), 12.20 (q); mass spectrum m/e 432 (4%, $M^+ - C_2H_5O$), 386 (100%, $M^+ - C_7H_7$); exact mass: calcd for $C_{26}H_{26}NO_3S$ ($M^+ - C_2H_5O$) 432.1633, found 432.162.

Photochemical Isomerization of Vinyl Ester 13-*E*. A degassed solution of the ester **13-*E*** (6.85 g, 14.3 mmol) in dry CH_3CN (270 mL) [along with benzophenone sensitizer (3.9 g, 21.5 mmol)] was irradiated for 24 h over 2 days using a medium-pressure mercury vapor lamp, Pyrex filter. After concentration a yellow oil results. Plug filtration through silica gel (300 g) using 20% methylene chloride–hexane as eluent removed the benzophenone. The esters were separated by medium-pressure liquid chromatography using ethyl acetate–hexane (1:5), affording 1.98 g of **13-*Z*** and 4.03 g of **13-*E*** to obtain an 88% recovery of material with the ratio of **13-*Z*:13-*E*** being 33:67.

(5*S*)-(*Z*)-5-(*N*-Benzyl-*p*-toluenesulfonamido)-2,3-dimethyl-6-phenylhex-3-en-2-ol (14-*Z*). To a solution of the ester **13-*Z*** (1.50 g, 3.12 mmol) in dry ether (120 mL) at −78 °C was added dropwise methylmagnesium bromide (3.0 M in ether, 3.12 mL, 9.36 mmol). The resulting heterogeneous solution was allowed to warm to 0 °C over a period of 1 h. The reaction mixture was poured into saturated aqueous ammonium chloride and extracted twice with ether. The crude product was chromatographed on silica gel (100 g); elution with ether–hexane (1:3) afforded **14-*Z*** (1.31 g, 90%) as a colorless oil: $[\alpha]^{25}_D$ −22.2° (c 2.2); ^{1}H NMR ($CDCl_3$) δ 7.74 (d, 2 H, J = 8 Hz), 7.49–7.03 (m, 10 H), 6.89 (d, 1 H, J = 8 Hz), 6.84 (d, 1 H, J = 8 Hz), 5.72 (m, 1 H), 4.95 (qd, 1 H, J = 1.5, 10 Hz), 4.53 (AB quartet, 2 H, J_{AB} = 16 Hz), 2.92–2.55 (m, 2 H), 2.40 (s, 3 H), 1.40 (d, 3 H, J = 1.5 Hz), 1.11 (s, 3 H), 0.71 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 143.60 (s), 142.92 (s), 138.62 (s), 138.54 (s), 138.24 (s), 129.49 (d), 129.27 (d), 128.34 (d), 128.10 (d), 127.32 (d), 126.23 (d), 123.93 (d), 74.62 (s), 56.83 (d), 48.79 (t), 41.71 (t), 29.46 (q), 28.66 (q), 23.10 (q), 21.44 (q); mass spectrum m/e 432 (11%, $M^+ - OCH_3$), 404 (6%, $M^+ - (CH_3)_2COH$), 386 (56%, 404 − H_2O), 372 (100%, $M - C_7H_7$); exact mass: calcd for $C_{27}H_{30}NO_2S$ ($M^+ - OCH_3$) 432.200, found 432.199.

(5*S*)-(*E*)-5-(*N*-Benzyl-*p*-toluenesulfonamido)-2,3-dimethyl-6-phenylhex-3-en-2-ol (14-*E*). To a solution of the ester **13-*E*** (900 mg, 1.87 mmol) in dry ether (20 mL) at −78 °C was added dropwise methyllithium (1.2 M in ether, 4.10 mL, 4.87 mmol). After 20 min at −78 °C the reaction mixture was poured into saturated aqueous ammonium chloride and extracted twice with ether. The crude product was chromatographed on silica gel (100 g); elution with ether–hexane (1:3) afforded **14-*E*** (790 mg, 91%) as a colorless oil: $[\alpha]^{25}_D$ +6.7° (c 0.57); ^{1}H NMR ($CDCl_3$) δ 7.74 (d, 2 H, J = 8 Hz), 7.50–7.03 (m, 10 H), 6.95 (d, 1 H, J = 8 Hz), 6.91 (d, 1 H, J = 8 Hz), 5.34 (qd, 1 H, J = 1.5, 10 Hz), 4.71 (H_M of CH_AH_BC(NTs, Bn)H_MCH_X=, 1 H, J_{MA} = 10 Hz), J_{MB} = 4 Hz, J_{MX} = 10 Hz), 4.49 (AB quartet, 2 H, J_{AB} = 16 Hz), 2.81 (dd, 1 H, J = 4, 13 Hz), 2.52 (dd, 1 H, J = 10, 13 Hz), 2.38 (s, 3 H), 1.07 (d, 3 H, J = 1.5 Hz), 0.96 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 145.74 (s), 143.10 (s), 138.76 (s), 138.52 (s), 137.88 (s), 129.57 (d), 129.44 (d), 128.41 (d), 128.07 (d), 127.32 (d), 126.25 (d), 119.02 (d), 73.11 (s), 57.73 (d), 48.58 (t), 41.25 (t), 28.25 (q), 28.18 (q), 21.43 (q), 12.78 (q); exact mass: calcd for $C_{27}H_{30}NO_2S$ ($M^+ - OCH_3$) 432.200, found 432.199.

(2*S*)-(*Z*)-*N*,*N*-Benzyl-2-(4,5-dimethyl-1-phenyl)hexa-3,5-dienyl-*p*-toluenesulfonamide (15-*Z*). To a solution of alcohol **14-*Z*** (2.06 g, 4.47 mmol) and triethylamine (6.23 mL, 44.7 mmol) in methylene chloride (5 mL) at 0 °C was added methanesulfonyl chloride[17] (1.8 mL, 22.4 mmol). After 30 min, ether (20 mL) and water (20 mL) were added and the layers were separated. The aqueous phase was extracted once more with ether, and the combined extracts were washed with cold 5% aqueous hydrochloric acid, water, saturated aqueous sodium bicarbonate, and saturated NaCl solution and dried. The crude product was purified by column chromatography on silica gel (100 g). Elution with 5% ether–hexane afforded **15-*Z*** (2.0 g) 95% as a white solid: mp 65–67 °C; $[\alpha]^{25}_D$ −13.0° (c 1.08); ^{1}H NMR ($CDCl_3$) δ 7.71 (d, 2 H, J = 8 Hz), 7.45–7.05 (m, 10 H), 6.87 (d, 1 H, J = 8 Hz), 6.83 (d, 1 H, J = 8 Hz), 5.21 (qd, 1 H, J = 1.05, 10 Hz), 4.52 (m, 2 H), 4.38 (AB quartet, 2 H, J_{AB} = 15 Hz), 3.82 (br s,1 H, $W_{1/2}$ = 5 Hz), 2.92 (dd, 1 *H*, J = 5, 13 Hz), 2.69 (dd, 1 H, J = 10, 13 Hz), 2.38 (s, 3 H), 1.53 (d, 3 H), J =1.5 Hz), 1.20 (d, 3 H, J = 1 Hz); ^{13}C NMR ($CDCl_3$) δ 144.26 (s), 143.12 (s), 141.72 (s), 138.67 (s), 138.44 (s), 137.92 (s), 129.70 (d), 129.42 (d), 129.33 (d), 128.46 (d), 128.33 (d), 127.97 (d), 127.32 (d), 126.02 (d), 122.78 (d), 112.54 (t), 59.27 (d), 50.14 (t), 42.88 (t), 22.67 (q), 21.33 (q), 20.99 (q); mass spectrum m/e 445 (1%, M^+), 354 (100%, $M^+ - C_7H_7$); exact mass: calcd for $C_{28}H_{31}NO_2S$ 445.208, found 445.207.

(2*S*)-(*E*)-*N*,*N*-Benzyl-2-(4,5-dimethyl-1-phenyl)hexa-3,5-dienyl-*p*-toluenesulfonamide (15-*E*). Treatment of the alcohol **14-*E*** (1.0 g, 2.16 mmol) in a similar manner to that described for preparation of diene **15-*Z***, afforded diene **15-*E*** (990 mg, 95%): $[\alpha]^{25}_D$ +47.6° (c 2.20); ^{1}H NMR ($CDCl_3$) δ 7.71 (d, 2 H, J = 8 Hz), 7.45–7.05 (m, 10 H), 6.96 (d, 1 H, J = 8 Hz), 6.92 (d, 1 H, J = 8 Hz), 5.35 (qd, 1 H, J = 1.5, 10 Hz), 2.99 (dd, 1 H, J = 4, 13 Hz), 2.60 (dd, 1 H, J = 10, 13 Hz), 2.37 (s, 3 H), 1.59 (s, 3 H), 1.23 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 144.03 (s), 143.05 (s), 138.80 (s), 138.22 (s), 138.13 (s), 137.88 (s), 129.48 (d), 129.34 (d), 128.46 (d), 128.17 (d), 127.53 (d), 127.31 (d), 126.23 (d), 123.85 (d), 112.87 (t), 58.49 (d), 49.02 (t), 41.99 (t), 21.43 (q), 20.56 (q), 13.71 (q); mass spectrum m/e 445 (1%, M^+), 354 (100%, $M^+ - C_7H_7$); exact mass: calcd for $C_{28}H_{31}NO_2S$ 445.208, found 445.207.

(2*S*)-(*Z*)-*N*,*N*-Benzyl-2-(4,5-dimethyl-1-phenyl)hexa-3,5-dienylamine (16-*Z*). A mixture of the diene **15-*Z*** (500 mg, 1.16 mmol), Na_2HPO_4 (659 mg, 4.64 mmol), and finely ground 6% sodium amalgam (6.2 g) in methanol (10 mL) was stirred rapidly and heated to a gentle reflux.[18] After 12 h the reaction mixture was cooled to 25 °C and poured into water and extracted with ether (3×). The combined extracts were washed with water and saturated NaCl solution and dried. The crude product was filtered through a small plug of silica gel (ether), affording diene **16-*Z*** (324 mg, 97%): $[\alpha]^{25}_D$ −3.0° (c 1.74); ^{1}H NMR ($CDCl_3$) δ 7.4–7.05 (m, 10 H), 5.09 (qd, 1 H, J = 1.5, 9 Hz), 4.68 (br s, 1 H, $W_{1/2}$ = 5 Hz), 4.43 (br s, 1 H, $W_{1/2}$ = 5 Hz), 3.66 (AB quartet, 2 H, J_{AB} = 13 Hz), 2.74 (d, 2 H, J = 7 Hz), 1.79 (d, 3 H, J = 1.5 Hz), 1.61 (d, 3 H, J = 1 Hz); ^{13}C NMR ($CDCl_3$) δ 145.2 (s), 141.12 (s), 140.82 (s), 139.09 (s), 129.53 (d), 128.57 (d), 128.25 (d), 127.93 (d), 126.67 (d), 126.17 (d), 112.35 (t), 57.67 (d), 51.66 (t), 43.07 (t), 23.20 (q), 21.88 (q); mass spectrum m/e 291 (1%, M^+), 200 (100%, $M^+ - C_7H_7$); exact mass: calcd for $C_{21}H_{25}N$ 291.199, found 291.196.

(2*S*)-(*E*)-*N*,*N*-Benzyl-2-(4,5-dimethyl-1-phenyl)hexa-3,5-dienylamine (16-*E*). Treatment of the diene **15-*E*** (220 mg, 0.494 mmol) in a similar manner to that described for the preparation of diene **15-*Z***, afforded diene **16-*E*** (154 mg, 95%): $[\alpha]^{25}_D$ −6.4° (c 0.77); ^{1}H NMR ($CDCl_3$) δ 7.40–7.05 (m, 10 H), 5.50 (dd, 1 H, J = 1.5, 9 Hz), 4.98 (br s, 1 H, $W_{1/2}$ = 4 Hz), 4.93 (br s, 1 H, $W_{1/2}$ = 5 Hz), 3.75 (dd, 1 H, J = 7, 14 Hz), 3.72 (AB quartet, 2 H, J_{AB} = 14 Hz), 2.78 (d, 2 H, J = 7 Hz), 1.93 (s, 3 H), 1.62 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 144.46 (s), 140.55 (s), 138.60 (s), 136.60 (s), 130.84 (d), 129.42 (d), 128.42 (d), 128.29 (d), 127.97 (d), 126.74 (d), 126.25 (d), 111.93 (t), 56.91 (d), 51.51 (t), 42.47 (t), 21.02 (q), 14.13 (q); mass spectrum m/e 291 (1%, M^+), 200 (100%, $M^+ - C_7H_7$); exact mass: calcd for $C_{21}H_{25}N$ 291.199, found 291.199.

(*E*)-5-(*N*-Benzyl-*p*-toluenesulfonamido)-3-methyl-6-phenylhex-3-en-2-one (*dl*-18-*E*). A solution of the aldehyde **12** (15.0 g, 38.2 mmol) and (3-oxo-2-butyl)triphenylphosphorane **17** (25.3 g, 76.3 mmol) in dry THF (150 mL) was stirred at 25 °C for 5 days (reaction ca. 80% complete by

TLC analysis). Silica gel (50 g) was then added, the volatiles were evaporated, and the mixture was placed on top of a column of silica gel (400 g). Elution with methylene chloride gave *dl*-**18**-*E* (12 g) which was crystallized from methanol (11.0 g, 65%): mp 125.5–127 °C; ^{1}H NMR ($CDCl_3$) δ 7.74 (d, 2 H, J = 8 Hz), 7.5–6.8 (m, 12 H), 6.24 (qd, 1 H, J = 1.5, 10 Hz), 5.0–4.6 (m, 1 H), 4.52 (AB quartet, 2 H, J_{AB} = 16 Hz), 3.1–2.5 (m, 2 H), 2.42 (s, 3 H), 1.92 (s, 3 H), 1.23 (d, 3 H, J = 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 199.24 (s), 143.54 (s), 138.97 (s), 137.98 (d), 137.82 (s), 136.68 (d), 129.71 (d), 129.01 (d), 128.64 (d), 128.41 (d), 128.16 (d), 127.81 (d), 127.12 (d), 126.64 (d), 58.10 (d), 49.07 (t), 39.86 (t), 25.21 (q), 21.40 (q), 10.79 (q); mass spectrum m/e 404 (2%, $M^+ - COCH_3$), 356 (100%, $M^+ - C_7H_7$); exact mass: calcd for $C_{25}H_{26}NO_2S$ ($M^+ - COCH_3$) 404.168, found 404.168.

(*E*)-5-(*N*-Benzyl-*p*-toluenesulfonamido)-2,3-dimethyl-6-phenylhex-3-en-2-ol (*dl*-14-*E*). To a solution of the enone *dl*-**18**-*E* (1.33 g, 3.0 mmol) in dry THF–ether (20 mL, 1:1) at −78 °C was added methylmagnesium bromide (3.0 M in ether, 3.0 mL, 9.0 mmol). The resulting heterogeneous solution was allowed to warm to 0 °C over a period of 1 h. The reaction mixture was poured into saturated ammonium chloride and extracted twice with ether. The crude product was chromatographed on silica gel (100 g); elution with ether–hexane (1:3) afforded *dl*-**14***E* (1.41 g, 100%), identical in all respects (TLC, ^{1}H NMR) with that obtained above from **13**-*E* except for $[\alpha]^{25}_D$ which was close to zero.

5-(*N*-Benzyl-*p*-toluenesulfonamido)-3,4-epoxy-2,3-dimethyl-1-phenylhexan-2-ol (*dl*-19). To a solution of the racemic alcohol *dl*-**14**-*E* (1.075 g, 2.3 mmol) in methylene chloride (20 mL) at 0 °C was added solid *m*-chloroperoxybenzoic acid (85%, 0.542 g, 2.7 mmol). After 5 min the cooling bath was removed and stirring at 25 °C was continued for 1.5 h. The reaction mixture was then washed with aqueous sodium bisulfite and aqueous sodium bicarbonate, dried, and evaporated. The epoxide *dl*-**19** (1.08 g, 97%) was obtained as a white solid foam: ^{1}H NMR ($CDCl_3$) δ 7.79 (d, 2 H, J = 8 Hz), 7.6–6.9 (m, 12 H), 4.50 (AB quartet, 2 H, J_{AB} = 16 Hz), 3.83 (ddd, 1 H, J = 5, 10, 10 Hz), 3.25 (d, 1 H, J = 10 Hz), 3.05 (dd, 1 H, J = 5, 13 Hz), 2.63 (dd, 1 H, J = 10, 13 Hz), 2.39 (s, 3 H), 0.99 (s, 3 H), 0.74 (s, 3 H), 0.59 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 143.11 (s), 138.12 (s), 137.21 (s), 137.06 (s), 129.44 (d), 128.73 (d), 128.56 (d), 128.48 (d), 127.87 (d), 127.54 (d), 126.82 (d), 70.50 (s), 67.78 (s), 59.26 (d), 59.19 (d), 50.12 (t), 39.90 (t), 26.17 (q), 24.42 (q), 21.49 (q), 13.32 (q).

***N*,*N*-Benzyl-2-(4-methyl-3,4-epoxy-1-phenyl)hexa-5-enyl-*p*-toluenesulfonamide (*dl*-20).** To a solution of the epoxide *dl*-**19** (800 mg, 1.67 mmol) in pyridine (7.5 mL) at 25 °C was added phosphorus oxychloride (0.46 mL, 5.01 mmol). The mixture was heated at 60 °C for 1.5 h, then poured onto ice and extracted with ether (3×). The extract was washed with saturated aqueous copper sulfate solution (4×), and saturated NaCl solution and dried. Evaporation gave *dl*-**20** (745 mg, 97%) as a pale yellow oil, homogeneous by TLC analysis: ^{1}H NMR ($CDCl_3$) δ 7.82 (d, 2 H, J = 8 Hz), 7.5–6.9 (m, 12 H), 4.66 (br s, 2 H, $W_{1/2}$ = 5 Hz), 4.51 (AB quartet, 2 H, J_{AB} = 16 Hz), 3.70 (H_C of $CH_AH_BCH_CCH_D$, J_{CA} = 4 Hz, J_{CB} = 10 Hz, J_{CD} = 10 Hz), 3.06 (dd, 2 H, J = 4, 13 Hz), 2.87 (d, 1 H, J = 10 Hz), 2.67 (dd, 1 H, J = 10, 13 Hz), 2.39 (s, 3 H), 1.34 (d, 3 H, J = 1.5 Hz), 0.53 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 145.05 (s), 143.04 (s), 137.88 (s), 137.29 (s), 129.42 (d), 129.25 (d), 128.58 (d), 128.50 (d), 128.18 (d), 127.78 (d), 127.48 (d), 126.66 (d), 111.36 (t), 63.66 (s), 63.12 (d), 59.70 (d), 50.18 (t), 40.36 (t), 21.43 (q), 18.32 (q), 16.06 (q).

(*Z*)-*N*,*N*-Benzyl-2-(4,5-dimethyl-1-phenyl)hexa-3,5-dienyl-*p*-toluenesulfonamide (*dl*-15-*Z*). The allyl epoxide *dl*-**20** (1.86 g, 4.03 mmol) was dissolved in THF (20 mL) and cooled to −78 °C; lithium diphenylphosphide[22] (5.25 mmol, 7.0 mL of a 0.75 M solution) was added to produce a brick-red homogeneous solution. The solution was allowed to warm to 25 °C and stirred for an additional 4 h. During the course of this period the color was discharged and a cream-colored precipitate formed. Addition of methyl iodide (2.0 mmol, 1.25 mL) followed by stirring at 25 °C for 18 h afforded a yellow heterogeneous reaction mixture. Water was added and the mixture was extracted with ether. The crude product (containing methyldiphenylphosphine oxide) was purified by column chromatography on silica gel. Elution with methylene chloride–hexane (3:1) afforded 1.1 g (60%) of *Z* diene, uncontaminated with *E* diene as judged from NMR analysis.[23]

(*Z*)-(5*S*)-5-(*N*-Benzyl-*p*-toluenesulfonamido)-3-methyl-6-phenylhex-3-en-2-one (18-*Z*). To a solution of lithium diphenyl-2-pyridylmethane[24] and methyllithium (from diphenyl-2-pyridylmethane (5.66 g, 23.07 mmol) and methyllithium (1.6 M, 30 mL, 48 mmol)) in ether (100 mL) at −25 °C was added a solution of ester **13**-*Z* (5.51 g, 11.55 mmol) in ether (50 mL) over 30 min. After an additional 10 min the reaction mixture was added via cannula to a rapidly stirred mixture of ice and aqueous ammonium chloride.

The ether phase was separated and washed with cold 5% aqueous hydrochloric acid, water, saturated aqueous sodium bicarbonate, and saturated NaCl solution and dried. The crude product was purified by column chromatography on silica gel (200 g). Elution with ether–hexane (1:4) afforded enone **18**-*Z* as a pale yellow solid (4.16 g, 81%): mp 109–110 °C; $[\alpha]^{25}D$ +19.7° (*c* 1.72); ^{1}H NMR ($CDCl_3$) δ 7.62 (d, 2 H, J = 8 Hz), 7.46–6.85 (m, 12 H), 5.60 (qd, 1 H, J = 1.5, 10 Hz), 4.42 (AB quartet, 2 H, J_{AB} = 16 Hz), 2.95–2.50 (m, 2 H), 2.37 (s, 3 H), 1.78 (s, 3 H), 1.69 (d, 3 H, J = 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 202.50 (s), 142.76 (s), 138.31 (s), 137.81 (s), 137.60 (s), 133.54 (d), 129.23 (d), 128.66 (d), 128.41 (d), 128.10 (d), 127.60 (d), 127.24 (d), 126.16 (d), 58.37 (d), 50.38 (t), 41.13 (t), 28.70 (q), 21.40 (q), 20.46 (q); mass spectrum m/e 404 (10%, $M^+ - COCH_3$), 356 (100%, $M^+ - C_7H_7$); exact mass: calcd for $C_{25}H_{26}NO_2$ ($M^+ - COCH_3$) 404.168, found 404.168.

2-Trimethylsilylethyl Chloromethyl Ether (21). Gaseous hydrogen chloride was bubbled through a mechanically stirred mixture of 2-trimethylsilylethanol (52 g, 0.44 mol) and paraformaldehyde (14.54 g, 0.485 mmol) at such a rate that the internal temperature remained below 25 °C and until two homogeneous phases formed (ca. 30 min). The layers were separated and the top layer was diluted with pentane (200 mL) and dried over magnesium sulfate for 3 h at 0 °C, with stirring. The solution was filtered, calcium chloride (1 g) was added, and the pentane was evaporated; the product (90% yield) was stored over calcium chloride in the freezer: ^{1}H NMR ($CDCl_3$) δ 5.50 (s, 2 H), 3.78 (t, 2 H), 0.98 (t, 2 H), 0.03 (s, 9 H).[28]

(2-Trimethylsilylethoxymethyl)triphenylphosphonium Chloride (22b). A solution of 2-trimethylsilylethyl chloromethyl ether (**21**) (10 g, 0.06 mol) and triphenylphosphine (16.25 g, 0.063 mol) in benzene (300 mL) was heated at a gentle reflux for 18 h. The reaction mixture was cooled to 0 °C and the white precipitate was collected by suction filtration and washed with ether (500 mL). The product (25 g, 94%) was dried in a vacuum desiccator over P_2O_5: ^{1}H NMR ($CDCl_3$) δ 5.88 (d, 2 H, J = 4 Hz), 4.02 (t, 2 H), 1.02 (t, 2 H), 0.0 (s, 9 H).

(2*S*)-(*Z*,*E*)-*N*,*N*-Benzyl-2-(4,5-dimethyl-6-methoxy-1-phenyl)hexa-3,5-dienyl-*p*-toluenesulfonamide (23-*ZE*) and (2*S*)-(*Z*,*Z*)-*N*,*N*-Benzyl-2-(4,5-dimethyl-6-methoxy-1-phenyl)hexa-3,5-dienyl-*p*-toluenesulfonamide (23-*ZZ*). To a solution of potassium *tert*-butoxide (280 mg, 2.5 mmol) and *tert*-butyl alcohol (0.23 mL, 2.4 mmol) in dry THF (15 mL) at −78 °C was added solid (methoxymethyl)triphenylphosphonium chloride (**22a**: 842 mg, 2.46 mmol). After 10 min at −78 °C the cooling bath was removed; then after a further 10 min a solution of ketone **18**-*Z* (366 mg, 0.818 mmol) in THF (5 mL) was added. Stirring at 25 °C was continued for 1 h; the reaction mixture was then poured into water and extracted twice with ether. The extracts were washed with water and saturated NaCl solution and dried. Purification of the crude product by preparative TLC (ether–hexane, 1:1) gave an inseparable mixture of **23**-*ZE* and **23**-*ZZ* (250 mg, 64%, **23**-*ZE*:**23**-*ZZ* 7:1): mass spectrum m/e 384 (100%, $M^+ - C_7H_7$); exact mass: calcd for $C_{22}H_{26}NO_3S$ 384.163, found 384.164. **23**-*ZE*: ^{1}H NMR ($CDCl_3$) δ 7.69 (d, 2 H, J = 8 Hz), 7.4–6.75 (m, 12 H), 5.21 (qd, 1 H, J = 1.5, 10 Hz), 4.69 (q, 1 H, J = 1.5 Hz), 4.54 (d, 1 H, J = 15 Hz), 4.12 (d, 1 H, J = 15 Hz), 3.29 (s, 3 H), 2.39 (s, 3 H), 1.54 (d, 3 H, J = 1.5 Hz), 1.17 (d, 3 H, J = 1.5 Hz).

23-*ZZ*: ^{1}H NMR ($CDCl_3$) δ 7.66 (d, 2 H, J = 8 Hz), 7.4–6.75 (m, 12 H), 5.57 (q, 1 H, J = 1.5 Hz), 5.21 (qd, 1 H, J = 1.5, 10 Hz), 4.42 (d, 1 H, J = 15 Hz), 4.06 (d, 1 H, J = 15 Hz), 3.33 (s, 3 H), 2.39 (s, 3 H), 1.64 (d, 3 H, J = 1.5 Hz), 1.16 (d, 3 H, J = 1.5 Hz).

(2*S*)-(*Z*,*E*)-*N*,*N*-Benzyl-2-(4,5-dimethyl-6-methoxy-1-phenyl)hexa-3,5-dienylamine (25-*ZE*) and (2*S*)-(*Z*,*Z*)-*N*,*N*-Benzyl-2-(4,5-dimethyl-6-methoxy-1-phenyl)hexa-3,5-dienylamine (25-*ZZ*). Treatment[18] of a mixture **23**-*ZE* and **23**-*ZZ* (248 mg, 0.52 mmol) in a similar manner to that described for the preparation of **16**-*Z* afforded an inseparable mixture (161 mg, 96%) of **25**-*ZE* and **25**-*ZZ*.

25-*ZE*: ^{1}H NMR ($CDCl_3$) δ 7.4–7.1 (m, 10 H), 5.18 (q, 1 H, J = 1.5 Hz), 5.09 (qd, 1 H, J = 1.5, 10 Hz), 3.63 (AB quartet, 2 H, J_{AB} = 13 Hz), 3.34 (s, 3 H), 2.73 (m, 2 H), 1.75 (d, 3 H, J = 1.5 Hz), 1.49 (d, 3 H, J = 1.5 Hz).

25-*ZZ*: ^{1}H NMR ($CDCl_3$, in part) δ 5.68 (q, 1 H, J = 1.5 Hz), 5.21 (qd, 1 H, J = 1.5, 10 Hz), 3.46 (s, 3 H), 1.73 (d, 3 H, J = 1.5 Hz), 1.43 (d, 3 H, J = 1.5 Hz).

(2*S*)-(*Z*,*E*)-*N*,*N*-Benzyl-2-[6-(2′-trimethylsilyl)ethoxy-4,5-dimethyl-1-phenyl]hexa-3,5-dienyl-*p*-toluenesulfonamide (24-*ZE*) and (2*S*)-(*Z*,*Z*)-*N*,*N*-Benzyl-2-[6-(2′-trimethylsilyl)ethoxy-4,5-dimethyl-1-phenyl]hexa-3,5-dienyl-*p*-toluenesulfonamide (24-*ZZ*). To a solution of potassium *tert*-butoxide (585 mg, 5.22 mmol) in dry THF (70 mL) at −78 °C was added solid (2-trimethylsilylethoxymethyl)triphenylphosphonium chloride (2.65 g, 5.70 mmol). After 10 min at −78 °C the cooling bath was removed; then after an additional 10 min a solution of enone **18**-*Z* (850 mg, 1.90 mmol) in THF (5 mL) was added. The reaction mixture was stirred for 20 min, then poured into ice–water and extracted with ether (3×). The crude product was purified by column chromatography on silica gel (100 g). Elution with ether–hexane (1:1) gave a mixture of **24**-*ZE*/**24**-*ZZ* as a colorless oil (900 mg, 84%, **24**-*ZE*:**24**-*ZZ* 7:1).

24-*ZE*: ^{1}H NMR ($CDCl_3$) δ 7.69 (d, 2 H, J = 8 Hz), 7.4–6.8 (m, 12 H), 5.21 (qd, 1 H, J = 1.5, 10 Hz), 4.76 (q, 1 H, J = 1.5 Hz), 4.51 (d, 1 H, J = 16 Hz), 4.12 (d, 1 H, J = 16 Hz), 3.49 (m, 2 H), 2.80 (m, 2 H), 2.39 (s, 3 H), 1.54 (d, 3 H, J = 1.5 Hz), 1.19 (d, 3 H, J = 1.5 Hz), 0.89 (m, 2 H).

24-*ZZ*: ^{1}H NMR ($CDCl_3$, in part) δ 5.64 (q, 1 H, J = 1.5 Hz), 5.39 (qd, 1 H, J = 1.5, 10 Hz), 4.39 (d, 1 H, J = 16 Hz), 4.03 (d, 1 H, J = 16 Hz), 2.39 (s, 3 H), 1.64 (d, 3 H, J = 1.5 Hz), 1.18 (d, 3 H, J = 1.5 Hz).

(2*S*)-(*Z*,*E*)-*N*,*N*-Benzyl-2-[6-(2′-trimethylsilyl)ethoxy-4,5-dimethyl-1-phenyl]hexa-3,5-dienylamine (24-*ZE*) and (2*S*)-(*Z*,*Z*)-*N*,*N*-Benzyl-2-[6-(2′-trimethylsilyl)ethoxy-4,5-dimethyl-1-phenyl]hexa-3,5-dienylamine (26-*ZZ*). Treatment[18] of a mixture of **24-*ZE*** and **24-*ZZ*** (900 mg, 1.60 mmol) in a similar manner to that described for the preparation of **16-*Z*** afforded **26-*ZE*** (56 mg, higher R_f) and **26-*ZZ*** (311 mg, lower R_f) after separation by column chromatography on silica gel (ethyl acetate–hexane 2:3).

26-*ZE*: ^{1}H NMR ($CDCl_3$) δ 7.4–7.0 (m, 10 H), 5.23 (q, 1 H, J = 1 Hz), 5.09 (qd, 1 H, J = 1, 9 Hz), 3.85–3.32 (m, 5 H), 2.74 (m, 2 H), 1.75 (d, 3 H, J = 1.5 Hz), 1.51 (d, 3 H, J = 1.5 Hz), 0.89 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 142.05 (d), 140.57 (s), 139.25 (s), 138.94 (s), 129.75 (d), 128.74 (d), 128.35 (d), 128.17 (d), 128.86 (d), 126.21 (d), 113.59 (s), 69.44 (t), 57.73 (d), 51.47 (t), 43.20 (t), 23.75 (q), 18.59 (t), 12.89 (q).

26-*ZZ*: ^{1}H NMR ($CDCl_3$) δ 7.3–7.0 (m, 10 H), 5.73 (q, 1 H, J = 1.5 Hz), 5.18 (qd, 1 H, J = 1.5, 9 Hz), 3.85–3.25 (m, 5 H), 2.74 (m, 2 H), 1.74 (d, 3 H, J = 1.5 Hz), 1.42 (d, 3 H), J = 1.5 Hz), 0.88 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 142.66 (s), 141.20 (s), 141.20 (d), 137.51 (s), 131.02 (d), 130.94 (d), 129.65 (d), 129.35 (d), 127.48 (d), 127.96 (d), 114.50 (s), 70.87 (t), 59.92 (d), 53.07 (t), 43.36 (t), 23.87 (q), 20.03 (t), 18.74 (q); mass spectrum m/e 407 (6%, M^+), 288 (13%, $M^+ - (CH_3)_3SiCH_2CH_2 - H_2O$), 91 (100%); exact mass: calcd for $C_{26}H_{37}NOSi$ 407.2644, found 407.263.

(*E*,*Z*)-*N*,*N*-Benzyl-2-[6-(2′-trimethylsilyl)ethoxy-4,5-dimethyl-1-phenyl]hexa-3,5-dienyl-*p*-toluenesulfonamide (*dl*-33-*EZ*) and (*E*,*E*)-*N*,*N*-Benzyl-2-[6-(2′-trimethylsilyl)ethoxy-4,5-dimethyl-1-phenyl]hexa-3,5-dienyl-*p*-toluenesulfonamide (*dl*-27-*EE*). Treatment of enone *dl*-**18-*E*** (588 mg, 1.32 mmol) in a similar manner to that described for the preparation of **24-*ZE*** and **24-*ZZ*** afforded an inseparable mixture of *dl*-**27-*EZ*** and *dl*-**27-*EE*** (544 mg, 75%, 2.05:1).

dl*-27-*EZ: ^{1}H NMR ($CDCl_3$, in part) δ 8.71 (d, 2 H, J = 9 Hz), 7.5–6.9 (m, 12 H), 6.01 (br s, 1 H, $W_{1/2}$ = 3 Hz), 5.13 (qd, 1 H, J = 1, 10 Hz), 2.39 (s, 3 H), 1.44 (s, 3 H), 1.19 (s, 3 H).

dl*-27-*EE: ^{1}H NMR ($CDCl_3$, in part) 5.80 (br s, 1 H, $W_{1/2}$ = 3.5 Hz), 5.31 (qd, 1 H, J = 2, 10 Hz), 1.41 (d, 3 H, J = 1.5 Hz), 1.34 (d, 3 H, J = 1.5 Hz).

(*E*,*Z*)-*N*,*N*-Benzyl-2-[6-(2′-trimethylsilyl)ethoxy-4,5-dimethyl-1-phenyl]hexa-3,5-dienylamine (*dl*-28-*EZ*) and (*E*,*E*)-*N*,*N*-Benzyl-2-[6-(2′-trimethylsilyl)ethoxy-4,5-dimethyl-1-phenyl]hexa-3,5-dienylamine (*dl*-28-*EE*). Treatment of a mixture of *dl*-**27-*EZ*** and *dl*-**27-*EE*** (554 mg, 0.987 mmol) in a similar manner to that described for the preparation of **15-*Z*** afforded a mixture of *dl*-**28-*EZ*** and *dl*-**28-*EE*** (362 mg, 90%). Partial separation of *dl*-**28-*EZ*** and *dl*-**28-*EE*** could be achieved by column chromatography (silica gel, 10% ethyl acetate–hexane, *dl*-**28-*EZ***, slightly more mobile).

dl*-28-*EZ: ^{1}H NMR ($CDCl_3$) δ 7.3–7.0 (m, 10 H), 6.83 (br s, 1 H), 6.15 (br s, 1 H, $W_{1/2}$ = 1.5 Hz) 5.19 (qd, 1 H, J = 1, 10 Hz), 1.72 (s, 3 H), 1.49 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 144.97 (d), 140.29 (s), 136.42 (s), 130.82 (d), 129.57 (d), 129.35 (d), 128.01 (d), 127.82 (d), 127.44 (d), 117.67 (s), 71.30 (t), 57.94 (d), 52.72 (t), 44.20 (t), 19.91 (t), 15.25 (q), 12.45 (q); mass spectrum m/e 407 (4%, M^+), 288 (8%, $M^+ - (CH_3)_3SiCH_2CH_2 - H_2O$), 91 (100%); exact mass: calcd for $C_{26}H_{37}NOSi$ 407.2644, found 407.264.

dl*-28-*EE: ^{1}H NMR ($CDCl_3$, in part) δ 5.82 (br s, 1 H, $W_{1/2}$ = 1.5 Hz), 5.25 (qd, 1 H, J = 1, 10 Hz), 1.64 (d, 3 H, J = 1.5 Hz), 1.60 (d, 3 H, J = 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 143.39 (d), 140.42 (s), 137.16 (s), 115.82 (s), 71.34 (t), 57.65 (d), 52.74 (t), 43.49 (t), 19.96 (t), 17.99 (q), 17.42 (q).

Determination of Enantiomeric Purities of Enone *dl*-18-*E* and Dienes 15-*Z* and 24-*ZE*. Ozonolysis: General Procedure. Ozone was bubbled through a solution of enone *dl*-**18-*E*** (200 mg, 0.436 mmol) in ethanol (10 mL) at −78 °C until a blue color persisted (for dienes **15-*Z*** and **24-*ZE*** ozone was bubbled through for 30 min past the blue color to ensure complete oxidation). Nitrogen was then bubbled through the solution to remove excess ozone (10 min) and sodium borohydride (132 mg) in ethanol (5 mL) was added. After 1 h at 25 °C the reaction mixture was poured into water, neutralized at 0 °C, then extracted with ether (3×). Purification of the crude product by preparative TLC (ether) gave alcohol **11** (136 mg, 82%). (1) **11** derived from enone *dl*-**18-*E*** had $[\alpha]^{25}_D$ +0.05° (*c* 1.36). (2) **11** derived from diene **15-*Z*** had $[\alpha]^{25}_D$ −50.1° (*c* 1.56).

Chiral Shift Reagent Studies. The ^{1}H NMR (360 MHz) spectrum of racemic **11** containing 10 mol % of tris[3-[(trifluoromethyl)hydroxymethylene]-*d*-camphorato]europium(III) showed diastereotopic resonance pairs at δ 8.01 (d, J = 7.9 Hz) and 8.05 (d, J = 7.9 Hz), 7.81 (d, J = 6.6 Hz) and 7.71 (d, J = 6.9 Hz), 5.25 (d, J = 16.2 Hz) and 5.20 (d, J = 15.6 Hz), and 4.95 (d, J = 16.2 Hz) and 4.91 (d, J = 15.6 Hz) ppm, while that of **11**, derived from dienes **15-*Z*** and **24-*ZE*** by the above ozonolysis procedure, showed only the later, higher field signals of each resonance pair.

(2′*S*)-3,3-Dimethyl-6-oxocyclohex-1-enyl-1-((*Z*)-*N*,*N*-benzyl-2′-[4′,5′-dimethyl-1′-phenyl]hexa-3′,5′-dienyl)carboxamide (30). To a suspension of 2-chloro-1-methylpyridinium iodide[32] (140 mg, 0.55 mmol) in triethylamine (0.21 mL, 1.5 mmol) and methylene chloride (1 mL) at 0 °C was added a solution of 3,3-dimethyl-6-oxocyclohex-1-enecarboxylic acid in methylene chloride (2 mL) over 5 min. After 5 min a solution of diene **16-*Z*** (145 mg, 0.5 mmol) in methylene chloride (1.5 mL) was added. After 30 min at 0 °C, ether (25 mL) was added and the solution was washed with cold 5% aqueous hydrochloric acid, saturated aqueous sodium bicarbonate, and saturated NaCl solution and dried. Purification by preparative TLC (ether–hexane 9:1) afforded amide **30** (194.5 mg, 85%) as a colorless oil: $[\alpha]^{25}_D$ +13.7° (*c* 0.95); ^{1}H NMR ($CDCl_3$, in part) δ 7.6–6.95 (m, 10 H), 6.48 (br s, 1 H); mass spectrum m/e 441 (11%, M^+), 350 (100%, $M^+ - C_7H_7$); exact mass: calcd for $C_{30}H_{35}NO_2$ 441.267, found 441.267.

(2′*S*)-3,3-Dimethyl-6-oxocyclohex-1-enyl-1-((*Z*,*E*)-*N*,*N*-benzyl-2′-[6′-(trimethylsilyl)ethoxy-4′,5′-dimethyl-1′-phenyl]hexa-3′,5′-dienyl)carboxamide (31). In a similar manner to that described for the preparation of amide **30**, diene **26-*ZE*** (224 mg, 0.5 mmol) gave amide **31** (155 mg, 56%): $[\alpha]^{25}_D$ +50.97° (*c* 1.55); ^{1}H NMR ($CDCl_3$, in part) δ 7.6–6.9 (m, 10 H), 6.23 (s, 1 H), 5.78 (br s, 1 H), 5.62 (d, 1 H, J = 10 Hz); mass spectrum m/e 466 (14%, $M^+ - (CH_3)_3SiCH_2CH_2$, 438 (24%, $M^+ - (CH_3)_3SiCH_2CH_2 - H_2O$), 91 (100%).

(2′*S*)-3,3-Dimethyl-6-oxocyclohex-1-enyl-1-((*Z*,*Z*)-*N*,*N*-benzyl-2′-[6′-(trimethylsilyl)ethoxy-4′,5′-dimethyl-1′-phenyl]hexa-3′,5′-dienyl)carboxamide (32). In a similar manner to that described for the preparation of amide **30**, diene **26-*ZE*** (224 mg, 0.5 mmol) gave **32** (237 mg, 85%): $[\alpha]^{25}_D$ +5.17° (*c* 2:37); ^{1}H NMR ($CDCl_3$, in part) δ 7.6–6.9 (m, 10 H), 6.41 (s, 1 H), 5.45 (d, 1 H, J = 10 Hz), 5.42 (br s, 1 H); mass spectrum m/e 466 (15% $M^+ - C_7H_7$), 456 (14%, $M^+ - (CH_3)_3SiCH_2CH_2$), 438 (28%, $M^+ - (CH_3)_3SiCH_2CH_2 - H_2O$), 91 (100%); exact mass: calcd for $C_{28}H_{40}NO_3Si$ ($M^+ - C_7H_7$) 466.278, found 466.275.

(3*S*,3a*R*,6a*S*,10a*S*)-3,3a,6,6a,7,8,9,10-Octahydro-2,3-dibenzyl-4,5,7,7-tetramethyl-1*H*-benz[*d*]isoindole-1,10-dione (33). A carefully deoxygenated solution of amide **30** (150 mg) in toluene (15 mL) was heated to reflux for 40 h. The reaction mixture was then concentrated and purified by column chromatography on silica gel (30 g). Elution with ether–hexane (3:2) gave **33** (150 mg) as a white solid: mp 133–133.5 °C; $[\alpha]^{25}_D$ +107.5° (*c* 0.55); IR ($CHCl_3$) 1705, 1680 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.25–7.10 (m, 10 H, aryl), 5.17 (d, J_{AB} = 15.4 Hz, H_A), 3.91 (d, J_{AB} = 15.4 Hz, H_B), 3.20 (dd, J_{CE} = 5.3 Hz, J_{DE} = 9.8 Hz, J_{EF} < 1 Hz, H_E), 3.05 (dd, J_{CE} = 5.3 Hz, J_{CD} = 13.2 Hz, H_C), 2.81 (ddd, J_{MN} = J_{KN} = 14.2 Hz, J_{LN} = 5.8 Hz, H_N), 2.51 (d, J_{GJ} = 6.4 Hz, H_J), 2.50 (dd, J_{CD} = 13.2 Hz, J_{DC} = 9.8 Hz, H_D), 2.45 (ddd, J_{MN} = 14.2 Hz, J_{KM} = 4.0 Hz, J_{LM} = 4.5 Hz, H_M), 2.39 (br s, J_{EF} < 1 Hz, H_F), 2.11 (ddq, J_{GI} = 17.5 Hz, J_{GJ} = 6.4 Hz, $J_{CH_3(5)g}$ = 1.5 Hz, H_G), 1.89 (d, J_{GI} = 17.5 Hz, H_J), 1.88 (ddd, J_{KL} = 15.5 Hz, J_{KM} = 4.0 Hz, J_{KN} = 14.2 Hz, H_K), 1.74 (ddd, J_{KL} = 15.5 Hz, J_{LM} = 4.5 Hz, J_{LN} = 5.8 Hz, H_L), 1.55 (br s, C_6-CH_3), 1.05 (s, CH_3), 0.90 (d, $J_{CH_3(5)g}$ = 1.5 Hz C_5-CH_3), 0.82 (s, CH_3); ^{13}C NMR ($CDCl_3$) δ 212.0 (s), 172.7 (s), 138.0 (s), 136.5 (s), 129.5 (d), 128.7 (d), 128.4 (d), 128.0 (s), 127.7 (d), 127.3 (d), 126.7 (d), 123.2 (s), 62.8 (d), 62.1 (s), 44.9 (d), 44.6 (t), 43.8 (d), 41.7 (t), 39.0 (t), 36.2 (t), 33.2 (s), 30.7 (q), 29.6 (t), 23.1 (q), 19.8 (q), 16.1 (q). Anal. Found: C, 81.75; H, 8.12; N, 3.16. $C_{30}H_{35}NO_2$ requires C, 81.59; H, 7.99; N, 3.17. For the structural parameters of an X-ray study on *racemic* tricyclic **33** prepared from *dl*-**16-*Z***, see ref 12.

(3*S*,3a*R*,6a*S*,7*S*,10a*S*)-3,3a,6,6a,7,8,9,10-Octahydro-2,3-dibenzyl-7-(2′-trimethylsilyl)ethoxy-4,5,7,7-tetramethyl-1*H*-benz[*d*]isoindole-1,10-dione (34) and 3(*N*),4-Dibenzyl-8-(2′-trimethylsilyl)ethoxy-6,7,13,13-tetramethyl-2-oxo-3-aza-9-oxatricyclo[8.4.0.0^{5,10}]tetradeca-1,6-diene (35). A solution of amide **31** (220 mg, 0.395 mmol) in deoxygenated toluene (25 mL) was heated to a gentle reflux for 15 h. The reaction mixture was cooled, concentrated, and then chromatographed on silica gel (30 g). Elution with ether–hexane (1:1) gave **34** (174 mg, 79%) as a colorless oil and **35** (32 mg, 15%).

34: $[\alpha]^{25}_D$ +30.0° (*c* 1.60); ^{1}H NMR ($CDCl_3$, 470 MHz) δ 7.4–6.95 (m, 10 H), 5.13 (d, 1 H, J = 15.3 Hz), 3.99 (d, 1 H, J = 15.3 Hz), 3.77 (dd, 1 H, J = 1, 5.1 Hz), 3.73 (m, 1 H), 3.33 (m, 1 H), 3.11 (dd, 1 H, J = 4.9, 10.1 Hz), 2.98 (dd, 1 H, J = 4.9, 13.2 Hz), 2.95 (d, 1 H, J = 5.1 Hz), 2.72 (ddd, 1 H, J = 5.2, 13.8, 14.5 Hz), 2.49 (dd, 1 H, J = 10.3, 13.2 Hz), 2.42 (ddd, J = 4.0, 4.4, 14.5 Hz), 2.37 (br s, 1 H, J = 1 Hz),

1.58 (ddd, 1 H, J = 4.4, 5.2, 15.5 Hz), 1.57 (s, 3 H), 1.23 (s, 3 H), 0.95 (m, 1 H), 0.87 (s, 3 H), 0.86 (s, 3 H), 0.85 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 212.58 (s), 174.02 (s), 139.01 (s), 137.75 (s), 133.72 (s), 130.81 (d), 130.04 (d), 129.82 (d), 129.01 (d), 128.78 (d), 128.07 (d), 125.66 (s), 78.97 (d), 68.89 (t), 64.89 (d), 62.61 (s), 46.71 (d), 46.20 (d), 46.20 (t), 43.97 (s), 40.60 (t), 37.01 (t), 34.65 (t), 33.67 (q), 25.84 (q), 19.82 (t), 17.98 (q), 14.94 (q); IR ($CHCl_3$) 1709, 1679 cm^{-1}; mass spectrum m/e 456 (32%, $M^+ - (CH_3)_3SiCH_2CH_2$), 438 (55%, $M^+ - (CH_3)_3SiCH_2CH_2 - H_2O$), 91 (100%); exact mass: calcd for $C_{30}H_{34}NO_3$ ($M^+ - (CH_3)_3SiCH_2CH_2$) 456.254, found 456.253.

35: ^{1}H NMR ($CDCl_3$ 470 MHz, in part) δ 7.4-7.0 (m, 10 H), 6.49 (s, 1 H), 5.41 (d, 1 H, J = 14.9 Hz), 4.57 (s, 1 H), 3.94 (m, 1 H), 3.47 (m, 1 H), 3.21 (dd, 1 H, J = 6.6, 7.7 Hz), 3.20 (d, 1 H, J = 14.9 Hz), 2.87 (dd, 1 H, J = 6.6, 13.3 Hz), 2.75 (dd, 1 H, J = 7.7, 13.3 Hz), 2.31 (m, 1 H), 1.97 (br s, 1 H); ^{13}C NMR ($CDCl_3$) 169.35 (s), 145.58 (d), 138.94 (s), 138.70 (s), 134.11 (s), 131.11 (d), 130.14 (d), 129.85 (d), 129.41 (d), 128.54, 128.31, 127.14, 127.53, 97.95 (d), 72.29 (s), 66.85 (t), 59.68 (d), 49.59 (t), 47.38 (d), 44.36 (t), 35.33 (t), 34.19 (t), 33.35 (s), 29.91 (q), 29.76 (q), 19.67 (t), 18.18 (q), 16.04 (q); IR ($CHCl_3$) 1635 cm^{-1}; mass spectrum m/e 557 (3%, M^+), 438 (100%, $M^+ - (CH_3)_3SiCH_2CH_2 - H_2O$).

Acknowledgment. We thank the National Science Foundation (CHE 79-03953) and the National Institute of Health (AI-13073) for their generous support of this work. The carbon-13 NMR data reported in this investigation were obtained on the departmental CFT-20 and Varian XL 200 instruments provided by NSF Grants 7842 and CHE 800-4246. We thank Dr. Preston Conrad and Professor J. Grutzner for providing those spectra. We also thank the Purdue University Biological Magnetic Resonance Laboratory (NIH RR01077) for access to the 470-MHz ^{1}H NMR spectrometer and John Saddler and Phil Hamann for providing those spectra.

Registry No. 8, 13505-32-3; **9**, 82495-70-3; **10**, 82495-71-4; **11**, 74974-70-2; **12**, 74974-71-3; **13-*Z***, 74974-72-4; **14-*Z***, 74974-74-6; **14-*E***, 74974-79-1; EL-**14-*E***, 82536-02-5; **15-*Z***, 74974-75-7; EL-**15-*Z***, 82535-49-7; **15-*E***, 74974-80-4; **16-*Z***, 74974-77-9; **16-*E***, 74974-78-0; **17**, 26487-92-3; EL-**18-*E***, 82495-72-5; **18-Z**, 82569-77-5; EL-**17**, 82495-73-6; EL-**20**, 82495-74-7; **21**, 76513-69-4; **229**, 4009-98-7; **226**, 82495-75-8; **23-*EZ***, 82495-76-9; **23-*ZZ***, 82495-77-0; **24-*EZ***, 82495-78-1; **24-*ZZ***, 82495-79-2; **25-*EZ***, 82495-80-5; **25-*ZZ***, 82495-81-6; **26-*EZ***, 82495-82-7; **26-*ZZ***, 82495-83-8; EL-**27-*ZE***, 82535-50-0; EL-**27-*EE***, 82535-51-1; EL-**28-*ZE***, 82535-52-2; DL-**28-*EE***, 82535-53-3; **29**, 82495-84-9; **30**, 74974-81-5; **31**, 82495-85-0; **32**, 82495-86-1; **33**, 74974-82-6; **34**, 82522-07-4; **35**, 82511-63-5; L-(-)-phenylalanine, 63-91-2.

Supplementary Material Available: Tables of ^{13}C NMR of amino dienes (2 pages). Ordering information is given on any current masthead page.

Conjugate Addition of β-Keto Ester Dianions to Vinyl Sulfones: A New Procedure for Seven-Ring Annulation. Synthesis of a Chiral Cytochalasin C Intermediate via an Intramolecular Diels-Alder Reaction of a Chiral *Z* Diene[1,2]

Stephen G. Pyne,[3] D. C. Spellmeyer, S. Chen, and P. L. Fuchs*

Contribution from the Department of Chemistry, Purdue University, West Lafayette, Indiana 49707. *Received November 24, 1981*

Abstract: Conjugate addition reactions of dimethylhydrazone anions and β-keto ester dianions to a chiral sterically hindered vinyl sulfone are reported. Further functionalization of the resulting α-sulfonyl-stabilized anion by alkylation with allyl bromide followed by reductive desulfonylation, ozonolysis, and intramolecular aldol reaction provides an enolized α-carboalkoxy enone, the net result being a new annulation sequence for the synthesis of seven-membered rings. Determination of the relative stereochemistry of conformationally mobile cis- and trans-fused bicyclo[5.4.0] systems by combined Karplus/molecular mechanics calculations is described. Cyclization of a pair (**40**, **3**) of chiral *Z* dienes via an intramolecular Diels-Alder reaction stereospecifically affords chiral polycyclic adducts (**41**, **4**) that are potential precursors for cytochalasin C.

Pursuant to our goal of the total synthesis of *l*(-)-cytochalasin C (**5**), we wished to prepare the trans-fused bicyclo[5.4.0] system **3** and effect its cyclization to lactam **4**. Confidence in the viability of the *Z* diene bearing a chiral substituent at the pentadienylic center to serve as a cyclization substrate was bolstered by our earlier model studies.[1] Cyclization of diene **3** to lactam **4**[4] would *simultaneously create five new asymmetric relationships* induced by the specified C-3 center (the four-starred "standard" centers subject to Diels-Alder control as well as the ultimate relationship that results from the diene selecting a single diastereotopic face of the dienophile).

The plan for synthesis of the cyclization substrate **3** was based upon the union of the previously prepared chiral dienyl amine **1**[1] and oxocycloheptencarboxylic acid **2**. Synthesis of **2** was envisaged to arise from an annulation approach with chiral vinyl sulfone *d*-**8**, which in turn was to be prepared from the previously available racemic sulfide alcohol *dl*-**6**[5] (Scheme I).

Synthesis of Chiral Vinyl Sulfone *d*-8. Treatment of racemic sulfide alcohol *dl*-**6**[5] with 2 equiv of *m*-chloroperoxybenzoic acid in methylene chloride smoothly affords β-hydroxy sulfone *dl*-**7**. Subsequent reaction of *dl*-**7** with phosphorus oxychloride in pyridine provides *racemic* vinyl sulfone *dl*-**8**.

Sulfide alcohol *dl*-**6**[5] also provides a ready entry to the chiral vinyl sulfones *d*-**8** and *l*-**8**. Reaction of *dl*-**6** with excess neat α-phenethyl isocyanate[6] at 140 °C for 18 h affords a near-quantitave yield of the diastereomeric sulfide urethanes **9**/**10**. Although it was possible to purify urethane **9** by direct crystallization, it was more convenient to simply oxidize the crude **9**/**10** mixture with *m*-chloroperoxybenzoic acid to afford a mixture of sulfone urethanes **11**/**12**. Separation of the individual diastereomers **11** and **12** proved to be exceptionally convenient and could

(1) Cytochalasin Support Studies. 5. For paper 4, see: Pyne, S. G.; Hensel, M. J.; Fuchs, P. L. *J. Am. Chem. Soc.*, preceding paper in this issue.
(2) Syntheses via Vinyl Sulfones. 9. For paper 8 in this series, see ref 5.
(3) Postdoctoral Research Associate.
(4) Lactam **4** is a potential substrate for enolate-promoted fragmentation to establish the macrocyclic moiety of cytochalasin C. See: Clark, D. A.; Fuchs, P. L. *J. Am. Chem. Soc.* **1979**, *101*, 3567.
(5) Musser, A. K.; Fuchs, P. L. *J. Org. Chem.* **1982**, *47*, 3121.
(6) Gracheva, R. A.; Terent'ev, A. P.; Bezruchka, V. T. *Zh. Org. Khim., Engl. Transl.* **1969**, *5*, 1044.

0002-7863/82/1504-5728$01.25/0