°C. After 20 min, a solution of the alcohol (48 mg, 0.085 mmol) in CH_2Cl_2 (1.8 mL) was added dropwise at −78 °C, and the reaction mixture was stirred at the same temperature for 20 min. After addition of triethylamine (0.6 mL, 4.3 mmol) at −78 °C, the reaction mixture was stirred at −78 °C for 20 min and warmed to 23 °C. The reaction was quenched with water at 0 °C, extracted with CH_2Cl_2, washed with brine, dried (Na_2SO_4), and concentrated. The residue was dissolved in ether, passed through a short silica gel column, and concentrated to give the crude dialdehyde **24**. To a stirred solution of the crude dialdehyde **24** in THF (0.2 mL) and water (0.2 mL) was added acetic acid (0.6 mL) at 0 °C. The reaction mixture was warmed to 60 °C and stirred at the same temperature for 12 h. After being cooled to 0 °C, the reaction was quenched with saturated aqueous $NaHCO_3$, extracted with ethyl acetate, washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by flash chromatography (ethyl acetate) to give **25** (17 mg, 60% in two steps, mixture of diastereomers at hemiacetal position): ^1H NMR ($CDCl_3$) δ 5.70 (dd, J = 6.0, 5.0 Hz, $^3/_4$ H), 5.65 (dd, J = 5.5, 1.8 Hz, $^1/_4$ H), 4.98 (s, $^1/_4$ H), 4.75 (s, $^3/_4$ H), 4.36 (d, J = 7.6 Hz, $^3/_4$ H), 4.31 (d, J = 7.6 Hz, $^1/_4$ H), 4.00–4.10 (m, 1 H), 2.78 (dq, J = 7.6, 7.3 Hz, 1 H), 1.04 (d, J = 7.3 Hz, 3 H), 0.88 (s, 9 H), 0.12 (s, 6 H); IR ($CHCl_3$) 3600, 3400 cm^{-1}; MS m/z 330 (M^+), 329 ($M^+ - H$), 313 ($M^+ - OH$), 295, 273 ($M^+ - C_4H_9$), 225, 73 (base peak); HR-MS (M^+) calcd for $C_{16}H_{30}O_5Si$ 330.1862, found 330.1840; $[\alpha]^{20}_D$ +22.8° (c 0.68, $CHCl_3$).

(1*R*,2*R*,6*S*,8*S*,9*S*,10*S*)-2-[(*tert*-Butyldimethylsilyl)oxy]-10-methyl-5,7-dioxatricyclo[6.2.1.0^{2,6}]undec-3-en-9-ol (26). To a stirred solution of **25** (17 mg, 0.052 mmol) in CH_2Cl_2 (0.8 mL) was added thiophenol (6 μL, 0.058 mmol) and boron trifluoride diethyl etherate (13 μL, 0.11 mmol) at −78 °C. The reaction mixture was stirred at −78 °C for 1 h and warmed to 0 °C. After being stirred at 0 °C for 30 min, the reaction was quenched with saturated aqueous $NaHCO_3$, extracted with CH_2Cl_2, washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by flash chromatography (hexane–ether, 2:3) to give the corresponding thioether (18 mg, 83%) as a colorless oil. To a stirred solution of the thioether (18 mg, 0.043 mmol) and $NaHCO_3$ (8 mg, 0.095 mmol) in CH_2Cl_2 (0.4 mL) was added a solution of *m*-chloroperbenzoic acid (9 mg, 0.05 mmol) in CH_2Cl_2 (0.35 mL) at 0 °C. After being stirred at the same temperature for 10 min, the reaction was quenched with saturated aqueous Na_2SO_3, extracted with ethyl acetate, washed with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), passed through a short silica gel column, and concentrated to give the corresponding sulfoxide. The crude sulfoxide was dissolved in toluene (1 mL), and the solution was refluxed for 40 min. After being cooled to 23 °C, the reaction mixture was concentrated. The residue was purified by flash chromatography (hexane–ether, 1:1) to give **26** (5 mg, 38% in two steps) as a colorless solid: ^1H NMR (C_6D_6) δ 6.10 (d, J = 2.9 Hz, 1 H), 5.51 (s, 1 H), 4.61 (d, J = 2.9 Hz, 1 H), 3.90–4.00 (m, 2 H), 2.88 (dq, J = 7.0, 7.0 Hz, 1 H), 1.83 (ddd, J = 12.8, 6.5, 3.0 Hz, 1 H), 1.67 (d, J = 6.5 Hz, 1 H), 1.59 (d, J = 12.8 Hz, 1 H), 0.90–1.10 (m, 12 H), 0.10 (s, 3 H), 0.09 (s, 3 H); IR ($CHCl_3$) 3600, 3450, 1610 cm^{-1}; MS m/z 255 ($M^+ - C_4H_9$), 198, 157, 129, 97, 75 (base peak), 73; HR-MS ($M^+ - C_4H_9$) calcd for $C_{12}H_{19}O_4Si$ 255.1053, found 255.1062; $[\alpha]^{20}_D$ −145.8° (c 0.19, $CHCl_3$).

(1*R*,2*R*,6*S*,8*S*,10*S*)-2-[(*tert*-Butyldimethylsilyl)oxy]-10-methyl-5,7-dioxatricyclo[6.2.1.0^{2,6}]undec-3-en-9-one (2). To a stirred solution of **26** (4.5 mg, 0.013 mmol) in DMF (0.3 mL) was added pyridinium dichromate (50.8 mg, 0.14 mmol) at 0 °C. After being stirred at 40 °C for 90 min, the reaction mixture was diluted with ether, passed through a short silica gel column, and concentrated. The crude product was purified by flash chromatography (hexane–ether, 3:1) to give **2** (4.4 mg, 98%) as a colorless oil: ^1H NMR (C_6D_6) δ 6.02 (d, J = 2.9 Hz, 1 H), 5.52 (s, 1 H), 4.56 (d, J = 2.9 Hz, 1 H), 3.77 (d, J = 2.8 Hz, 1 H), 3.00 (dq, J = 2.5, 7.7 Hz, 1 H), 1.71 (d, J = 6.0 Hz, 1 H), 1.56 (dd, J = 14.1, 2.5 Hz, 1 H), 1.18 (ddd, J = 14.1, 6.0, 2.8 Hz, 1 H), 1.02 (d, J = 7.7 Hz, 3 H), 0.87 (s, 9 H), 0.01 (s, 3 H), 0.00 (s, 3 H); IR ($CHCl_3$) 1755, 1615 cm^{-1}; MS m/z 253 ($M^+ - C_4H_9$), 75 (base peak); HR-MS ($M^+ - C_4H_9$) calcd for $C_{12}H_{17}O_4Si$ 253.0896, found 253.0899; $[\alpha]^{20}_D$ − 110.2° (c 0.44, $CHCl_3$).

Acknowledgment. We are grateful to Yukari Sato for her technical assistance.

Supplementary Material Available: ^1H NMR spectra of **2**, **5–12**, **15**, **23**, **25**, and **26** (13 pages). Ordering information is given on any current masthead page.

New Methodology for the Synthesis of Protected, Primary Pentadienylamines

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The utility of forming *N*-*tert*-butoxycarbonyl- (Boc) and *N*-phthalimido-protected primary 2(*E*),4(*E*)-pentadienylamines from aldehydes and ketones is described. When diethyl [(*E*)-4-[*N*-(*tert*-butoxycarbonyl)-amino]-2-buten-1-yl]phosphonate (**33*E***) is treated with sodium bis(trimethylsilyl)amide at −78 °C followed by aldehydes or ketones, the desired Boc-protected 2(*E*),4(*E*)-pentadienylamines are obtained in good yields. When diethyl [(*E*)-4-(*N*-phthalimido)-2-buten-1-yl]phosphonate (**17*E***) is subjected to similar conditions, the corresponding 2(*E*),4(*E*)-pentadienylphthalimides are obtained in good yields. In all cases, the 2*E*,4*E* isomer is the predominant isomer formed under these conditions and can be obtained in isomerically pure form from a simple recrystallization.

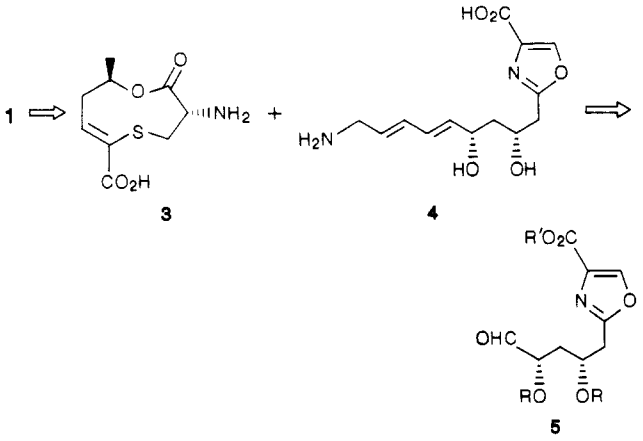
The 1-amino-2(*E*),4(*E*)-pentadiene system is found in a wide variety of natural products. The antibiotics aurodox[1] and efrotomycin,[2] for example, are two of the most prominent members of the elfamycins. Mocimycin (kirromycin), heneicomycin, and dihydromocimycin constitute the remaining members of this family of narrow-spectrum antibiotics.[3] Neooxazolomycin[4] and oxazolomycin[5] are

(1) Aurodox has also been called X-108 and goldinamycin. For an excellent review of the isolation, characterization, synthesis, and biological activity of aurodox, see: Maeher, H.; Leach, M.; Williams, T. H.; Blount, J. F. *Can. J. Chem.* **1980**, *58*, 501–526 and references cited therein.

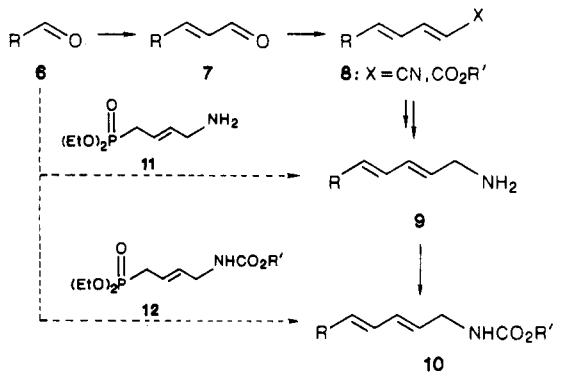
(2) For references related to the isolation, characterization, and biological activity of efrotomycin, see: Dewey, R. S.; Arison, B. H.; Hannah, J.; Shih, D. H.; Albers-Schoenberg, G. *J. Antibiot.* **1985**, *38*, 1691–1698.

0022-3263/89/1954-3359$01.50/0

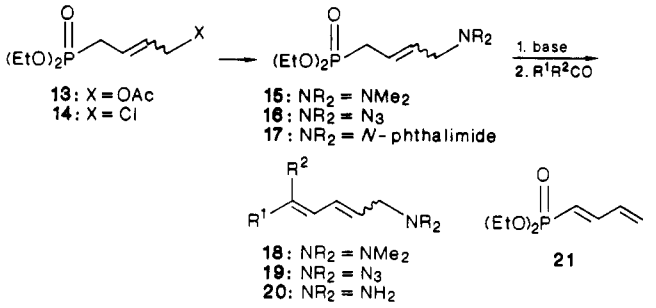
Scheme I



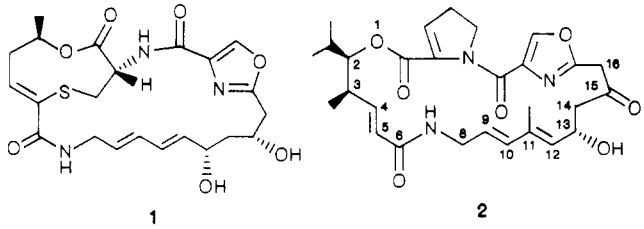
Scheme II



Scheme III



from another family of antibiotics that have an interesting biological profile. Recently, two cytotoxic polyenylisoxazoles have been isolated from *Streptomyces* species. Curromycin A was obtained from a genetically modified *Streptomyces hygroscopicus*[6] and curromycin B from the nonmodified bacterium.[7] Our interest in synthesizing the primary pentadienylamine moiety is due to its presence in the several members of the streptogramin family of antibiotics such as griseoviridin 1 and virginiamycin M_1 2.



Because of their useful biological properties as well as their complex framework, the streptogramin antibiotics have been the target of numerous synthetic efforts. The most common approach to griseoviridin, for example, involves disconnection of the two amide linkages to provide the oxazole–diene system 4 and the highly functionalized lactone 3 (Scheme I). We have already synthesized the lactone portion of griseoviridin, 3,[8,9] and we have developed a route to the 4-carboalkoxy-2-substituted-oxazoles.[10,11]

Our approach to the oxazole–diene 4 involves the synthesis and homologation of the functionalized aldehyde 5. Based on this strategy, we needed to develop a method for the conversion of aldehydes to pentadienylamines. Meyers[12] and Nicolaou[13] have recently addressed this problem. Though both of their approaches represent useful methods for the preparation of allylic amines, they are less desirable for the synthesis of pentadienylamines because of the series of multiple transformations that are required to obtain the desired compounds.

In general, the synthesis of the pentadienylamines from carbonyl compounds has often involved the initial conversion of the carbonyl group to an enal such as 7 (Scheme II). Such intermediates can be converted to either a dienyl nitrile or dienyl ester such as 8 and then to the desired

(3) For recent work with elfamycin antibiotics, the reader is directed to the following articles: (a) Kempf, A. J.; Wilson, K. E.; Hensens, O. D.; Monaghan, R. L.; Zimmerman, S. B.; Dulaney, E. L. *J. Antibiot.* **1986**, *39*, 1361–1367. (b) Nicolaou, K. C. *Chem. Ber.* **1985**, *21*, 813–817. (c) Parmeggiani, A.; Swart, G. W. M. *Annu. Rev. Microbiol.* **1985**, *39*, 557–577; *Chem. Abstr.* **1985**, *103*, 205158*z*. (d) Chinali, G. *Boll-Soc. Ital. Biol. Sper.* **1981**, *57*, 1706–1712; *Chem. Abstr.* **1982**, *96*, 85296*f*. (e) Parmeggiani, A.; Sander, G. *Top. Antibiot. Chem.* **1980**, *5*, 159–221; *Chem. Abstr.* **1981**, *94*, 41924*p*. (f) Zimmerman, S. B.; Chalmers, J. H., Jr.; Dewey, R. S.; Stapley, E. O.; Hernandez, S. *J. Antibiot.* **1979**, *32*, 665–666. (g) Wolf, H.; Chinali, G.; Parmeggiani, A. *Eur. J. Biochem.* **1977**, *75*, 67–75; *Chem. Abstr.* **1977**, *87*, 78932*w*.

(4) (a) Takahashi, K.; Kawabata, M.; Uemura, D.; Iwadare, S.; Mitomo, R.; Nakano, F.; Matsuzaki, A. *Tetrahedron Lett.* **1985**, *26*, 1077–1078. For recent synthetic approaches to neooxazolomycin, see: (b) Kende, A. S.; DeVita, R. J. *Tetrahedron Lett.* **1988**, *29*, 2521–2524.

(5) For information regarding the isolation, characterization, and biological activity of oxazolomycin, see: (a) Mori, T.; Takahashi, K.; Kashiwabara, M.; Uemura, D.; Katayama, C.; Iwadare, S.; Shizuri, Y.; Mitomo, R.; Nakano, F.; Matsuzaki, A. *Tetrahedron Lett.* **1985**, *26*, 1073–1076. (b) Takahashi, K.; Mori, T.; Kashiwabara, M.; Uemura, D.; Katayama, C.; Iwadare, S.; Shizuri, Y.; Mitomo, R.; Nakano, F.; Matsuzaki, A. *Tennen Yuki Kagobutsu Toronkai Koen Yoshishu* **1983**, *26*, 189–196; *Chem. Abstr.* **1984**, *100*, 167719*m*.

(6) Ogura, M.; Nakayama, H.; Furihata, K.; Shimazu, A.; Seto, H.; Otake, N. *J. Antibiot.* **1985**, *38*, 669.

(7) (a) Ogura, M.; Nakayama, H.; Furihata, K.; Shimazu, A.; Seto, H.; Otake, N. *Agric. Biol. Chem.* **1985**, *49*, 1909–1910; *Chem. Abstr.* **1985**, *103*, 101560*h*. (b) Okabe, T.; Isono, F.; Kashiwagi, M.; Takahashi, M.; Nishimura, T.; Suzuki, H.; Tanaka, N. *J. Antibiot.* **1985**, *38*, 964–965.

(8) Butera, J.; Rini, J.; Helquist, P. *J. Org. Chem.* **1985**, *50*, 3676–3678.

(9) For other approaches to the ene–thiol lactone portion of griseoviridin, see: (a) Liu, L.; Tanke, R. S.; Miller, M. J. *J. Org. Chem.* **1986**, *51*, 5332–5337. (b) Meyers, A. I.; Amos, R. A. *J. Am. Chem. Soc.* **1980**, *102*, 870–872.

(10) Connell, R.; Scavo, F.; Helquist, P.; Åkermark, B. *Tetrahedron Lett.* **1986**, *27*, 5559–5562.

(11) For papers dealing with the synthesis of other key portions of the streptogramin antibiotics, see the following papers and the references cited therein: (a) Schlessinger, R. H.; Iwanowicz, E. J.; Springer, J. P. *J. Org. Chem.* **1986**, *51*, 3073–3075. (b) Meyers, A. I.; Lawson, J. P.; Walker, D. G.; Linderman, R. J. *J. Org. Chem.* **1986**, *51*, 5111–5123. (c) Fujita, E. *Heterocycles* **1984**, *21*, 41–60. (d) Nagao, Y.; Yamada, S.; Hagiwara, Y.; Fujita, E. *Tennen Yuki Kagobutsu Toronkai Koen Yoshishu* **1983**, *26*, 476–483; *Chem. Abstr.* **1984**, *100*, 209476*n*. (e) Wood, R. D.; Ganem, B. *Tetrahedron Lett.* **1983**, *24*, 4391–4392. (f) Nagao, Y.; Yamada, S.; Fujita, E. *Tetrahedron Lett.* **1983**, *24*, 2291–2294. (g) Nagao, Y.; Yamada, S.; Fujita, E. *Tetrahedron Lett.* **1983**, *24*, 2287–2290. (h) Meyers, A. I.; Walker, D. G. *J. Org. Chem.* **1982**, *47*, 2999–3000. (i) Wood, R. D.; Ganem, B. *Tetrahedron Lett.* **1982**, *23*, 707–710. (j) Meyers, A. I.; Lawson, J.; Amos, R. A.; Walker, D. G.; Spohn, R. F. *Pure Appl. Chem.* **1982**, *54*, 2537–2544.

(12) (a) Meyers, A. I.; Lawson, L. P.; Carver, D. R. *J. Org. Chem.* **1981**, *46*, 3119–3123. (b) Meyers, A. I.; Lawson, J. P. *Tetrahedron Lett.* **1981**, *22*, 3163–3166.

(13) Dolle, R. E.; Nicolaou, K. C. *J. Am. Chem. Soc.* **1985**, *107*, 1691–1694.

pentadienylamines. The use of allylic phosphono esters[14] and phosphono nitriles[15] allows for the direct conversion of **6** to **8**, but the subsequent transformation of pentadienyl esters and nitriles to pentadienylamines such as **9** still requires a number of steps.

Meyers has improved upon this approach by converting the enal **7** to a pentadienylphthalimide via modified Schweizer reaction.[16] Since that time, a number of other useful amino phosphonates and amino phosphinates have been developed to convert carbonyl compounds into allylic amino compounds.[17] In this paper, we describe our efforts directed toward the synthesis and application of a variety of phosphonates such as **11** and **12** as more general reagents for the very direct preparation of primary pentadienylamines from aldehydes and ketones.[18]

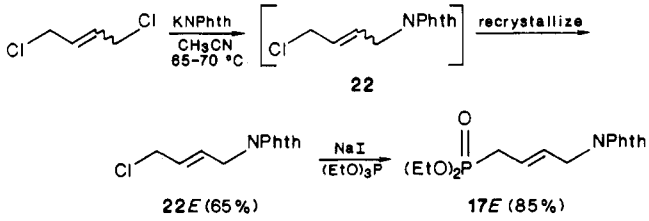
Results and Discussion

Our approach to phosphonates such as **11** began with the readily available acetoxyphosphonate **13**. We had shown in earlier work that this type of phosphonate could be converted into the corresponding dimethylamino phosphonate **15** through a palladium-catalyzed reaction with dimethylamine. Amino phosphonates such as **15** were useful for the conversion of aldehydes and ketones into tertiary pentadienyldimethylamines **18** (Scheme III).[19] Based on the success of this approach, we began our work in this area by exploring the palladium-catalyzed conversion of **13** to phosphonates such as **16** and **17**.

When acetoxyphosphonate **13** was treated with sodium azide by using Murahashi's conditions,[20] the desired azide **16** was obtained along with a substantial amount of the dienylphosphonate **21**. This type of elimination was not surprising due to the tendency of these activated π-allyls to undergo elimination when treated with base.[21,22]

Since the azide **16** could not be separated from the diene **21**,[23] nor could the formation of **21** be suppressed, we began to study the palladium-catalyzed reaction of the chlorophosphonate **14**.[24] The chlorophosphonate was prepared in 74% yield via an Arbuzov reaction of the corresponding 1,4-dichloro-2-butene.[25] We found that when **14** was treated with sodium azide in THF under palladium-catalyzed conditions,[26] the desired azidophosphonate **16** was obtained in 81% yield.[27]

Scheme IV



The conversion of **16** to the desired phosphonate amine **11** was explored; however, all attempts to effect this reduction led to the formation of a complex mixture of products.[28] Although the consumption of **16** could be observed by GC and TLC, we were unable to isolate anything resembling the desired phosphonate amine. The condensation of **16** with aldehydes and ketones was briefly attempted. However, we obtained none of the desired pentadienyl azide **19** by this approach. We also explored the palladium-catalyzed substitution of **13** with phthalimide,[29] but found that when either **13** or **14** were subjected to palladium-catalyzed reactions with potassium phthalimide, only the dienylphosphonate **21** was obtained.

Because these phosphonate compounds were so sensitive to elimination, a different approach to the phosphono phthalimide **17** was explored. A solution of predominantly *trans*-1,4-dichloro-2-butene was treated with potassium phthalimide in acetonitrile to provide the chloro phthalimide **22** (Scheme IV). Although this compound was obtained as a mixture of *E* and *Z* isomers, it was possible to obtain the pure *E* isomer **22*E*** by recrystallization from acetone. Treatment of **22*E*** with triethyl phosphite and sodium iodide provided the phosphonate phthalimide **17*E*** as a low-melting solid.[30]

We attempted to deprotect the phthalimido phosphonate **17*E*** in order to prepare the amino phosphonate **11**. Unfortunately, all such attempts led to elimination of the phthalimide group and formation of the diene **21**. Apparently, the phosphonate was not stable to the basic conditions and elevated temperatures that were required for deprotection. Although we were unable to synthesize

(14) For recent examples, see: (a) Murali, D.; Rao, G. S. K. *Synthesis* **1987**, 254–256. (b) Forbes, J. E.; Pattenden, G. *Tetrahedron Lett.* **1987**, *28*, 2771–2774. (c) Moorhoff, C. M.; Schneider, D. F. *Tetrahedron Lett.* **1987**, *28*, 559–562. (d) Williams, D. R.; White, F. H. *J. Org. Chem.* **1987**, *52*, 5067–5079.

(15) For recent examples, see: (a) Mead, D.; Asato, A. E.; Denny, M.; Liu, R. S. H.; Hanzawa, Y.; Taguchi, T.; Yamada, A.; Kobayashi, N.; Hosada, A.; Kobayashi, Y. *Tetrahedron Lett.* **1987**, *28*, 259–262. (b) Hopf, H.; Krause, N. *Tetrahedron Lett.* **1986**, *27*, 6177–6180.

(16) Schweizer, E. E.; Smucker, L. D.; Votral, R. J. *J. Org. Chem.* **1966**, *31*, 467.

(17) For related work involving the synthesis of allylic amines via the condensation of phosphonates and phosphoranes with aldehydes and ketones, see: (a) Valerio, R. M.; Alewood, P. F.; Johns, R. B. *Synthesis* **1988**, 786–789. (b) Bicknell, A. J.; Burton, G.; Elder, J. S. *Tetrahedron Lett.* **1988**, *27*, 3361–3364.

(18) For a related synthesis of *N*-acyl-1,1-disubstituted-pentadienylamines via allylic phosphinoylamines, see: Cavalla, D.; Cruse, W. B.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1883–1889.

(19) Nikaido, M.; Aslanian, R.; Scavo, F.; Helquist, P.; Åkermark, B.; Bäckvall, J.-E. *J. Org. Chem.* **1984**, *49*, 4738–4740.

(20) Murahashi, S.-I.; Tanigawa, Y.; Imada, Y.; Taniguchi, Y. *Tetrahedron Lett.* **1986**, *27*, 227–230. In this work, we obtained the best results when the palladium(0) catalyst was generated in situ. This was done by treating palladium dibenzylideneacetone [$Pd(dba)_2$] with the appropriate amount of phosphine ligand prior to the addition of the electrophile.

(21) For other examples of the elimination of π-allyl palladium complexes, see: (a) Coste-Manière, I. C.; Zahra, J. P.; Waegell, B. *Tetrahedron Lett.* **1988**, *29*, 1017–1020. (b) Trost, B. M.; Tometzki, G. B. *J. Org. Chem.* **1988**, *53*, 915–917. (c) Trost, B. M.; Mignani, S. *J. Org. Chem.* **1986**, *51*, 3435–3439. (d) Åkermark, B.; Nyström, J. E.; Rein, T.; Bäckvall, J. E.; Helquist, P.; Aslanian, R. *Tetrahedron Lett.* **1984**, *25*, 5719–5722 and references cited in these articles.

(22) This facile elimination has been shown to be a useful method for the synthesis of phosphoryl and sulfonyl dienes: Åkermark, B.; Nyström, J.-E.; Rein, T.; Bäckvall, J.-E.; Helquist, P.; Aslanian, R.; *Tetrahedron Lett.* **1984**, *25*, 5719–5722.

(23) We did not attempt to distill the azide for fear of its decomposition and/or detonation.

(24) Keinan has demonstrated that although certain activated π-allyl complexes derived from allylic acetates may eliminate palladium hydride, the π-allyls derived from the corresponding chlorides are much more resistant to elimination. Keinan, E.; Roth, Z., private communication.

(25) Pariza, R. J.; Fuchs, P. L. *J. Org. Chem.* **1985**, *50*, 4252–4266.

(26) The allylic chloride was added to a THF suspension of $Pd(dba)_2$ (5 mol %), diphenylphosphinoethane (15 mol %), and sodium azide.

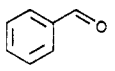
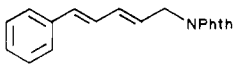
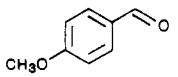
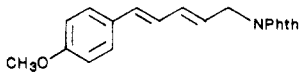
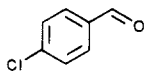
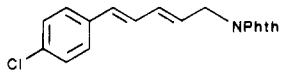
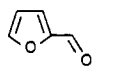
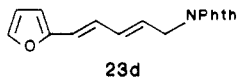
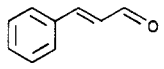
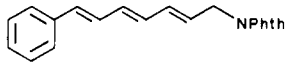
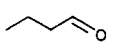
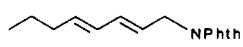
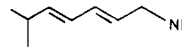
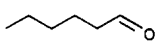
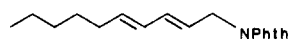
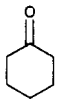
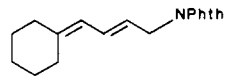
(27) It was interesting to note that while the palladium-catalyzed conversion of **14** to **16** was complete in 3 h at 23 °C, the uncatalyzed reaction required several days to approach completion (ca. 60% after 3 days at 23 °C).

(28) We attempted to reduce the azide to the corresponding amine using methods described earlier in the literature: (a) Vaultier, M.; Knouzi, N.; Carrié, R. *Tetrahedron Lett.* **1983**, *24*, 763–764. (b) Koziara, A.; Osowska-Pacewicka, K.; Zawadzki, S.; Zwierzak, A. *Synthesis* **1985**, 202–204. For a recent review regarding the synthesis and transformation of organic azides, see: (c) Scriven, E. F. V.; Turnbull, K. *Chem. Rev.* **1988**, *88*, 297–362.

(29) Inoue, Y.; Taguchi, M.; Toyofuku, M.; Hashimoto, H. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 3021–3022.

(30) In some cases, a small amount of the *Z* isomer of **17** was observed. In such cases, the phosphonate was subjected to a low-temperature recrystallization (−20 °C) from ethyl ether. This allowed for the isolation of the pure *E* isomer, **17*E***.

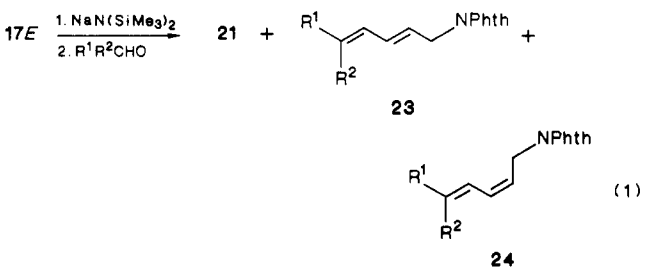
Table I. Condensation Reactions of 17*E* with Aldehydes and Ketones

R^1R^2CO	major isomer	yield,[a,b] %	isomer ratio[c]
	 **23a**	72	87:13
	 **23b**	41	82:18
	 **23c**	54	84:16
	 **23d**	81	82:18
	 **23e**	47	85:15
	 **23f**	36	85:15
	 **23g**	37	88:12
	 **23h**	36	81:19
	 **23i**	41	94:6

[a] Refers to the isolated yield of both isomers. [b] Percent yield was based on the conversion of the carbonyl compound to the corresponding pentadienylphthalimide. [c] Refers to 2*E*,4*E*:2*Z*,4*E* ratio of isomers as determined by ^{1}H NMR integration CH_2NPhth protons.

11 by this route, we had developed a route to the pure *E* isomer of the phosphonate phthalimide, **17*E***. We therefore decided to subject this phosphonate to condensation reactions with aldehydes in order to obtain pentadienylphthalimides. This approach would allow for the direct conversion of aldehydes and ketones into 1-phthalimido-2(*E*),4(*E*)-pentadienes.

When **17*E*** was subjected to the usual condensation conditions (THF, LDA, −78 °C), the desired pentadienylphthalimides **23** and **24** were obtained along with a substantial amount of the dienylphosphonate **21** (eq 1).[31]



(1)

The conditions of the reaction were modified in order to improve upon the yield of pentadienylphthalimide formation. Unlike the Schweizer reaction employed by Meyers, the elimination of phthalimide was not reversible at low temperatures. Thus, when the dienylphosphonate **21** was formed at low temperatures, the phthalimide anion did not seem to add to the diene system to regenerate the phosphonate anion of **17**.[32] Although the elimination of phthalimide from **17*E*** could not be completely suppressed, it was possible to obtain synthetically useful amounts of the desired 2(*E*),4(*E*)-pentadienylphthalimides **23** from a variety of aldehydes and ketones. The results from the condensation of **17*E*** with various carbonyl compounds are listed (Table I).

As the table indicates, the yields for forming pentadienylphthalimides varied from aldehyde to aldehyde. The highest isolated yields were obtained from aromatic and conjugated aromatic aldehydes. Lower yields of pentadienylphthalimides were obtained when aliphatic aldehydes were employed. Although the major products were the 2*E*,4*E* isomers (**23**), and the bond formed in the reaction was exclusively trans, we were surprised to find that small amounts of the 2*Z*,4*E* isomer **24** were also formed from **17*E***. These results indicated that the pure (*E*)-phosphonate **17*E*** must have isomerized at some point in the condensation reaction.[33]

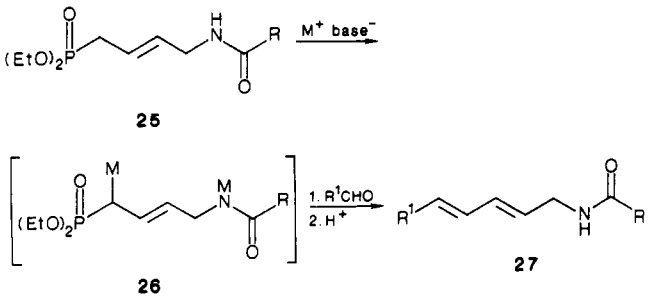
This undesired isomerization was enhanced when lithium bases were used and was minimized when sodium

(31) The elimination of imides, amides (and amines) is facilitated under mild conditions, when the nitrogen substituent is either 1,2 or 1,4 relative to a phosphonate. For examples of this type of elimination with amino phosphonates, see: Darling, S. D.; Subramanian, N. *Tetrahedron Lett.* **1975**, 3279–3282.

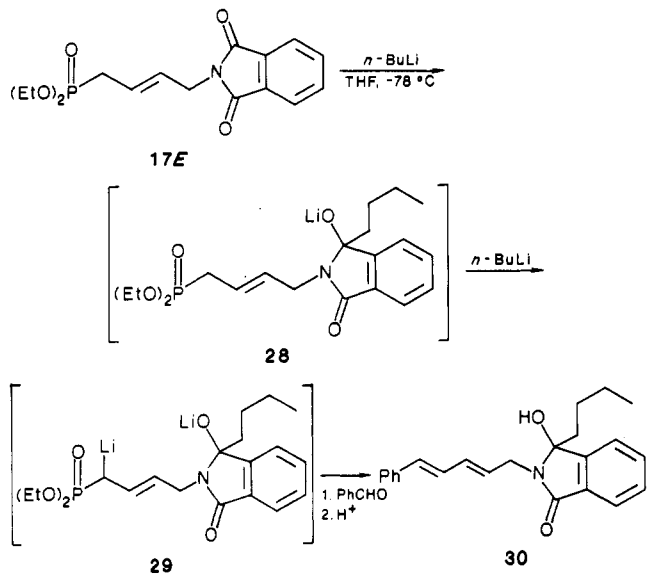
(32) Phosphoryl dienes of this type were known to be susceptible to nucleophilic attack at the 4-position, leading to the formation of 4-substituted phosphonates. Pudovik, A. N.; Konovalova, I. V.; Ishmaeva, E. A. *Zh. Obshch. Khim.* **1962**, *32*, 237.

(33) Corey has shown that pure *E* allylic phosphonium salts and phosphonates can isomerize under the conditions of the condensation reactions: Corey, E. J.; Erickson, B. W. *J. Org. Chem.* **1974**, *39*, 821–825. We were unable to isolate any of the unreacted *Z* isomer of **17** after condensation reactions. Apparently whatever (*Z*)-phosphonate that formed either was condensed with the aldehyde or eliminated the phthalimide to provide the phosphonate diene **21**.

Scheme V



Scheme VI



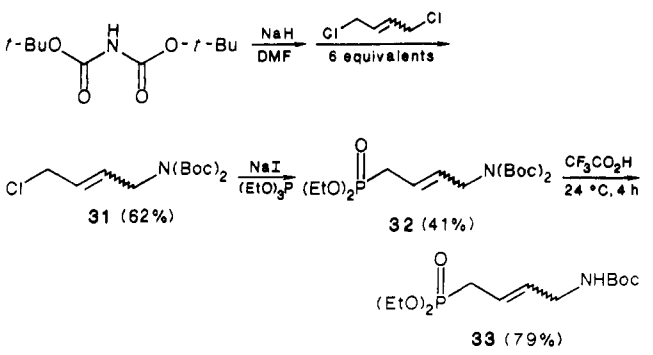
bases were used. When potassium bases were utilized (KOtBu, KDA), elimination of phthalimide was the major pathway. The highest yields of **23** were obtained when the phosphonate **17*E*** was treated with sodium bis(trimethylsilyl)amide at −78 °C, followed by addition of the carbonyl compound at −78 °C. When the anion was generated at higher temperatures, only formation of diene **21** was observed. Once the aldehyde was added, slow warming of this solution to 25 °C (over ca. 4–6 h) led to the highest selectivity and greatest yield of the desired 2(*E*),4(*E*)-pentadienylphthalimides.

After studying the condensation of **17*E*** in some detail, we sought to develop an alternative phosphonate–amine derivative that would be less susceptible to elimination and lead to isomerically pure products. One way to suppress the elimination of the amine moiety would be through the formation of a dianion such as **26** (Scheme V). Generating an anion on the amido group would reduce its tendency to eliminate when the anion of the phosphonate is formed.[34]

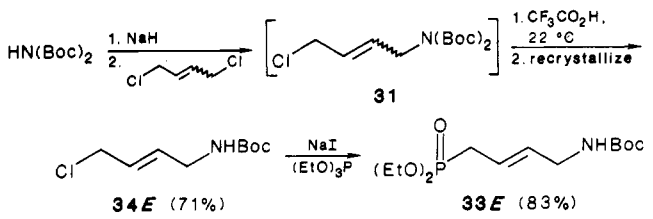
We were also interested in seeing whether generation of the dianion would suppress the isomerization of the phosphonate during the condensation reaction. Our optimism regarding this aspect of the condensation arose as a result of an experiment with the phthalimido phosphonate **17*E***. It was noted that when **17*E*** was treated with *n*-butyllithium followed by benzaldehyde, none of the pentadienylphthalimide **23** was formed (Scheme VI). Instead, **30** was obtained in isomerically pure form as the 2*E*,4*E* isomer.

(34) Warren has used a similar approach in his synthesis of allylic amines and carbonyl compounds. Cavalla, D.; Cruse, W. B.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1883–1889.

Scheme VII



Scheme VIII



This product appears to result from carbonyl addition of *n*-butyllithium to form **28**. When the dianion **29** was formed by reaction of the second equivalent of *n*-butyllithium, the amide residue becomes less inclined to eliminate. Benzaldehyde was therefore able to condense with the phosphonate portion of **29** to provide the unexpected pentadienylphthalide **30**.

Based on this observation, we set out to synthesize phosphonate amines in which the nitrogen was partially protected. We chose to prepare Boc-protected amines due to the chemical stability of the carbamate group and ease of deprotection.[35] We had demonstrated earlier that partially protected primary amines are easily obtained from the corresponding diprotected amines through a selective hydrolysis.[36] Hence, our approach to phosphonates such as **12** began with the synthesis of the diprotected amino phosphonate **32**. The commercially available iminodicarbamate[37] was deprotonated and treated with an excess of predominantly *trans*-1,4-dichloro-2-butene. The resulting chloride **31** was converted to the corresponding phosphonate **32** via a sodium iodide catalyzed Arbuzov reaction (Scheme VII).

As expected, **32** was not useful in condensation reactions and rapidly eliminated the iminodicarbamate when treated with base. The phosphonate was therefore partially deprotected to provide the monoprotected phosphonate amine **33**. Unlike **17*E***, this compound was a heavy oil, and it was not possible to obtain the pure *E* isomer of this phosphonate. When this isomeric mixture of phosphonates was subjected to condensation conditions, mixtures of 2*E*,4*E* and 2*Z*,4*E* isomers were obtained.

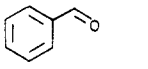
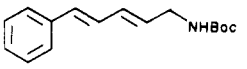
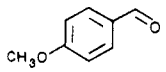
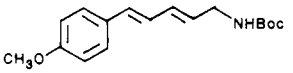
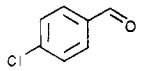
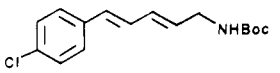
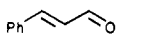
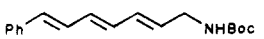
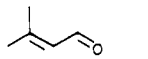
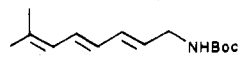
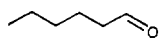
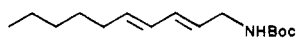
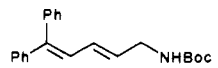
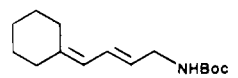
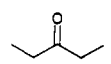
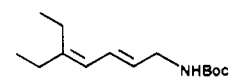
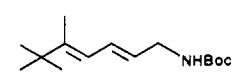
To improve on the isomer distribution, the sequence used to synthesize the Boc-protected amino phosphonate was altered (Scheme VIII). Rather than isolate the bisprotected amine, **31**, the oily mixture was treated directly with trifluoroacetic acid at 22 °C to provide a solid residue. This residue was recrystallized from hexane and then acetone to provide the pure *E* isomer **34*E*** as white needles in 71% overall yield from the iminodicarbamate. As ex-

(35) Greene, T. W. In *Protective Groups in Organic Chemistry*; Wiley: New York, 1981.

(36) Connell, R. D.; Rein, T.; Åkermark, B.; Helquist, P. *J. Org. Chem.* **1988**, *53*, 3845–3849.

(37) Aldrich Chemicals, Inc.

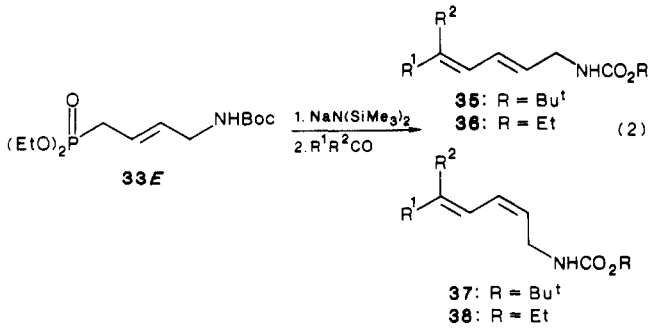
Table II. Condensation Reactions of Aldehydes and Ketones with 33*E*

R^1R^2CO	product[a]	yield,[b,c] %	% 2*E*,4*E*
	 **35a**	64 (81)[d]	>99
	 **35b**	58 (78)[d]	>98
	 **35c**	51 (71)[d]	96
	 **35d**	53	>96
	 **35e**	64	>85[e]
	 **35f**	65	88
	 **35g**	67 (93)[d]	100
	 **35h**	74	94
	 **35i**	47	94
	 **35j**	51	100

[a] Major isomer shown. [b] Refers to the isolated yield of all isomers. [c] Yield based on the conversion of the carbonyl compound to the corresponding pentadienylamine. [d] Yield in parentheses is based on recovered carbonyl compound. [e] Two other isomers were observed.

pected, isomerically pure **34*E*** was then converted to the desired Boc-protected amino phosphonate **33*E*** in good yield and in isomerically pure form.

When **33*E*** was treated with 2.2 equiv of base followed by either aldehydes or ketones, the desired Boc-protected 2(*E*),4(*E*)-pentadienylamines **35** were obtained along with a small amount of the Boc-protected 2(*Z*),4(*E*)-pentadienylamines **37** (eq 2). We varied the amount and the type



(2)

of base used in these reactions and found that sodium bis(trimethylsilyl)amide was still best suited for these types of reactions. Unlike the reactions with the phosphonate phthalimide **17*E***, it was necessary to quench these reactions at −10 to 0 °C. If these reaction mixtures are allowed to warm to 24 °C and remain at this temperature for long periods of time, the products tended to decompose. The major pathway of this decomposition appears to be formation of the corresponding ethyl carbamates **36** and **38**.[38] However, this and other byproducts were not formed when the reaction was quenched at 0 °C and quickly worked up. After determining the best conditions for the condensation reaction, a variety of aldehydes and ketones were subjected to condensation reactions with **33*E***. The results of this work are summarized in Table II.

From the results in Table II, it is clear that the Boc-protected amino phosphonate **33*E*** will react with a variety of carbonyl compounds to provide the desired 2(*E*),4(*E*)-pentadienylamines, protected as their *tert*-butyl carbamates. Although the reaction worked well with cinnamaldehyde and 3-methyl-2-butenal, the reaction with crotonaldehyde led to a mixture of products.[39] Another anomaly was observed when acetophenone or *p*-bromoacetophenone was subjected to the usual conditions of the reaction. In both cases, only a trace of the desired carbamate was obtained along with unreacted starting material. With the exception of these two cases, the reaction worked well with a wide variety of aldehydes and ketones.

(38) This product was presumably obtained from transesterification of the Boc-protected pentadienylamine by ethoxide formed from the phosphonate after the condensation.

(39) This may be the result of a competing Michael addition, which is well precedented for condensation reactions of conjugated aldehydes. For examples, see: (a) Binns, M. R. Haynes, R. K.; Katsifis, A. G.; Schober, P. A.; Vonwiller, S. C. *J. Am. Chem. Soc.* **1988**, *110*, 5411–5423 and references cited therein. (b) Moorhoff, C. M.; Schneider, D. F. *Tetrahedron Lett.* **1987**, *28*, 559–562.

In all the cases, the formation of the 2*E*,4*Z* isomer was not observed. Hence the double bond that was formed in the reaction was exclusively of the *E* configuration as it was in the case of the phthalimido phosphonate **17*E***. The formation of a small amount of the 2*Z*,4*E* isomer was observed in a few of the examples. However, this isomer was by far the minor component, being formed in less than 10% in all of the examples. In many of the cases where a mixture of 2*Z*,4*E* isomer was formed, it was possible to obtain the pure 2*E*,4*E* isomer by recrystallization of the mixture from acetone or ethyl ether. Even though not all the products were crystalline, it was often possible to separate the mixtures by radial chromatography and obtain fractions that were further enriched in the 2*E*,4*E* isomer.

In closing, we have developed two new and useful protected, primary allylic amino phosphonates. The phosphonate phthalimide **17*E*** allows for the direct conversion of aldehydes and ketones to pentadienylphthalimides. Although only modest to good yields of the desired products are obtained, the starting phosphonate is easy to synthesize, and the major isomer that is formed in the reaction is easily recrystallized from the isomeric mixture. With the Boc-protected amino phosphonate **33*E***, we have developed a simple and convenient route to convert aldehydes and ketones into Boc-protected, primary pentadienylamines. Again, the phosphonate used to effect this transformation is easy to prepare and obtain in isomerically pure form. Based on the ease of preparation, the isomeric selectivity of the transformation, the stability of these protected amines, and the ease by which they are deprotected,[40] we are confident that this method will be used extensively in the synthesis of complex, natural products.

Experimental Section

Reagents. Anhydrous tetrahydrofuran (THF) was freshly distilled under nitrogen from deep purple or dark blue solutions of sodium benzophenone radical anion or dianion. Dimethylformamide was dried over activated 4-Å molecular sieves, and acetonitrile was distilled from calcium hydride prior to use. All aldehydes and ketones were either distilled or recrystallized prior to their use in condensation reactions. The 1,4-dichloro-2-butene was distilled prior to use. The first fraction containing the cis isomer was set aside while the later fractions containing predominantly the trans isomer were used to prepare the phosphonates.

Equipment. All reactions were carried out in oven-dried glassware (120 °C), which was cooled under nitrogen. Crude products were purified by flash column chromatography using 250 mesh silica gel or were purified by radial chromatography with a Chromatotron. Thin-layer chromatography (TLC) was performed on aluminum-backed silica gel plates, and visualization was accomplished with a UV light or an iodine vapor chamber.

Instrumentation. HPLC purification was performed with a Waters HPLC, equipped with an M-45 pump and an R407 differential refractometer. Mass spectral data were obtained by using electron impact ionization (EI) at 70 eV. Melting points were obtained in open-ended capillaries and are corrected.

(*E*)-1-Chloro-4-(*N*-phthalimido)-2-butene (22*E*). A suspension of predominantly *trans*-1,4-dichloro-2-butene[41] (103.6 g, 0.828 mol) and potassium phthalimide (30.7 g, 0.166 mol) was stirred and warmed to 75–80 °C in an oil bath. After 12 h at this temperature, the flask was cooled to 23 °C, and the slurry was poured into a separatory funnel containing ether (300 mL) and CH_2Cl_2 (80 mL). The organic portion was then washed with water (2 × 30 mL) and saturated aqueous NaCl (1 × 40 mL). The yellow solution was dried ($MgSO_4$) and concentrated via rotary evaporation (pressure 10–11 Torr, bath temperature less than 30 °C). The excess 1,4-dichloro-2-butene was distilled off under reduced pressure (10–11 Torr, bath temperature at 45–50 °C) to provide a yellow solid residue. This residue was heated in refluxing hexane, cooled to 0 °C, and filtered to remove any of the excess 1,4-dichloro-2-butene. The white residue was then recrystallized from acetone to provide 25.37 g (65%) of **22*E*** as a white solid. Only one isomer, presumably the *E* isomer, was observed by ^1H and ^{13}C NMR. **22*E***: mp 101–102 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.86 (dd, J = 5.45 Hz, J = 3.10 Hz, 2 H, phth-*H*), 7.73 (dd, J = 5.41 Hz, J = 3.09 Hz, 2 H, phth-*H*), 5.87 (m, 2 H, C*H*=C*H*), 4.32 (dd, $J_{3,4}$ = 3.71 Hz, $J_{2,4}$ = 0.51 Hz, 2 H, CH_2N), 4.03 (d, $J_{1,2}$ = 4.5 Hz, 2 H, CH_2Cl); ^{13}C NMR (50 MHz, $CDCl_3$) δ 166.70 (NC=O), 133.23, 131.35, 128.88, 127.17, 122.61, 43.51 (CH_2Cl), 38.41 (CH_2N); IR ($CDCl_3$) 1700 cm^{-1}; mass spectrum EI (rel intensity) 237 (20, M + 2), 235 (38, M^+), 200 (100, M^+ - Cl).

Anal. Calcd for $C_{12}H_{10}ClNO_2$: C, 61.16; H, 4.28. Found: C, 61.12; H, 4.24.

Diethyl [(*E*)-4-(*N*-Phthalimido)-2-buten-1-yl]phosphonate (17*E*). A suspension of sodium iodide (0.69 g, 4.67 mmol), **22*E*** (11.00 g, 46.71 mmol), and triethyl phosphite (8.54 g, 51.38 mmol) was warmed to 100–110 °C in an oil bath. After 30 h at this temperature, the flask was cooled to 23 °C, and the yellow oil was poured into a separatory funnel containing ether (250 mL). The organic layer was washed with water (1 × 20 mL), saturated aqueous $Na_2S_2O_3$ (2 × 20 mL), and saturated aqueous NaCl (1 × 40 mL). The solution was then dried ($MgSO_4$) and concentrated in vacuo to provide a colorless oil. This oil was diluted with 3 mL of CH_2Cl_2 and purified by radial chromatography (40% ethyl acetate in hexane) to provide 13.42 g (85%) of a colorless oil. When this oil was obtained as a mixture of the 2*E* and 2*Z* isomers, the pure *E* isomer was obtained by diluting the mixture with ether (3 mL), placing the solution in a freezer at −20 °C for 24 h, and decanting off the mother liquor containing mainly the *Z* isomer. The remaining ether was stripped off in vacuo (20–23 °C, 0.01 Torr) to provide 55–75% of **17*E*** as a white solid. Only one isomer could be detected by ^1H and ^{13}C NMR spectroscopy: mp 35–36 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, J = 5.65 Hz, J = 3.10 Hz, 2 H, phth-*H*), 7.73 (dd, J = 5.30 Hz, J = 3.10 Hz, 2 H, phth-*H*), 5.73 (m, 2 H, C*H*=C*H*), 4.28 (m, 2 H, CH_2N), 4.10 (m, 4 H, CH_3CH_2OP), 2.63 (m, 2 H, CH_2P), 1.29 (t, 6 H, CH_3CH_2OP); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.75 (NC=O), 133.94, 132.03, 128.54 (d, $J_{P,C}$ = 14.82 Hz, PCH_2CH=CH), 123.58 (d, $J_{P,C}$ = 11.46 Hz, PCH_2CH=*C*H), 123.22, 61.98 (d, $J_{P,C}$ = 6.47 Hz, CH_2OP), 39.13 (CH_2N), 30.22 (d, $J_{P,C}$ = 139.57 Hz, PCH_2), 16.36 (d, $J_{P,C}$ = 5.73 Hz, $POCH_2CH_3$); IR (neat) 1700 cm^{-1}; mass spectrum EI (rel intensity) 337 (100, M^+), 199 (85, M^+ - $(EtO)_2P(O)$).

Anal. Calcd for $C_{16}H_{20}NO_5P$: C, 56.97; H, 5.98. Found: C, 56.89; H, 5.77.

(2*E*,4*E*)-5-Phenyl-1-(*N*-phthalimido)-2,4-pentadiene (23a). A solution of **17*E*** (0.465 g, 1.35 mmol) in THF (13.5 mL) was stirred at 23 °C for 5 min and cooled to −78 °C. After 15 min at −78 °C, a 1.0 M solution of sodium bis(trimethylsilyl)amide in THF[37] (1.35 mL, 1.35 mmol) was added dropwise over 2 min. During the addition, the clear, colorless solution became cloudy as a white suspension was observed. When the addition was complete, the solution took on a lime green color. After 15 min at −78 °C, freshly distilled benzaldehyde (0.130 g, 1.25 mL, 1.23 mmol) was added, and the dark green solution faded to a light green color. The solution was stirred at −78 °C for 30 min and then allowed to warm to 23 °C over a 7-h period.

General Workup. The yellow solution was poured into ether (150 mL). The ether portion was washed with water (2 × 10 mL) and saturated aqueous NaCl (1 × 10 mL), dried ($MgSO_4$), and concentrated to provide a white solid residue. This residue was dissolved in a minimal amount of CH_2Cl_2 and purified by radial chromatography (10% ethyl acetate in hexane) to provide 0.240 g (72%) of a white solid. Preliminary ^1H NMR analysis of this crude product indicated an 87:13 ratio of the 2*E*,4*E* and 2*Z*,4*E* isomers (the presence of the 2*Z*,4*E* isomer was indicated by a dd at 4.2 ppm). This crude product was recrystallized from acetone to provide the pure 2*E*,4*E* isomer **23a** as white needles: mp 160–162 °C (lit.[12] mp 160–161.5 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, J = 5.58 Hz, J = 3.09 Hz, 2 H, phth-*H*), 7.75 (dd, J = 5.43 Hz, J = 3.22 Hz, 2 H, phth-*H*), 7.28 (m, 5 H, Ar-*H*), 6.71

(40) For complete experimental details on the deprotection of Boc-protected, pentadienylamines, see: Zwierzak, A.; Pilichowska, S. *Synthesis* **1982**, 922–924.

(41) Purchased from Aldrich Chemical Co. as an 85% mixture of the *E* isomer. The remainder was predominantly the *Z* isomer.

(dd, $J_{4,5}$ = 15.62 Hz, $J_{3,4}$ = 10.41 Hz, 1 H, ArCH=C*H*CH=CH), 6.54 (d, $J_{4,5}$ = 15.68 Hz, 1 H, ArC*H*=CHCH=CH), 6.51 (ddt, $J_{2,3}$ = 15.07 Hz, $J_{3,4}$ = 10.42 Hz, $J_{1,3}$ = 1.21 Hz, 1 H, CH=CHC*H*=CHCH$_2$N), 5.96 (dtd, $J_{2,3}$ = 15.13 Hz, $J_{1,2}$ = 6.48 Hz, $J_{2,4}$ = 0.8 Hz, 1 H, CHCH=C*H*CH$_2$N), 4.28 (dd, $J_{1,2}$ = 6.50 Hz, $J_{1,3}$ = 1.21 Hz, 2 H, CH=CHC*H*$_2$N); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.90 (N*C*=O), 136.98, 134.00, 133.95, 133.37, 132.16, 128.56, 127.65, 126.52, 126.39, 123.29, 39.35 (CHCH$_2$N); mass spectrum CI/isobutane (rel intensity) 292 (18, M + 3), 291 (22, M + 2), 290 (100, M + 1), 289 (10, M$^+$).

Anal. Calcd for $C_{19}H_{15}NO_2$: C, 78.87; H, 5.22. Found: C, 78.88; H, 5.17.

(2*E*,4*E*)-5-(4′-Methoxyphenyl)-1-(*N*-phthalimido)-2,4-pentadiene (23b). Prepared as above by treating **17*E*** (0.440 g, 1.30 mmol) in THF (14.3 mL) at −78 °C with 0.95 M solution of sodium bis(trimethylsilyl)amide in THF (1.37 mL, 1.30 mmol). The green solution was initially stirred at −76 °C for 10 min, and then 4-methoxybenzaldehyde (0.161 g, 1.18 mmol) was added. The pale green solution was then allowed to warm to 23 °C over a 7-h period. Workup as above provided a solid residue which was dissolved in CH_2Cl_2 (2.0 mL) and purified by radial chromatography (10% ethyl acetate in hexane) to provide 0.154 g (41%) of a white solid. Preliminary ^{1}H NMR analysis of this crude product indicated an 82:18 ratio of the 2*E*,4*E* and 2*Z*,4*E* isomers (the presence of the 2*Z*,4*E* isomer was indicated by a dd at 4.48 ppm as well as a singlet at 3.83 ppm). This crude product was recrystallized from acetone to provide the pure 2*E*,4*E* isomer, **23b**, as white needles: mp 160–162 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 5.51 Hz, *J* = 3.06 Hz, 2 H, phth-*H*), 7.78 (dd, *J* = 5.44 Hz, *J* = 3.11 Hz, 2 H, phth-*H*), 7.29 (d, *J* = 8.76 Hz, 2 H, Ar-*H*), 6.82 (d, *J* = 8.77 Hz, 2 H, Ar-*H*), 6.59 (dd, $J_{4,5}$ = 15.24 Hz, $J_{3,4}$ = 10.14 Hz, 1 H, ArCH=C*H*CH=CH), 6.49 (d, $J_{4,5}$ = 14.79 Hz, 1 H, ArC*H*=CHCH=CH), 6.42 (dd, $J_{2,3}$ = 14.78 Hz, $J_{3,4}$ = 9.92 Hz, 1 H, CH=CHC*H*=CHCH$_2$N), 5.80 (dt, $J_{2,3}$ = 14.75 Hz, $J_{1,2}$ = 6.62 Hz, 1 H, CHCH=C*H*CH$_2$N), 4.35 (d, $J_{1,2}$ = 6.44 Hz, 2 H, CH=CHC*H*$_2$N), 3.80 (s, 3 H, OC*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.86 (N*C*=O), 159.28 (CH$_3$O*C*), 134.28, 133.87, 132.92, 132.15, 129.77, 127.60, 125.62, 125.29, 123.21, 114.00, 55.21 (O*C*H$_3$), 39.35 (CHCH$_2$N); mass spectrum EI (rel intensity) 320 (10, M + 1), 319 (44, M$^+$), 173 (18), 172 (100), 157 (20).

Anal. Calcd for $C_{20}H_{17}NO_3$: C, 75.22; H, 5.37. Found: C, 75.22; H, 5.41.

(2*E*,4*E*)-5-(4′-Chlorophenyl)-1-(*N*-phthalimido)-2,4-pentadiene (23c). Prepared as above by treating **17*E*** (0.728 g, 1.78 mmol) in THF (23.0 mL) at −78 °C with 0.95 M solution of sodium bis(trimethylsilyl)amide in THF (2.25 mL, 2.13 mmol). The solution was stirred at −78 °C for 10 min, and then 4-chlorobenzaldehyde (0.273 g, 1.94 mmol) was added. The pale green solution was then allowed to warm to 23 °C over a 7-h period. Workup as above provided a solid residue, which was dissolved in CH_2Cl_2 (2.0 mL) and purified by radial chromatography (10% ethyl acetate in hexane) to provide 0.339 g (54%) of a white solid. Preliminary ^{1}H NMR analysis of this crude product indicated an 84:16 ratio of the 2*E*,4*E* and 2*Z*,4*E* isomers (the presence of the 2*Z*,4*E* isomer was indicated by a dd at 4.51 ppm). The solid was recrystallized twice from acetone to provide **23c** as fine white needles: mp 184–186 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 5.54 Hz, *J* = 3.07 Hz, 2 H, phth-*H*), 7.75 (dd, *J* = 5.45 Hz, *J* = 3.07 Hz, 2 H, phth-*H*), 7.28 (m, 4 H, Ar-*H*), 6.68 (dd, $J_{4,5}$ = 15.39 Hz, $J_{3,4}$ = 10.26 Hz, 1 H, ArCH=C*H*CH=CH), 6.50 (d, $J_{4,5}$ = 15.42 Hz, 1 H, ArC*H*=CHCH), 6.43 (ddt, $J_{2,3}$ = 15.03 Hz, $J_{3,4}$ = 10.27 Hz, 1 H, CH=CHC*H*=CHCH$_2$N), 5.87 (dt, $J_{2,3}$ = 15.05 Hz, $J_{1,2}$ = 6.53 Hz, 1 H, CHCH=C*H*CH$_2$N), 4.38 (dd, $J_{1,2}$ = 6.39 Hz, $J_{1,3}$ = 0.88 Hz, 2 H, CH=CHC*H*$_2$N); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.87 (N*C*=O), 135.51, 133.97, 133.69, 133.24, 132.16, 131.98, 128.75, 128.26, 127.54, 127.18, 123.31, 39.32 (CHCH$_2$N); mass spectrum CI/isobutane (rel intensity) 326 (42, M + 3), 325 (22, M + 2), 324 (100, M + 1), 308 (80).

Anal. Calcd for $C_{19}H_{14}ClNO_2$: C, 70.48; H, 4.36. Found: C, 70.19; H, 4.48.

(2*E*,4*E*)-5-(2′-Furyl)-1-(*N*-phthalimido)-2,4-pentadiene (23d). Prepared as above by treating **17*E*** (0.348 g, 1.03 mmol) in THF (11.3 mL) at −78 °C with 0.95 M solution of sodium bis(trimethylsilyl)amide in THF (1.21 mL, 1.03 mmol). The green slurry was stirred at −78 °C for 10 min, and then furfuraldehyde (0.086 g, 0.074 mL, 0.898 mmol) was added. The pale green solution was then allowed to warm to 23 °C over a 7-h period. Workup as above provided an orange solid residue, which was dissolved in CH_2Cl_2 (2.0 mL) and purified by radial chromatography (10% ethyl acetate in hexane) to provide 0.202 g (81%) of a white solid. Preliminary ^{1}H NMR analysis of this crude product indicated an 82:18 ratio of the 2*E*,4*E* and 2*Z*,4*E* isomers (the presence of the 2*Z*,4*E* isomer was indicated by a dd at 4.50 ppm). The solid was recrystallized twice from acetone to provide isomerically pure **23d** as fine white needles: mp 168–170 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 5.48 Hz, *J* = 3.08 Hz, 2 H, phth-*H*), 7.73 (dd, *J* = 5.45 Hz, *J* = 3.07 Hz, 2 H, phth-*H*), 7.34 (d, *J* = 1.44 Hz, 1 H, furan-*H*), 6.62 (dd, $J_{4,5}$ = 15.62 Hz, $J_{3,4}$ = 10.74 Hz, 1 H, CH=C*H*CH=CHCH$_2$N), 6.37 (dd, $J_{2,3}$ = 14.84 Hz, $J_{3,4}$ = 10.98 Hz, 1 H, CH=CHC*H*=CHCH$_2$N), 6.36 (b m, 1 H, furan-*H*), 6.33 (d, $J_{4,5}$ = 15.16 Hz, 1 H, C*H*=CHCH=CHCH$_2$), 6.25 (b d, *J* = 2.3 Hz, 1 H, furan-*H*), 5.85 (dt, $J_{2,3}$ = 15.05 Hz, $J_{1,2}$ = 6.51 Hz, 1 H, CH=C*H*CH$_2$N), 4.36 (d, $J_{1,2}$ = 6.48 Hz, 2 H, CH=CHC*H*$_2$N); ^{13}C NMR (50 MHz, $CDCl_3$) δ 167.64 (N*C*=O), 152.79, 142.22, 133.90, 133.57, 132.11, 126.59, 126.19, 123.24, 120.63, 111.52, 108.67, 39.24 (*C*H$_2$N); IR ($CDCl_3$) 1708 cm^{-1} (C=O); mass spectrum CI/isobutane (rel intensity) 281 (10, M + 2), 280 (42, M + 1), 279 (8, M$^+$), 190 (100).

Anal. Calcd for $C_{17}H_{13}NO_3$: C, 73.10; H, 4.69. Found: C, 72.96; H, 4.51.

(2*E*,4*E*,6*E*)-7-Phenyl-1-(*N*-phthalimido)-2,4,6-heptatriene (23e). Prepared as above by treating **17*E*** (0.406 g, 1.20 mmol) in THF (13.5 mL) at −78 °C with 0.95 M solution of sodium bis(trimethylsilyl)amide in THF (1.27 mL, 1.20 mmol). The green slurry was stirred at −70 °C for 10 min, and then cinnamaldehyde (0.144 g, 0.138 mL, 1.09 mmol) was added. The solution was allowed to warm to 23 °C over a 7-h period. Workup as above provided a solid residue, which was dissolved in CH_2Cl_2 (2.0 mL) and purified by radial chromatography (10% ethyl acetate in hexane) to provide 0.162 g (47%) of a white solid. Preliminary ^{1}H NMR analysis of this crude product indicated an 85:15 ratio of the 2*E*,4*E*,6*E* and 2*Z*,4*E*,6*E* isomers (the presence of the 2*Z*,4*E*,6*E* isomer was indicated by a dd at 4.45 ppm). The solid was recrystallized twice from acetone to provide **23e** as fine white needles: mp 164–166 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 5.58 Hz, *J* = 3.09 Hz, 2 H, phth-*H*), 7.72 (dd, *J* = 5.43 Hz, *J* = 2.37 Hz, 2 H, phth-*H*), 7.28 (m, 5 H, Ar-*H*), 6.78 (dd, $J_{6,7}$ = 15.50 Hz, $J_{5,6}$ = 9.91 Hz, 1 H, ArCH=C*H*CH=CH), 6.53 (d, $J_{6,7}$ = 15.59 Hz, 1 H, ArC*H*=CHCH), 6.34 (m, 2 H) and 6.32 (dd, *J* = 14.57 Hz, *J* = 10.10 Hz, 1 H, CHC*H*=C*H*CH=CHCH$_2$N), 5.78 (dt, $J_{2,3}$ = 15.14 Hz, $J_{1,2}$ = 6.73 Hz, 1 H, CHCH=C*H*CH$_2$N), 4.34 (d, $J_{1,2}$ = 6.64 Hz, 2 H, CH=CHC*H*$_2$N); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.82 (N*C*=O), 137.15, 133.94, 133.91, 133.89, 133.06, 132.12, 131.75, 128.65, 128.55, 127.54, 126.38, 126.33, 123.23, 39.34 (CHCH$_2$N); IR ($CDCl_3$) 3020, 2990, and 1708 cm^{-1}; mass spectrum EI (rel intensity) 316 (8, M + 1), 315 (20, M$^+$), 168 (100), 167 (62), 153 (58).

Anal. Calcd for $C_{21}H_{17}NO_2$: C, 79.97; H, 5.44. Found: C, 79.93; H, 5.44.

(2*E*,4*E*)-1-(*N*-Phthalimido)-2,4-octadiene (23f). Prepared as above by treating **17*E*** (0.4515 g, 1.66 mmol) in THF (18.3 mL) at −78 °C with 0.95 M solution of sodium bis(trimethylsilyl)amide in THF (1.74 mL, 1.66 mmol). The green slurry was stirred at −75 °C for 10 min, and then butanal (0.109 g, 0.133 mL, 1.51 mmol) was added. The pale green solution was then allowed to warm to 23 °C over a 7-h period. Workup as above provided an oil, which was purified by radial chromatography (5% ethyl acetate in hexane) to provide 0.140 g (36%) of a white solid. Preliminary ^{1}H NMR analysis of this crude product indicated an 85:15 ratio of the 2*E*,4*E* and 2*Z*,4*E* isomers (the presence of the 2*Z*,4*E* isomer was indicated by a dd at 4.40 ppm). The solid was recrystallized from acetone to provide **23f** as white needles: mp 85–87 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 5.58 Hz, *J* = 3.09 Hz, 2 H, phth-*H*), 7.75 (dd, *J* = 5.43 Hz, *J* = 3.22 Hz, 2 H, phth-*H*), 6.26 (dd, $J_{2,3}$ = 15.15 Hz, $J_{3,4}$ = 10.45 Hz, 1 H, CH$_2$CH$_2$CH=CHC*H*=CH), 5.98 (dd, $J_{4,5}$ = 15.17 Hz, $J_{3,4}$ = 10.44 Hz, 1 H, CH=C*H*CH=CH$_2$CH$_2$N), 5.64 (dt, $J_{4,5}$ = 15.12 Hz, $J_{5,6}$ = 6.96 Hz, 1 H, CH$_3$CH$_2$CH$_2$C*H*=CHCH), 5.56 (dt, $J_{2,3}$ = 15.15 Hz, $J_{1,2}$ = 6.53 Hz, 1 H, CH=C*H*CH$_2$N), 4.24 (dd, $J_{1,2}$ = 6.84 Hz, $J_{1,3}$ = 0.54 Hz, 2 H, CH=CH$_2$C*H*$_2$N), 1.97 (dt, $J_{6,7}$ = 7.23 Hz, $J_{5,6}$ = 6.75 Hz, 2 H, CH$_3$CH$_2$C*H*$_2$CH=CH), 1.32 (m, 2 H, CH$_3$C*H*$_2$CH$_2$), 0.81 (t, $J_{7,8}$ = 7.37 Hz, 3 H, C*H*$_3$CH$_2$); ^{13}C NMR (50 MHz, $CDCl_3$) δ

167.76 (NC=O), 135.94, 134.14, 133.77, 132.08, 129.00, 123.43, 123.11, 39.22 (CH_2N), 34.56 ($CH_2CH_2CH_3$), 22.17 ($CH_2CH_2CH_3$), 13.55 ($CH_2CH_2CH_3$); IR ($CDCl_3$) 1705 cm^{-1} (C=O); mass spectrum CI/isobutane (rel intensity) 257 (22, M + 2), 256 (100, M + 1), 255 (12, M^+).

Anal. Calcd for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71. Found: C, 75.35; H, 6.59.

(2*E*,4*E*)-6-Methyl-1-(*N*-phthalimido)-2,4-heptadiene (23g). Prepared as above by treating **17*E*** (0.707 g, 2.10 mmol) in THF (23.0 mL) at −78 °C with 0.95 M solution of sodium bis(trimethylsilyl)amide in THF (2.10 mL, 2.00 mmol). The green slurry was stirred at −78 °C for 10 min, and then isobutyraldehyde (0.137 g, 0.173 mL, 1.90 mmol) was added. The solution was then allowed to warm to 23 °C over a 7-h period. Workup as above provided an oil, which was purified by radial chromatography (5% ethyl acetate in hexane) to provide 0.140 g (36%) of a yellow oil. Preliminary ^1H NMR analysis of this crude product indicated an 85:15 ratio of the 2*E*,4*E* and 2*Z*,4*E* isomers (the presence of the 2*Z*,4*E* isomer was indicated by a dd at 4.24 ppm as well as a dd at 6.05 ppm with J = 11.03 Hz and J = 10.49 Hz). The oil was recrystallized from ethyl ether (at −20 °C) to provide **23g** as white needles: mp 44–46 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.86 (dd, J = 5.49 Hz, J = 3.10 Hz, 2 H, phth-*H*), 7.73 (dd, J = 5.44 Hz, J = 3.08 Hz, 2 H, phth-*H*), 6.25 (ddd, $J_{2,3}$ = 15.20 Hz, $J_{3,4}$ = 10.23 Hz, $J_{1,3}$ = 0.96 Hz, 1 H, CH=CHC*H*=CHCH$_2$N), 5.95 (ddd, $J_{4,5}$ = 15.40 Hz, $J_{3,4}$ = 10.30 Hz, $J_{4,6}$ = 0.76 Hz, 1 H, $(CH_3)_2$CHCH=C*H*CH=CH), 5.69 (dd, $J_{4,5}$ = 15.32 Hz, $J_{5,6}$ = 6.41 Hz, 1 H, $(CH_3)_2$CHC*H*=CHCH), 5.65 (dt, $J_{2,3}$ = 15.09 Hz, $J_{1,2}$ = 6.59 Hz, 1 H, CHCH=C*H*CH$_2$N), 4.15 (dd, $J_{1,2}$ = 6.51 Hz, $J_{1,3}$ = 0.88 Hz, 2 H, CH=CHC*H*$_2$N), 2.30 (m, 1 H, $(CH_3)_2$C*H*CH=CH), 0.98 (d, $J_{6,7}$ = 6.76 Hz, 6 H, (CH_3)$_2$CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.82 (*N*C=O), 143.03, 134.34, 133.80, 132.18, 126.01, 123.64, 123.15, 39.30 (CH_2N), 30.99 (CHCH(CH_3)$_2$), 22.10 (CHCH(CH_3)$_2$); mass spectrum CI/isobutane (rel intensity) 258 (10, M + 3), 257 (24, M + 2), 256 (100, M + 1), 255 (10, M^+).

Anal. Calcd for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71. Found: C, 75.43; H, 6.85.

General Procedure for the Isolation of the 2*Z*,4*E* Isomer from the Isomeric Mixture. (2*E*,4*E*)-1-(*N*-Phthalimido)-2,4-decadiene (23h). Prepared as above by treating **17*E*** (0.490 g, 1.45 mmol) in THF (16.0 mL) at −78 °C with 0.95 M solution of sodium bis(trimethylsilyl)amide in THF (1.53 mL, 1.45 mmol). The solution was stirred at −75 °C for 10 min, and then hexanal (0.132 g, 0.158 mL, 1.32 mmol) was added. The solution was allowed to warm to 23 °C over a 7-h period. Workup as above provide a yellow oil, which was purified by flash chromatography (5.0% ethyl acetate in hexane) to provide 0.134 g (36%) of a low-melting solid. Preliminary ^1H NMR analysis of this crude product indicated an 81:19 ratio of the 2*E*,4*E* and 2*Z*,4*E* isomers. The semisolid was transferred to a Craig tube and recrystallized from ethyl ether to provide **23h** as white needles: mp 71–73 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, J = 5.45 Hz, J = 3.05 Hz, 2 H, phth-*H*), 7.71 (dd, J = 5.46 *Hz*, J = 3.05 Hz, 2 H, phth-*H*), 6.25 (ddt, $J_{2,3}$ = 15.09 Hz, $J_{3,4}$ = 10.20 Hz, $J_{1,3}$ = 1.12 Hz, 1 H, CH=CHC*H*=CHCH$_2$N), 5.97 (ddt, $J_{4,5}$ = 14.93 Hz, $J_{3,4}$ = 10.19 Hz, $J_{4,6}$ = 1.09 Hz, 1 H, CH$_2$CH=C*H*CH=CHCH$_2$N), 5.69 (dt, $J_{4,5}$ = 15.21 Hz, $J_{5,6}$ = 6.84 Hz, 1 H, $CH_3(CH_2)_3CH_2CH$=CH), 5.58 (dt, $J_{2,3}$ = 15.12 Hz, $J_{1,2}$ = 6.42 Hz, 1 H, CHCH=C*H*CH$_2$N), 4.28 (dd, $J_{1,2}$ = 6.54 Hz, $J_{1,3}$ = 1.00 Hz, 2 H, CH=CHC*H*$_2$N), 2.04 (dt, $J_{6,7}$ = 6.73 Hz, $J_{5,6}$ = 6.69 Hz, 2 H, $CH_3(CH_2)_3CH_2$CH=CH), 1.40 (m, 6 H, $CH_3(CH_2)_3CH_2$), 0.83 (t, $J_{9,10}$ = 6.70 Hz, 3 H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.96 (*N*C=O), 136.41, 134.29, 133.89, 132.22, 128.91, 123.43, 123.25, 39.36 (CHCH$_2$N), 32.56, 31.35, 28.80, 22.49, 14.00; mass spectrum EI (rel intensity) 283 (80, M^+), 212 (62), 160 (88), 148 (70), 136 (100), 130 (58), 80 (78).

Anal. Calcd for $C_{18}H_{21}NO_2$: C, 76.30; H, 7.47. Found: C, 76.36; H, 7.41.

(2*Z*,4*E*)-1-(*N*-Phthalimido)-2,4-decadiene (24h). The mother liquid from the previous recrystallization was now enriched with the 2*Z*,4*E* isomer. This yellow oil was purified by HPLC (1% ethyl acetate in hexane) to provide **24h** a colorless oil. Due to the complexity of proton NMR spectrum, the following ^1H NMR data was obtained largely from high-field decoupling experiments: ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (m, 2 H, phth-*H*), 7.76 (m, 2 H, phth-*H*), 6.57 (dddt, $J_{4,5}$ = 15.00 Hz, $J_{3,4}$ = 9.61 Hz, $J_{4,6}$ = 1.40 Hz, $J_{2,4}$ = 1.13 Hz, 1 H, CH$_2$CH=C*H*CH=CHCH$_2$N), 6.13 (dd, $J_{2,3}$ = 11.28 Hz, $J_{3,4}$ = 10.19 Hz, 1 H, CH=CHC*H*=CHCH$_2$N), 5.79 (dt, $J_{4,5}$ = 14.96 Hz, $J_{5,6}$ = 6.91 Hz, 1 H, $CH_3(CH_2)_3CH_2$C*H*=CH), 5.36 (dt, $J_{2,3}$ = 10.68 Hz, $J_{1,2}$ = 7.39 Hz, 1 H, CHCH=C*H*CH$_2$N), 4.41 (dd, $J_{1,2}$ = 7.35 Hz, $J_{1,3}$ = 1.35 Hz, 1 H, CH=CHC*H*$_2$N), 2.16 (td, $J_{6,7}$ = 6.84 Hz, $J_{5,6}$ = 6.51 Hz, 2 H, $CH_3(CH_2)_3CH_2$CH=CH), 1.43 (m, 2 H, $CH_3CH_2CH_2CH_2CH_2$CH), 1.32 (m, 4 H, $CH_3CH_2CH_2CH_2$), 0.90 (t, $J_{9,10}$ = 7.06 Hz, 3 H, CH_3CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.85 (*N*C=O), 138.07, 133.72, 132.54, 132.11, 124.45, 123.06, 121.18, 34.89 (CHCH$_2$N), 32.71, 31.29, 28.69, 22.37, 13.89.

(2*E*)-4-Cyclohexylidene-1-(*N*-phthalimido)-2-butene (23i). Prepared as above by treating **17*E*** (0.451 g, 1.35 mmol) in THF (14.8 mL) at −78 °C with 0.95 M solution of sodium bis(trimethylsilyl)amide in THF (1.42 mL, 1.35 mmol). The green solution was stirred at −75 °C for 10 min, and then freshly distilled cyclohexanone (0.120 g, 0.127 mL, 1.22 mmol) was added. The pale green solution was then allowed to warm to 23 °C over a 7-h period. Workup as above provided an oil, which was purified by radial chromatography (5% ethyl acetate in hexane) to provide 0.140 g (41%) of a white solid. Preliminary ^1H NMR analysis of this crude product indicated a 94:6 ratio of the 2*E* and 2*Z* isomers (the presence of the 2*Z* isomer was indicated by a dd at 4.44 ppm). The solid was recrystallized from acetone to provide **23i** as white needles: mp 129–130.5 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.84 (dd, J = 5.31 Hz, J = 3.08 Hz, 2 H, phth-*H*), 7.71 (dd, J = 5.46 Hz, J = 3.00 Hz, 2 H, phth-*H*), 6.59 (dd, $J_{2,3}$ = 15.01 Hz, $J_{3,4}$ = 10.98 Hz, 1 H, C=CHC*H*=CHCH$_2$N), 5.73 (d, $J_{3,4}$ = 10.95 Hz, 1 H, C=C*H*CH=CHCH$_2$N), 5.62 (dt, $J_{2,3}$ = 15.00 Hz, $J_{1,2}$ = 6.78 Hz, 1 H, CHCH=C*H*CH$_2$N), 4.31 (d, $J_{1,2}$ = 6.70 Hz, 2 H, C=CHCH=CHC*H*$_2$N), 2.26 (b s, 2 H, C*H*$_2$C=CH), 2.10 (b s, 2 H, C*H*$_2$C=CH), 1.57 (b s, 6 H, $CH_2CH_2CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.87 (*N*C=O), 144.91, 133.79, 132.20, 130.05, 123.41, 123.14, 120.75, 39.67 (CH_2N), 37.20, 29.23, 28.37, 27.69, 26.65; IR ($CDCl_3$) 1710 cm^{-1} (C=O); mass spectrum CI/isobutane (rel intensity) 283 (20, M + 2), 282 (100, M + 1), 281 (10, M^+).

Anal. Calcd for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.81. Found: C, 76.70; H, 6.79.

Condensation of 17*E* with Benzaldehyde Using *n*-Butyllithium. Formation of 30. A solution of **17*E*** (0.324 g, 0.961 mmol) in THF (4.0 mL) was stirred at 23 °C for 10 min and cooled to −78 °C. A 1.42 M solution of *n*-butyllithium in hexane (0.744 mL, 1.06 mmol) was added dropwise over 2 min, and the clear, colorless solution took on an orange-red color. After the mixture was stirred for 1 min at −78 °C, freshly distilled benzaldehyde (0.114 g, 1.08 mmol) was added, and the solution was stirred at −78 °C for 2 h. The mixture was allowed to warm to 23 °C over a 5-h period and was poured into a separatory funnel containing ethyl acetate (70 mL). The organic portion was washed with water (2 × 10 mL) and saturated aqueous NaCl (1 × 10 mL) and was dried ($MgSO_4$). The solution was concentrated to a yellow oil and purified by flash chromatography (20% ethyl acetate in hexane) to provide 0.067 g (21%) of **30** as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.35 (m, 9 H, Ar-*H*), 6.72 (dd, $J_{4,5}$ = 15.02 Hz, $J_{3,4}$ = 10.14 Hz, 1 H, PhCH=C*H*CH), 6.58 (d, $J_{4,5}$ = 15.02 Hz, 1 H, PhC*H*=CH), 6.41 (ddt, $J_{2,3}$ = 14.87 Hz, $J_{3,4}$ = 10.06 Hz, $J_{1,3}$ = 1.16 Hz, 1 H, NCH$_2$CH=C*H*CH), 5.87 (dt, $J_{2,3}$ = 14.72 Hz, $J_{1,2}$ = 6.12 Hz, 1 H, NCH$_2$C*H*=CH), 4.10 (ddd, J_{gem} = 15.39 Hz, $J_{1,2}$ = 6.09 Hz, $J_{1,3}$ = 0.85 Hz, 1 H, NC*H*(H)CH=CH), 3.91 (ddd, J_{gem} = 15.45 Hz, $J_{1,2}$ = 6.09 Hz, $J_{1,3}$ = 1.05 Hz, 1 H, NCH(*H*)-CH=CH), 3.30 (b s, 1 H, NCO*H*), 2.10 (m, 2 H, C(OH)-CH_2CH$_2$CH$_2$CH$_3$), 1.20 (m, 4 H, CH$_2$CH_2CH_2CH$_3$), 0.78 (t, J = 7.01 Hz, 3 H, CH$_2$CH_3); ^{13}C NMR of the racemic mixture (100 MHz, $CDCl_3$) δ 167.26 (NC=O), 146.82, 137.13, 133.22, 132.63, 132.32, 131.12, 129.45, 129.05, 128.97, 128.92, 128.57, 128.28, 128.00, 127.54, 126.65, 126.35, 123.22, 121.66, 91.55 NCOH), 40.11, 35.83, 25.42 ($CH_2CH_2CH_3$), 22.26 (CH_2CH_3), 13.76 (CH_3).

(*E*)-1-Chloro-4-[*N*-(*tert*-butoxycarbonyl)amino]-2-butene (34*E*). Into a 1-L round-bottom flask was added sodium hydride (6.62 g, 0.276 mol) and the di-*tert*-butyl iminodicarboxylate (50.00 g, 0.23 mol). The flask was fitted with a nitrogen inlet and a vent needle and placed in a 0 °C cold bath, and DMF (500 mL) was slowly added. (**Caution**: gas evolution becomes brisk!!!) When the gas evolution subsided, the gray solution began to froth, and the flask had to be swirled manually. At this point, the slurry was added to a cold (0 °C) solution of 1,4-dichloro-2-butene (212 g, 1.70 mol) in DMF (300 mL). After the solution was stirred at

0 °C for 10 min, the flask was then removed from the ice bath and warmed to 60–65 °C. After 3 h, the orange solution was cooled to 23 °C and poured into a separatory funnel containing ether (800 mL). The organic portion was then washed with cold (0 °C) water (2 × 50 mL), 1 N aqueous $NaHSO_4$ (3 × 40 mL), 1 N aqueous $NaHCO_3$ (3 × 40 mL), and saturated aqueous NaCl (1 × 30 mL). The solution was dried ($MgSO_4$) and concentrated via rotary evaporation (pressure at 10–11 Torr, bath temperature less than 30 °C). The residual oil was transferred to a 500-mL conical flask, and the excess 1,4-dichloro-2-butene was distilled off under reduced pressure (0.1 Torr, bath temperature at 30–40 °C) to provide a yellow residue.

The residue was diluted with methylene chloride (900 mL), and the flask was placed in a water bath, which was maintained at 20–22 °C. The solution was stirred vigorously, as trifluoroacetic acid (39.33 g, 0.345 mol) in CH_2Cl_2 (50 mL) was added to this yellow oil (**Caution**: gas evolution occurs upon addition). When gas evolution was no longer observed (ca. 3.5 h), the solution was poured into a separatory funnel and washed with cold (0 °C) 1 N aqueous $NaHCO_3$ (5 × 40 mL) and saturated aqueous NaCl (2 × 30 mL). The solution was dried ($MgSO_4$) and concentrated by rotary evaporation to provide a solid residue. The solid was recrystallized two times from hexane to provide 33.57 g (71%) of **34*E*** as white needles in isomerically pure form: mp 72–74 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 5.78 (m, 2 H, C*H*=C*H*), 4.06 (d, $J_{1,2}$ = 5.2 Hz, 2 H, CHCH_2Cl), 3.76 (m, 3 H, CHCH_2N*H*), 1.45 (s, 9 H, OC(CH_3)$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.66 (*C*OO-C(CH_3)$_3$), 131.61 and 127.19 (*C*H=*C*H), 79.48 (O*C*(CH_3)$_3$), 44.23 (CH_2Cl), 41.56 (CH*C*H_2NH), 28.29 (OC(*C*H_3)$_3$); IR ($CDCl_3$) 2960, 2910, 1750, 1700 cm^{-1}.

Anal. Calcd for $C_9H_{16}ClNO_2$: C, 52.56; H, 7.84. Found: C, 52.36; H, 7.67.

Diethyl [(*E*)-4-[*N*-(*tert*-Butoxycarbonyl)amino]-2-buten-1-yl]phosphonate (33*E*). A suspension of sodium iodide (4.10 g, 27.53 mmol), **34*E*** (28.30 g, 0.138 mol), and triethyl phosphite (50.35 g, 0.302 mol) was warmed to 90–100 °C in an oil bath. After 20 h at this temperature, the flask was cooled to 23 °C, and the yellow oil was poured into a separatory funnel containing ether (400 mL). The ether layer was washed with saturated aqueous $Na_2S_2O_3$ (4 × 30 mL) and saturated aqueous NaCl (3 × 30 mL) and dried ($MgSO_4$). The solution was concentrated in vacuo to provide a yellow oil, which was purified by Kugelrohr distillation (110–115 °C oven temperature, 0.01–0.05 Torr) to provide 35.02 g (83%) of **33*E*** as a viscous, colorless oil in isomerically pure form: ^1H NMR (300 MHz, $CDCl_3$) δ 5.58 (m, 2 H, C*H*=C*H*), 4.80 (b s, 1 H, CH_2N*H*), 4.12 (m, 4 H, POC$H_2$$CH_3$), 3.62 (b m, 2 H, C$H_2$NH), 2.58 (dd, $J_{P,H}$ = 21.74 Hz, $J_{1,2}$ = 6.21 Hz, 2 H, PCH_2CH), 1.44 (s, 9 H, COOC(CH_3)$_3$), 1.33 (t, J = 7.06 Hz, 6 H, CH_2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.58 (*C*OO-C(CH_3)$_3$), 132.70 (d, $J_{P,C}$ = 14.41 Hz, PCH_2*C*H=CH), 120.54 (d, $J_{P,C}$ = 11.03 Hz, PCH_2CH=*C*H), 79.12 (O*C*(CH_3)$_3$), 61.78 (d, $J_{P,C}$ = 6.70 Hz, PO*C*$H_2$$CH_3$), 42.01 (*C*$H_2$NH), 29.92 (d, $J_{P,C}$ = 139.95 Hz, P*C*H_2CH), 28.13 (OC(*C*H_3)$_3$), 16.12 (d, $J_{P,C}$ = 5.96 Hz, POCH_2*C*H_3); mass spectrum CI/isobutane (rel intensity) 308 (100, M + 1), 252 (62, M + 1 − C_4H_8), 208 (42, M + 1 − CO_2 − C_4H_8).

Anal. Calcd for $C_{13}H_{26}NO_5P$: C, 50.81; H, 8.53. Found: C, 50.60; H, 8.59.

(2*E*,4*E*)-1-[*N*-(*tert*-Butoxycarbonyl)amino]-5-phenyl-2,4-pentadiene (35a). Prepared as above by treating the phosphonate **33*E*** (0.870 g, 2.83 mmol) in THF (22.6 mL) at −78 °C with a 1.0 M solution of sodium bis(trimethylsilyl)amide in THF (5.78 mL, 5.78 mmol). After the yellow solution was stirred at −78 °C for 50 min, benzaldehyde (0.273 g, 2.57 mmol) was added. The solution was then allowed to warm to −10 °C over a 4-h period. Workup as above provided a yellow oil, which was purified by radial chromatography (2.5% ethyl acetate in hexane) to provide 0.426 g (64%) of a white solid. ^1H NMR analysis of the product indicated the presence of a trace amount of another isomer. The solid was recrystallized twice from acetone to provide **35a** in isomerically pure form as fine white needles: mp 74–75.5 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.30 (m, 5 H, Ar-*H*), 6.75 (dd, $J_{4,5}$ = 15.66 Hz, $J_{3,4}$ = 10.42 Hz, 1 H, ArCH=C*H*CH=CH), 6.53 (d, $J_{4,5}$ = 15.69 Hz, 1 H, ArC*H*=CHCH), 6.31 (dd, $J_{2,3}$ = 15.22 Hz, $J_{3,4}$ = 10.41 Hz, 1 H, CHC*H*=CHCH_2NH), 5.79 (dt, $J_{2,3}$ = 15.11 Hz, $J_{1,2}$ = 6.21 Hz, 1 H, CH=C*H*CH_2N), 4.66 (b s, 1 H, CH_2N*H*), 3.83 (b t, 2 H, CHCH_2NH), 1.46 (s, 9 H, COOC(CH_3)$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.70 (N*C*=O), 137.12, 132.31, 131.78, 130.34, 128.56, 128.09, 127.51, 126.30, 79.42 (O*C*(CH_3)$_3$), 42.45 (*C*H_2NH), 28.39 (OC(*C*H_3)$_3$).

Anal. Calcd for $C_{16}H_{21}NO_2$: C, 74.09; H, 8.16. Found: C, 74.10; H, 8.16.

(2*E*,4*E*)-1-[*N*-(*tert*-Butoxycarbonyl)amino]-5-(4′-methoxyphenyl)-2,4-pentadiene (35b). Prepared as above by treating the phosphonate **33*E*** (1.088 g, 3.54 mmol) in THF (28.3 mL) at −78 °C with a 1.0 M solution of sodium bis(trimethylsilyl)amide in THF (7.25 mL, 7.25 mmol). After the yellow solution was stirred at −78 °C for 10 min, 4-methoxybenzaldehyde (0.438 g, 3.22 mmol) was added. The solution was then allowed to warm to −5 °C over a 5-h period and stirred at −5 °C for 1 h. Workup as above provided a yellow oil, which was purified by radial chromatography (10% ethyl acetate in hexane) to provide 0.548 g (59%) of an isomeric mixture along with 0.104 g (24%) of the unreacted aldehyde. ^1H NMR analysis of the mixture indicated only a small amount (<2.0%) of another isomer. The solid was recrystallized twice from acetone to provide **35b** in isomerically pure form as fine white needles: mp 98–99.5 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.30 (d, J = 8.73 Hz, 2 H, Ar-*H*), 6.85 (d, J = 8.78 Hz, 2 H, Ar-*H*), 6.63 (dd, $J_{4,5}$ = 15.55 Hz, $J_{3,4}$ = 10.23 Hz, 1 H, ArCH=C*H*CH=CH), 6.45 (d, $J_{4,5}$ = 15.65 Hz, 1 H, ArC*H*=CHCH), 6.26 (dd, $J_{2,3}$ = 15.11 Hz, $J_{3,4}$ = 10.11 Hz, 1 H, CH=CHC*H*=CHCH_2N), 5.71 (dt, $J_{2,3}$ = 15.12 Hz, $J_{1,2}$ = 6.19 Hz, 1 H, CHCH=C*H*CH_2N), 4.78 (b s, 1 H, CH_2N*H*), 3.77 (b s, 5 H, CH=CHCH_2N and OCH_3), 1.46 (s, 9 H, OC(CH_3)$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.12 (CH_3O*C*), 155.66 (NHC=O), 131.98, 131.80, 129.86, 129.07, 127.45, 126.04, 113.98, 79.27 (O*C*(CH_3)$_3$), 55.21 (O*C*H_3), 42.51 (CHCH_2NH), 28.75 (OC(*C*H_3)$_3$); IR ($CDCl_3$) 1701 cm^{-1} (C=O); mass spectrum EI (rel intensity) 289 (36, M^+), 233 (98, M^+ − C_4H_8), 188 (12, M^+ − C_4H_8 − CO_2), 172 (100).

Anal. Calcd for $C_{17}H_{23}NO_3$: C, 70.56; H, 8.01. Found: C, 70.60; H, 7.92.

(2*E*,4*E*)-1-[*N*-(*tert*-Butoxycarbonyl)amino]-5-(4′-chlorophenyl)-2,4-pentadiene (35c). Prepared as above by treating **33*E*** (1.085 g, 3.53 mmol) in THF (28.3 mL) at −78 °C with a 1.0 M solution of sodium bis(trimethylsilyl)amide in THF (7.54 mL, 7.54 mmol). The solution was stirred at −78 °C for 10 min, and then 4-chlorobenzaldehyde (0.451 g, 3.21 mmol) was added. The suspension became homogeneous after 15 min at −78 °C, and the yellow solution was allowed to warm to −10 °C over 5 h. After the solution was stirred at −10 °C for 30 min, workup as above provided an oil. The oil was purified by radial chromatography (2.5% ethyl acetate in hexane) to provide 0.130 g (29%) of the unreacted aldehyde and 0.447 g (51%) of a solid, isomeric mixture. ^1H NMR analysis of this mixture indicated the presence of ca. 4% of the 2*Z*,4*E* isomer (6.24 ppm, dd, J = 11.11 Hz, J = 10.79 Hz, CH=CHC*H*=CHCH_2N); the remaining isomer was the 2*E*,4*E* isomer. The solid was recrystallized twice from acetone to provide **35c** in isomerically pure form as fine white needles: mp 117–118.5 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.25 (m, 4 H, Ar-*H*), 6.72 (dd, $J_{4,5}$ = 15.63 Hz, $J_{3,4}$ = 10.40 Hz, 1 H, ArCH=C*H*CH=CH), 6.46 (d, $J_{4,5}$ = 15.66 Hz, 1 H, ArC*H*=CHCH=CH), 6.30 (dd, $J_{2,3}$ = 15.16 Hz, $J_{3,4}$ = 10.41 Hz, 1 H, CH=CHC*H*=CHCH_2NH), 5.81 (dt, $J_{2,3}$ = 15.15 Hz, $J_{1,2}$ = 6.08 Hz, 1 H, CHCH=C*H*CH_2NH), 4.67 (b s, 1 H, CH_2N*H*), 3.83 (b t, 2 H, CHCH_2NH), 1.46 (s, 9 H, COOC(CH_3)$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.69 (N*C*=O), 135.64, 133.06, 131.43, 131.03, 130.91, 128.73, 128.69, 127.44, 79.48 (O*C*(CH_3)$_3$), 42.40 (CHCH_2NH), 28.38 (OC(*C*H_3)$_3$); mass spectrum EI (rel intensity) 295 (3, M + 2), 293 (8, M^+), 239 (24, M + 2 − C_4H_8), 237 (M^+ − C_4H_8), 193 (12, M^+ − C_4H_8 − CO_2), 176 (100).

Anal. Calcd for $C_{16}H_{20}ClNO_2$: C, 65.41; H, 6.86. Found: C, 65.24; H, 6.68.

(2*E*,4*E*,6*E*)-1-[*N*-(*tert*-Butoxycarbonyl)amino]-7-phenyl-2,4,6-heptatriene (35d). Prepared as above by treating **33*E*** (1.074 g, 3.49 mmol) in THF (28.0 mL) at −78 °C with a 1.0 M solution of sodium bis(trimethylsilyl)amide in THF (7.46 mL, 7.46 mmol). The yellow solution was stirred at −78 °C for 10 min, and then cinammaldehyde (0.414 g, 3.17 mmol) was added. The solution was allowed to warm to −10 °C over 5 h and stirred at −10 to −5 °C for 30 min. Workup as above provided a yellow oil, which was purified by radial chromatography (2.5% ethyl acetate in hexane) to provide 0.480 g (53%) of a white solid. Preliminary ^1H NMR analysis of this crude product indicated that a trace amount (less than 4%) of two isomers had been formed. It was

not possible to determine what the two minor isomers were due to their low concentration in the mixture. The solid was recrystallized twice from acetone to provide **35d** in isomerically pure 2*E*,4*E*,6*E* isomer as fine white needles: mp 115–117 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (m, 5 H, Ar-*H*), 6.80 (dd, $J_{6,7}$ = 15.57 Hz, $J_{5,6}$ = 9.80 Hz, 1 H, ArCH=C*H*CH=CH), 6.55 (d, $J_{6,7}$ = 15.58 Hz, 1 H, ArC*H*=CHCH), 6.30 (m, 3 H, CHC*H*=C*HCH*=$CHCH_2N$), 5.71 (dt, $J_{2,3}$ = 14.41 Hz, $J_{1,2}$ = 6.13 Hz, 1 H, CHCH=C*H*CH_2N), 4.70 (b s, 1 H, CH_2NH), 3.80 (b t, 2 H, $CHCH_2NH$), 1.45 (s, 9 H, $OC(CH_3)_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.68 (*N*C=O), 137.120, 132.90, 132.61, 132.25, 131.64, 130.23, 128.77, 128.54, 127.45, 126.26, 79.31 ($OC(CH_3)_3$), 42.41 (CH_2NH), 28.34 ($OC(CH_3)_3$); mass spectrum EI (rel intensity) 285 (18, M^+), 229 (63, $M^+ - C_4H_8$), 168 (100).

Anal. Calcd for $C_{18}H_{23}NO_2$: C, 75.76; H, 8.12. Found: C, 75.59; H, 8.18.

(2*E*,4*E*)-1-[*N*-(*tert*-Butoxycarbonyl)amino]-7-methyl-2,4,6-octatriene (35e). Prepared as above by treating **33*E*** (1.081 g, 3.51 mmol) in THF (28.1 mL) at −78 °C with a 1.0 M solution of sodium bis(trimethylsilyl)amide in THF (7.19 mL, 7.19 mmol). The yellow solution was stirred at −78 °C for 10 min, and then 3-methyl-2-butenal (0.268 g, 3.19 mmol) was added. The solution was allowed to warm to 0 °C over 5 h. Workup as above provided a yellow oil, which was purified by radial chromatography (2.5% ethyl acetate in hexane) to provide 0.481 g (64%) of a colorless oil. Preliminary ^{1}H NMR analysis of this crude product indicated the major product to be the 2*E*,4*E* isomer (**35e**). However, two pairs of singlets centered at 1.90 and 1.83 ppm were observed (for $CH=C(CH_3)_2$), indicating the presence of two additional isomers. Because no other significant peaks from these isomers were observed, we were unable to determine which geometric isomers were formed. Because the two isomers appeared in such small amounts (less than 15% of the isomeric mixture), we are only able to report ^{1}H NMR data for the major isomer, the 2*E*,4*E* isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.39 (dd, $J_{4,5}$ = 14.58 Hz, $J_{5,6}$ = 11.17 Hz, 1 H, CHCH=C*H*CH=$C(CH_3)_2$), 6.21 (dd, $J_{2,3}$ = 14.85 Hz, $J_{3,4}$ = 10.62 Hz, 1 H, $HNCH_2CH$=C*H*CH=CHCH), 6.07 (dd, $J_{4,5}$ = 14.56 Hz, $J_{3,4}$ = 10.65 Hz, 1 H, $HNCH_2CH$=CHC*H*=CHCH), 5.84 (d, $J_{5,6}$ = 11.07 Hz, 1 H, CH=CHC*H*=$C(CH_3)_2$), 5.61 (dt, $J_{2,3}$ = 14.80 Hz, $J_{1,2}$ = 6.42 Hz, 1 H, $HNCH_2C$*H*=CHCH), 4.61 (b s, 1 H, *H*NCH_2CH), 3.78 (b t, 2 H, $HNCH_2CH$=CH), 1.79 (s, 3 H, CH=C(C*H*$_3$)CH_3), 1.77 (s, 3 H, CH=C(CH_3)C*H*$_3$), 1.45 (s, 9 H, $OC(CH_3)_3$); ^{13}C NMR data reported for the mixture containing primarily the 2*E*,4*E* isomer (75 MHz, $CDCl_3$) δ 155.66 (*N*C=O), 147.10, 139.55, 136.48, 132.38, 129.52, 129.01, 128.17, 128.07, 125.10, 124.13, 79.28 ($OC(CH_3)_3$), 42.49 ($CHCH_2N$), 28.36 ($OC(CH_3)_3$), 26.10 ($C(CH_3)CH_3$), 18.35 ($C(CH_3)CH_3$); mass spectrum EI (rel intensity) 237 (22, M^+), 181 (63, $M^+ - C_4H_8$), 136 (10, $M^+ - C_4H_8 - CO_2$), 120 (100), 57 (50, C_4H_9).

Anal. Calcd for $C_{14}H_{23}NO_2$: C, 70.85; H, 9.77. Found: C, 70.64; H, 9.60.

(2*E*,4*E*)-1-[*N*-(*tert*-Butoxycarbonyl)amino]-2,4-decadiene (35f). Prepared as above by treating **33*E*** (0.55 g, 1.79 mmol) in THF (14.8 mL) at −78 °C with a 1.0 M solution of sodium bis(trimethylsilyl)amide in THF (3.59 mL, 3.59 mmol). After the yellow solution was stirred at −78 °C for 10 min, hexanal (0.162 g, 1.63 mmol) was added. The solution was then allowed to warm to −10 °C over a 5-h period and workup as above provided a yellow oil. The oil was purified by radial chromatography (2.5% ethyl acetate in hexane) to provide 0.268 g (65%) of a colorless oil. ^{1}H NMR analysis of the product indicated that two isomers had been formed. Although the major isomer, the 2*E*,4*E* isomer (**35f**) was discernible in the mixture, it was difficult to obtain an accurate intergration of the two isomers due to the overlap of the signals. However, a crude intergration indicated that approximately 12% of the minor isomer had formed in the reaction: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.25 (ddt, $J_{2,3}$ = 14.73 Hz, $J_{3,4}$ = 10.30 Hz, 1 H, CH=CHC*H*=$CHCH_2N$), 5.97 (dd, $J_{4,5}$ = 14.90 Hz, $J_{3,4}$ = 10.35 Hz, 1 H, CH_2CH=C*H*CH=$CHCH_2N$), 5.60 (m, 2 H, CH_2CH=CHCH=C*H*CH_2N), 4.58 (b s, 1 H, CH_2NH), 3.88 (b m, CHC*H*$_2$NH, minor isomer) and 3.78 (b m, $CHCH_2NH$, major isomer), 2.10 (q, *J* = 7.04 Hz, 2 H, $CH_2CH_2CH_2CH$=CH), 1.46 (s, 9 H, $OC(CH_3)_3$), 1.32 (m, 6 H, $CH_3CH_2CH_2CH_2CH_2$), 0.88 (t, 3 H, CH_3CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) reported for the isomeric mixture δ 155.69 (NH*C*=O), 135.27, 132.74, 132.14, 129.26, 129.22, 127.47, 126.99, 124.63, 79.15 ($OC(CH_3)_3$), 42.41 ($CHCH_2NH$), 32.79, 32.53, 31.56, 28.38, 22.63, 22.49, 14.08, 14.00; IR (neat) 1705 cm^{-1} (C=O).

Anal. Calcd for $C_{15}H_{27}NO_2$: C, 71.10; H, 10.74. Found: C, 70.96; H, 10.88.

(2*E*)-1-[*N*-(*tert*-Butoxycarbonyl)amino]-5,5-diphenyl-2,4-pentadiene (35g). Prepared as above by treating **33*E*** (0.55 g, 1.79 mmol) in THF (14.4 mL) at −78 °C with a 1.0 M solution of sodium bis(trimethylsilyl)amide in THF (3.59 mL, 3.59 mmol). After the yellow solution was stirred at −78 °C for 10 min, benzophenone (0.297 g, 1.63 mmol) was added. The solution was then allowed to warm to −5 °C over a 5-h period and stirred at −5 °C for 1 h. Workup as above provided a yellow oil, which was purified by radial chromatography (5% ethyl acetate in hexane) to provide 0.365 g (67%) of **35g** as a white solid along with 0.083 g (28%) of the unreacted ketone. ^{1}H NMR analysis of the product indicated that only the 2*E* isomer had been formed. The solid was recrystallized from ethyl ether to provide white needles: mp 86–87 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (m, 10 H, Ar-*H*), 6.67 (d, $J_{3,4}$ = 10.95 Hz, 1 H, $(Ph)_2C$=C*H*CH=CH), 6.24 (ddt, $J_{2,6}$ = 15.17 Hz, $J_{3,4}$ = 10.99 Hz, $J_{1,3}$ = 1.32 Hz, 1 H, CHC*H*=$CHCH_2N$), 5.85 (dt, $J_{2,3}$ = 15.05 Hz, $J_{1,2}$ = 6.18 Hz, 1 H, CH=C*H*CH_2N), 4.60 (b s, 1 H, CH_2NH), 3.74 (b t, 2 H, CH_2NH), 1.41 (s, 9 H, $OC(CH_3)_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.62 (NH*C*=O), 142.60, 142.05, 139.53, 131.61, 130.29, 129.49, 128.16, 128.12, 127.43, 127.37, 127.32, 126.98, 79.29 ($OC(CH_3)_3$), 42.49 ($CHCH_2NH$), 28.33 ($OC(CH_3)_3$); IR ($CDCl_3$) 1704 cm^{-1} (C=O); mass spectrum EI (rel intensity) 335 (8, M^+), 279 (40, $M^+ - C_4H_8$), 105 (100), 57 (100, C_4H_9).

Anal. Calcd for $C_{22}H_{25}NO_2$: C, 78.77; H, 7.51. Found: C, 78.62; H, 7.54.

(2*E*)-1-[*N*-(*tert*-Butoxycarbonyl)amino]-4-cyclohexylidene-2-butene (35h). Prepared as above by treating **33*E*** (0.550 g, 1.79 mmol, 1.1 equiv) in THF (14.3 mL) at −78 °C with a 1 M solution of sodium bis(trimethylsilyl)amide in THF (3.58 mL, 3.58 mmol). After the solution was stirred at −78 °C for 15 min, cyclohexanone (0.159 g, 1.63 mmol, 1.0 equiv) was added. The cold bath was insulated with aluminum foil and was allowed to warm slowly to −10 °C. The orange yellow solution was then poured into ether (100 mL) and washed with aqueous 1 N $NaHSO_4$ (2 × 10 mL) and saturated aqueous NaCl (1 × 10 mL). The pale yellow solution was then dried ($MgSO_4$) and concentrated in vacuo to provide a yellow oil. This oil was purified by radial chromatography (2.5% ethyl acetate in hexane) to provide 0.299 g (74%) of white crystals. Preliminary ^{1}H NMR analysis of this crude product indicated a 94:6 ratio of the 2*E* and 2*Z* isomers (the presence of the 2*Z* isomer was indicated by a dd at 4.44 ppm). The solid was recrystallized from acetone to provide **35h** as white needles: mp 55.5–57 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.40 (dd, $J_{2,3}$ = 15.05 Hz, $J_{3,4}$ = 10.00 Hz, 1 H, C=CHC*H*=$CHCH_2N$), 5.75 (d, $J_{3,4}$ = 10.85 Hz, 1 H, C=C*H*CH=$CHCH_2N$), 5.62 (dt, $J_{2,3}$ = 15.03 Hz, $J_{1,2}$ = 6.29 Hz, 1 H, CH=C*H*CH_2N), 4.78 (b s, 1 H, CH_2NH), 3.76 (b t, 2 H, C=$CHCHCH_2NH$), 2.26 (b m, 2 H, CH_2C=CH), 2.10 (b m, 2 H, CH_2C=CH), 1.55 (b s, 6 H, $CH_2CH_2CH_2$), 1.44 (s, 9 H, $OC(CH_3)_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.74 (*N*C=O), 143.41, 127.45, 126.87, 120.90, 116.24, 78.95 ($OC(CH_3)_3$), 42.57 ($CHCH_2NH$), 37.06, 29.03, 28.27, 27.51, 26.65; IR ($CDCl_3$) 1700 (C=O) cm^{-1}; mass spectrum EI (rel intensity) 251 (4, M^+), 195 (10, $M^+ - C_4H_8$), 57 (100, C_4H_9).

Anal. Calcd for $C_{15}H_{25}NO_2$: C, 71.67; H, 10.03. Found: C, 71.56; H, 9.97.

(2*E*)-4-Cyclohexylidene-1-[*N*-(ethoxycarbonyl)amino]-2-butene (36h). If the above reaction was allowed to warm to room temperature prior to workup, a number of other spots are observed by TLC. One of the main byproducts is the ethyl carbamate derivative **36h**: mp 59–60 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.42 (dd, $J_{2,3}$ = 15.03 Hz, $J_{3,4}$ = 10.96 Hz, 1 H, C=CHC*H*=$CHCH_2N$), 5.75 (d, $J_{3,4}$ = 10.94 Hz, 1 H, C=C*H*CH=$CHCH_2N$), 5.62 (dt, $J_{2,3}$ = 15.04 Hz, $J_{1,2}$ = 6.34 Hz, 1 H, CHCH=C*H*CH_2N), 4.78 (b s, 1 H, CH_2NH), 4.12 (q, *J* = 7.08 Hz, 2 H, OCH_2CH_3), 3.82 (b t, *J* = 5.71 Hz, 2 H, $CHCH_2NH$), 2.26 (b m, 2 H, CH_2C=CH), 2.12 (b m, 2 H, CH_2C=CH), 1.55 (b s, 6 H, $CH_2CH_2CH_2$), 1.24 (t, *J* = 7.10 Hz, 3 H, OCH_2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.41 (*N*C=O), 144.00, 126.56, 120.85, 116.18, 60.71 (OCH_2CH_3), 43.02 ($CHCH_2NH$), 37.17, 29.17, 28.42, 27.65, 26.65, 14.59 (OCH_2CH_3); IR ($CDCl_3$) 1705 (C=O) cm^{-1}; mass spectrum EI (rel intensity) 223 (16, M^+), 195 (38, $M^+ - C_2H_4$), 150 (10, $M^+ - C_2H_4 - CO_2$), 134 (100).

(2*E*)-1-[*N*-(*tert*-Butoxycarbonyl)amino]-5-ethyl-2,4-heptadiene (35i). Prepared as above by treating **33*E*** (1.131 g, 3.68 mmol) in THF (29.4 mL) at −78 °C with a 1.0 M solution of sodium bis(trimethylsilyl)amide in THF (7.70 mL, 7.70 mmol). After the yellow solution was stirred at −78 °C for 20 min, 3-pentanone (0.288 g, 3.34 mmol) was added. The solution was then allowed to warm to 0 °C over a 5-h period, and workup as above to provide a yellow oil. This oil was purified by radial chromatography (2.5% ethyl acetate in hexane) to provide 0.373 g (47%) of a colorless oil. ^{1}H NMR analysis of the product indicated the presence of ca. 6% of the 2*Z* isomer. Unless otherwise stated, the following NMR data are for the 2*E* isomer (**35i**): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.39 (dd, $J_{2,3}$ = 15.04 Hz, $J_{3,4}$ = 10.93 Hz, $NCH_2CH{=}CHCH{=}C$, 2*E* isomer), 6.01 (d, $J_{3,4}$ = 10 Hz, $NCH_2CH{=}CHCH{=}C$, 2*Z* isomer), 5.75 (d, $J_{3,4}$ = 11.00 Hz, 1 H, $NHCH_2CH{=}CHCH{=}C$), 5.57 (dt, $J_{2,3}$ = 15.01 Hz, $J_{1,2}$ = 6.37 Hz, 1 H, $NHCH_2CH{=}CHCH$), 5.32 (dt, $J_{2,3}$ = 10 Hz, $J_{1,2}$ = 6.83 Hz, $NHCH_2CH{=}CHCH$, 2*Z* isomer), 4.55 (b s, 1 H, $NHCH_2CH{=}CH$), 3.90 (b t, $NHCH_2CH{=}CH$, 2*Z* isomer), 3.77 (b t, J = 5.85 Hz, 2 H, $NHCH_2CH{=}CH$), 2.17 (q, J = 7.41 Hz, 2 H, $C{=}CCH_2CH_3$), 2.08 (q, J = 7.47 Hz, 2 H, $C{=}CCH_2CH_3$), 1.45 (s, 9 H, $OC(CH_3)_3$), 1.02 (t, J = 7.41 Hz, 3 H, $C{=}CCH_2CH_3$), 1.00 (t, J = 7.62 Hz, 3 H, $C{=}CCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.70 ($NHC{=}O$), 147.09, 128.18, 127.08, 121.83, 79.25 ($OC(CH_3)_3$), 42.84 ($CHCH_2NH$), 29.43 (CH_2CH_3), 28.39 ($OC(CH_3)_3$), 23.79 (CH_2CH_3), 13.41 (CH_2CH_3), 12.57 (CH_2CH_3); mass spectrum EI (rel intensity) 239 (18, M^+), 183 (65, $M^+ - C_4H_8$), 154 (62), 122 (94), 59 (100, C_4H_9).

Anal. Calcd for $C_{14}H_{25}NO_2$: C, 70.25; H, 10.53. Found: C, 70.05; H, 10.40.

(2*E*,4*E*)-1-[*N*-(*tert*-Butoxycarbonyl)amino]-5,6,6-trimethyl-2,4-heptadiene (35j). Prepared as above by treating **33*E*** (1.27 g, 4.13 mmol) in THF (33.0 mL) at −78 °C with a 1.0 M solution of sodium bis(trimethylsilyl)amide in THF (8.45 mL, 8.45 mmol). After the yellow solution was stirred at −78 °C for 20 min, pinacolone (0.376 g, 3.75 mmol) was added. The solution was then allowed to warm to 0 °C over a 5-h period and worked up as above to provide a yellow oil. This oil was purified by radial chromatography (2.5% ethyl acetate in hexane) to provide 0.485 g (51%) of **35j** as a colorless oil. ^{1}H and ^{13}C NMR analysis of the product indicated only the 2*E* isomer had been formed: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.40 (b dd, $J_{2,3}$ = 14.95 Hz, $J_{3,4}$ = 10.71 Hz, 1 H, $HNCH_2CH{=}CHCH{=}C(CH_3)$), 5.90 (d, $J_{3,4}$ = 10.56 Hz, 1 H, $CH{=}CHCH{=}C(CH_3)$), 5.63 (dt, $J_{2,3}$ = 14.97 Hz, $J_{1,2}$ = 6.08 Hz, 1 H, $HNCH_2CH{=}CHCH{=}C$), 4.58 (b s, 1 H, $HNCH_2CH{=}CH$), 3.78 (b t, 2 H, $HNCH_2CH{=}CHCH$), 1.75 (s, 3 H, $CH{=}C(CH_3)C(CH_3)_3$), 1.45 (s, 9 H, $OC(CH_3)_3$), 1.05 (s, 9 H, $CH{=}C(CH_3)C(CH_3)_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.70 ($NHC{=}O$), 147.06, 129.03, 127.70, 120.34, 79.24 ($OC(CH_3)_3$), 42.79 ($CHCH_2NH$), 36.36 ($CH{=}C(CH_3)C(CH_3)_3$), 28.86 ($CH{=}C(CH_3)$), 28.39 ($OC(CH_3)_3$), 13.25 ($CH{=}C(CH_3)C(CH_3)_3$); mass spectrum EI (rel intensity) 253 (8, M^+), 197 (50, $M^+ - C_4H_8$), 140 (100), 57 (82, C_4H_9).

Anal. Calcd for $C_{15}H_{27}NO_2$: C, 71.10; H, 10.74. Found: C, 71.00; H, 10.81.

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Efficient Synthesis of Sterically and Optically Pure *E,Z* Conjugated Hydroxy Dienes. A New Approach to Hydroxyeicosatetraenoic Acids

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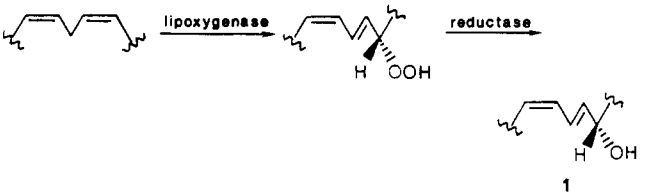
A new strategy for the synthesis of optically active *E,Z* conjugated hydroxy dienes, important intermediates for the synthesis of HETEs, is described. It involves as its key steps two successive chirality transfers starting from the tricyclic lactol **5**, easily obtained via an enzymatic pathway. This method is exemplified by the efficient synthesis of pure *S* and *R* enantiomers of 6-acetoxy-2(*Z*),4(*E*)-undecadien-1-ol (**6**).

Lipoxygenation of arachidonic acid, first observed in mammalian platelets,[1] has been now reported to occur in a number of different tissues and has been shown to lead to metabolites of great biological importance such as leukotrienes and HETEs[2] (hydroxyeicosatetraenoic acids). All the biological and biochemical properties of these substances are still not known, and since they are obtained only in minute amounts from natural sources, considerable synthetic efforts have been recently devoted to finding efficient methods for their synthesis.

Six different possible monohydroxylated metabolites (5-, 8-, 9-, 11-, 12-, and 15-HETEs) can be produced via the lipoxygenase pathway, depending on the oxidation site of arachidonic acid. But, regardless of the site involved, the final result is always the transformation of a (*Z,Z*)-1,4-diene moiety of arachidonic acid to an *E,Z* conjugated diene with a hydroxy group of *R* or *S* configuration next to the *E* double bond.



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