1516 J. Org. Chem. 1996, 61, 1516−1518

Synthesis and Cycloaromatization of (*Z*)-1,2,4-Heptatrien-6-ynes and (*Z*)-2,4,5-Hexatrienenitriles

Kung K. Wang* and Zhongguo Wang

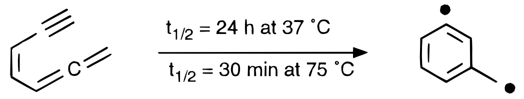
Department of Chemistry, West Virginia University, Morgantown, West Virginia 26506

Prem D. Sattsangi

Department of Chemistry, The Pennsylvania State University, Fayette Campus, Uniontown, Pennsylvania 15401

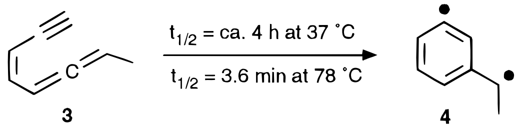
Received September 19, 1995

Cycloaromatization of (*Z*)-1,2,4-heptatrien-6-yne (**1**) to α,3-didehydrotoluene **2** is an attractive method for generating two radical centers simultaneously (eq 1).[1] While the process results in the loss of one chemical bond, the reaction has been estimated to be exothermic by ca. 15 kcal/mol. Converting a π bond of **1** to a σ bond in **2** along with gains from aromaticity and benzylic resonance are mainly responsible for making the process energetically favorable. Cyclization occurs at 37 °C with a half-life of ca. 24 h. At 75 °C, the half-life of the reaction is reduced to 30 min.



1 **2** (1)

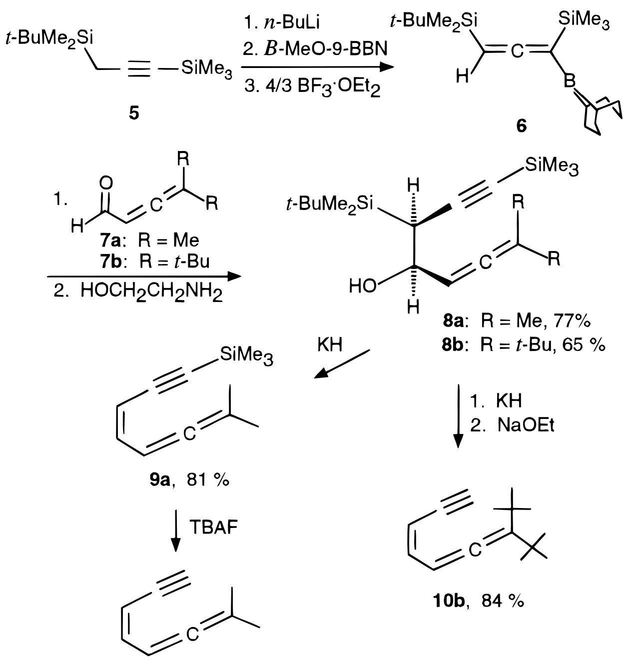
Introduction of a methyl substituent at the terminus of the allenic moiety accelerates the reaction rate by approximately 6-fold, and **3** cyclizes with a half-life of ca. 3.6 min at 78 °C (eq 2).[1] The formation of a more stable secondary benzylic radical in **4** is apparently responsible for the rate enhancement.



3 **4** (2)

We recently reported a simple synthetic method for the preparation of (*Z*)-3-hexene-1,5-diynes by condensation of (γ-(*tert*-butyldimethylsilyl)allenyl)borane **6** with the conjugated acetylenic aldehydes followed by the elimination step of the Peterson olefination reaction.[2] This method was also successfully applied to the synthesis of 1,2,4-heptatrien-6-ynes (enyne−allenes) by utilizing conjugated allenic aldehydes for condensation.[3] We now have utilized **6** for the synthesis of enyne−allenes **10a** and **10b**, and their rates of cycloaromatization to the corresponding α,3-didehydrotoluene biradicals were studied. Similarly, the aza analogues, (*Z*)-2,4,5-hexatrienenitriles **18a** and **18b** in which a cyano group replaces the acetylenic moiety of **10a** and **10b** were synthesized.

Scheme 1



10a, 57 %

Allenylborane **6** was prepared in situ by treating the readily available 3-(*tert*-butyldimethylsilyl)-1-(trimethylsilyl)-1-propyne (**5**)[4] with *n*-butyllithium followed by *B*-methoxy-9-borabicyclo[3.3.1]nonane (*B*-MeO-9-BBN) and $^{4}/_{3}BF_3{\cdot}OEt_2$ (Scheme 1).[2] Subsequent condensation with the conjugated allenic aldehydes **7**[3,5] furnished, after treatment with 2-aminoethanol, the condensation adducts **8** with high diastereoselectivity. The KH-induced syn elimination of hydroxytrimethylsilane from **8a** produced enyne−allene **9a** (*Z*:*E* = 96:4), which on exposure to tetrabutylammonium fluoride (TBAF) furnished the desilylated adduct **10a**. Conversion of **8b** to **10b** (*Z*:*E* > 99:1) was achieved in one operation by treatment with KH followed by desilylation with sodium ethoxide.

Compared to **3**, enyne−allene **10a** has an additional methyl substituent at the terminus of the allenic moiety, making it possible to produce a more stable tertiary benzylic radical center in **11** after cycloaromatization and, as a result, to increase the rate of reaction. Thermolysis of **10a** (0.122 g, 1.03 mmol, 0.2 M) in 5 mL of 1,4-cyclohexadiene at 37 °C for 15 h produced cumene (**12**, 43%), 1,2-dimethyl-1,2-diphenylethane (**13**, 2%), and the combination products **14a** and **14b** (1:1, 15%) (Scheme 2). The half-life of the reaction at 37 °C was determined to be ca. 70 min by using the ^{1}H NMR to monitor the disappearance of **10a** in C_6D_6 in the presence of an excess of 1,4-cyclohexadiene.

Enyne−allene **10b** having two sterically demanding *tert*-butyl groups exhibited a slower rate of cyclization ($t_{1/2}$ = ca. 60 min at 76 °C) when compared to **10a** (Scheme 3). Cycloaromatization was conducted in C_6D_6 in the presence of an excess of 1,4-cyclohexadiene, and the rate of the reaction was monitored by ^{1}H NMR. On thermolysis in refluxing benzene (80 °C) in the presence of an excess of 1,4-cyclohexadiene, the reaction was essentially complete within 5 h, and α,α-di-*tert*-butyltoluene (**16**) was isolated in 58% yield.

---

(1) Myers, A. G.; Kuo, E. Y.; Finney, N. S. *J. Am. Chem. Soc.* **1989**, *111*, 8057−8059.

(2) Wang, K. K.; Wang, Z.; Gu, Y. G. *Tetrahedron Lett.* **1993**, *34*, 8391−8394.

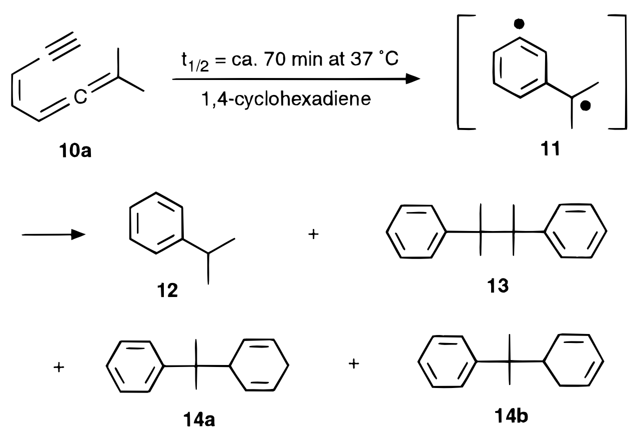
(3) (a) Andemichael, Y. W.; Gu, Y. G.; Wang, K. K. *J. Org. Chem.* **1992**, *57*, 794−796. (b) Andemichael, Y. W.; Huang, Y.; Wang, K. K. *J. Org. Chem.* **1993**, *58*, 1651−1652.

(4) (a) Furuta, K.; Ishiguro, M.; Haruta, R.; Ikeda, N.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2768−2776. (b) Yamakado, Y.; Ishiguro, M.; Ikeda, N.; Yamamoto, H. *J. Am. Chem. Soc.* **1981**, *103*, 5568−5570.

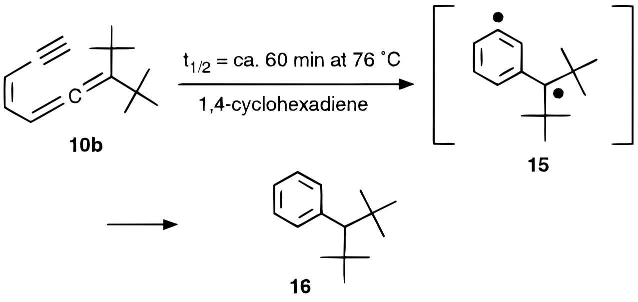
(5) Clinet, J.-C.; Linstrumelle, G. *Nouv. J. Chem.* **1977**, *1*, 373−374.

0022-3263/96/1961-1516$12.00/0 © 1996 American Chemical Society

Scheme 2



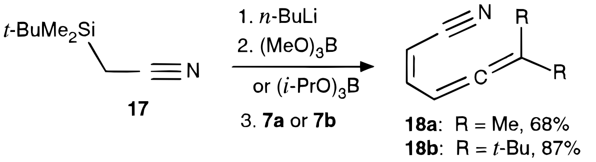
Scheme 3



When compared to **1**, the rate of cycloaromatization of **10b** is not significantly affected. Presumably, the small size of the hydrogen atom at the terminal position of the acetylenic moiety in **10b** minimizes the steric interactions even with the *tert*-butyl group, and the formation of a more stable tertiary benzylic radical in **15** partially compensates for the increased steric interactions.

It is worth noting that the benzylic radical center in **15** is an α,α-di-*tert*-butylbenzylic radical, which has been reported to be persistent in dilute solution at room temperature for several days.[6] For steric reasons, the α,α-di-*tert*-butylbenzylic radical prefers a conformation with the p-orbital of the radical center perpendicular to the π-bonds of the benzene ring, resulting in the loss of 13 kcal/mol of the resonance energy. This preference also eliminates the possibility of twisting the terminal allenic carbon of **10b** during the course of cyclization to allow at least a partial conjugation of the benzylic radical center with the benzene ring at the transition state in order to facilitate the rate of cyclization.[1,7]

(*Z*)-2,4,5-Hexatrienenitriles **18a** and **18b** were synthesized as the aza analogues of **10a** and **10b**, respectively. Sequential treatment of (*tert*-butyldimethylsilyl)acetonitrile (**17**)[4] with *n*-butyllithium, triisopropyl or trimethyl borate, and the allenic aldehydes **7** furnished **18a** (*Z*:*E* = 9:1) and **18b** (*Z*:*E* = 98:2) with high geometric purity (eq 3).



(3)

The conjugated nitrile **18a** exhibited much higher thermal stability than that of **10a** and showed no sign of change on prolonged storage at rt. Even after 10 min at 180 °C, a large portion of **18a** remained unreacted. A mixture of unidentified products was produced on thermolysis of **18a** in C_6D_6 in the presence of an excess of 1,4-cyclohexadiene at 200 °C for 30 min where the anticipated 2-isopropylpyridine was not detected.[8] The thermal stability of **18b** was even more remarkable, remaining unchanged even on heating in toluene-d_8 in the presence of an excess of 1,4-cyclohexadiene at 260 °C for 15 h.

Experimental Section

General procedures for manipulation of organoboranes and other organometallic reagents were described previously.[9] All reactions were conducted in oven-dried glassware under a nitrogen atmosphere. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl prior to use. The following reagents were purchased from Aldrich Chemical Co., Inc., and were used without further purification: *n*-butyllithium (2.5 M in hexanes), 1-(trimethylsilyl)-1-propyne, *tert*-butyldimethylsilyl chloride, 3-methyl-1,2-butadiene, TBAF, 1,4-cyclohexadiene, trimethyl borate, and triisopropyl borate. Potassium hydride (35 wt % dispersion in mineral oil) was also purchased from Aldrich, and mineral oil was removed by washing with pentane prior to use. 3-(*tert*-Butyldimethylsilyl)-1-(trimethylsilyl)-1-propyne (**5**),[4] (*tert*-butyldimethylsilyl)acetonitrile (**17**),[4] *B*-MeO-9-BBN,[10] and 4-methyl-2,3-pentadienal (**7a**)[3,5] were prepared according to the reported procedures. 5,5-Dimethyl-4-(1,1-dimethylethyl)-2,3-hexadienal (**7b**) was prepared in 80% isolated yield by treatment of 4,4-dimethyl-3-(1,1-dimethylethyl)-1,2-pentadiene[11] with *n*-butyllithium followed by *N*,*N*-dimethylformamide and acidic hydrolysis.[3,5] ^{1}H (270 MHz) and ^{13}C (67.9 MHz) NMR spectra were recorded in $CDCl_3$ or C_6D_6 using Me_4Si, $CHCl_3$ (^{1}H δ 7.26), $CDCl_3$ (^{13}C δ 77.02), C_6D_5H (^{1}H δ 7.15), or C_6D_6 (^{13}C δ 128.00) as internal standard. The isomer ratios were determined by integration of the ^{1}H NMR spectra.

(3*S*,4*R*)-3-(*tert*-Butyldimethylsilyl)-7-methyl-1-(trimethylsilyl)-5,6-octadien-1-yn-4-ol (8a). To 1.36 g of **5** (6.0 mmol) in 15 mL of THF was added 2.4 mL of a 2.5 M solution of *n*-butyllithium (6.0 mmol) in hexanes at −10 °C. After 30 min at −10 °C, 1.0 mL of *B*-MeO-9-BBN (0.92 g, 6.0 mmol) was introduced by a syringe. After an additional 45 min at 0 °C, 1.0 mL of $BF_3{\cdot}OEt_2$ (1.14 g, 8.0 mmol) was added and the reaction mixture was stirred at 0 °C for 20 min before 0.576 g (6.0 mmol) of **7a** was introduced. The reaction mixture was allowed to warm to rt. After 2 h, THF and hexanes were removed at reduced pressure under a slow stream of N_2, and the pressure was then restored with N_2. Hexane (20 mL) was added followed by 1.0 mL of 2-aminoethanol, and a white precipitate was formed almost immediately. After 15 min, the precipitate was removed by filtration, and the filtrate was washed with water, dried over $MgSO_4$, and concentrated. The residue was purified by column chromatography (silica gel/5% diethyl ether in hexanes) to furnish 1.481 g (4.6 mmol, 77%) of **8a** as a light yellow liquid: IR (neat) 3357, 2158, 1969, 1250, 843 cm^{-1}; ^{1}H (C_6D_6) δ 5.34 (1 H, d of septet, J = 5.1 and 2.8 Hz), 4.30 (1 H, ddd, J = 9.0, 5.1, and 2.6 Hz), 2.14 (1 H, d, J = 2.4 Hz), 2.03 (1 H, d, J = 9.0 Hz), 1.66 (3 H, d, J = 2.8 Hz), 1.60 (3 H, d, J = 2.8 Hz), 0.96 (9 H, s), 0.34 (3 H, s), 0.18 (9 H, s), 0.11 (3 H, s); ^{13}C (C_6D_6) δ 199.93, 106.74, 99.32, 94.81, 89.01, 68.88, 27.71, 27.20, 21.05, 20.46, 17.71, 0.36, −6.00, −6.50.

---

[6] Schreiner, K.; Berndt, A. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 144−145.

[7] Koga, N.; Morokuma, K. *J. Am. Chem. Soc.* **1991**, *113*, 1907−1911.

[8] Recently, a conference abstract concerning cycloaromatization of a (*Z*)-2,4,5-hexatrienenitrile to the corresponding aniline derivative appeared. Gillmann, T.; Heckhoff, S.; Weeber, T. *Abstracts of Papers*, 209th National Meeting of the American Chemical Society, Anaheim, CA, April 2−6, 1995; American Chemical Society: Washington, DC, 1995; ORGN 93.

[9] Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. *Organic Syntheses via Boranes*; Wiley-Interscience: New York, 1975.

[10] Kramer, G. W.; Brown, H. C. *J. Organomet. Chem.* **1974**, *73*, 1−15.

[11] Crandall, J. K.; Conover, W. W.; Komin, J. B.; Machleder, W. H. *J. Org. Chem.* **1974**, *39*, 1723−1729.

(3*S*,4*R*)-3-(*tert*-Butyldimethylsilyl)-8,8-dimethyl-7-(1,1-dimethylethyl)-1-(trimethylsilyl)-5,6-nonadien-1-yn-4-ol (8b). The same reaction procedure was repeated as described for **8a** except that 1.08 g (6.0 mmol) of **7b** was used to furnish 1.58 g (3.89 mmol, 65%) of **8b** as a light yellow liquid: IR (neat) 3561, 2158, 1941, 1249, 841 cm^{-1}; ^{1}H (CDCl$_3$) δ 5.30 (1 H, d, $J = 5.0$ Hz), 4.20 (1 H, ddd, $J = 10.1$, 5.1, and 1.8 Hz), 2.16 (1 H, d, $J = 1.8$ Hz), 2.02 (1 H, d, $J = 10.1$ Hz), 1.21 (9 H, s), 1.19 (9 H, s), 0.95 (9 H, s), 0.16 (3 H, s), 0.13 (9 H, s), 0.10 (3 H, s); ^{13}C (CDCl$_3$) δ 199.94, 125.12, 105.80, 97.41, 89.77, 68.90, 35.14, 34.76, 32.46, 32.18, 27.26, 26.98, 17.57, 0.17, −6.55, −6.70.

(*Z*)-7-Methyl-1-(trimethylsilyl)-3,5,6-octatrien-1-yne (9a). To a dispersion of 0.72 g (18 mmol) of KH in 20 mL of a 1:1 mixture of pentane and diethyl ether at 0 °C under N$_2$ was added 1.45 g (4.5 mmol) of **8a**. After 30 min of stirring, KH was removed by filtration, and the reaction mixture was washed with water, dried over MgSO$_4$, and concentrated. The residue was purified by column chromatography (silica gel/hexanes) to furnish 0.695 g (3.66 mmol, 81%) of **9a** (Z:E = 96:4) as a colorless liquid: IR (neat) 2144, 1947, 1250, 846 cm^{-1}; ^{1}H NMR (C$_6$D$_6$) δ 6.70 (1 H, dm, $J = 11.2$ and 1 Hz), 6.24 (1 H, t, $J = 10.9$ Hz), 5.32 (1 H, dd $J = 10.6$ and 0.9 Hz), 1.49 (6 H, d $J = 2.7$ Hz), 0.17 (9 H, s); ^{13}C NMR (C$_6$D$_6$) δ 207.70, 139.03, 107.93, 102.75, 101.32, 96.87, 91.25, 20.02, 0.03; MS *m/e* 190 (M$^+$), 175, 159, 131, 115, 84, 73.

(*Z*)-7-Methyl-3,5,6-octatrien-1-yne (10a). To a solution of 0.342 g (1.80 mmol) of **9a** in 10 mL of THF at 0 °C under N$_2$ was added 10 mL of a 1.0 M solution of TBAF in THF. The reaction mixture turned dark immediately. After 1 h of stirring at 0 °C, the reaction mixture was poured over a mixture of 15 mL of ice water and 25 mL of pentane contained in a separatory funnel. The organic layer was separated and washed with water, a 0.05 M solution of HCl, a saturated aqueous NaHCO$_3$ solution, and a saturated aqueous NaCl solution. The organic layer was then dried over MgSO$_4$ and concentrated. The residue was purified by column chromatography (silica gel/pentane) to furnish 0.122 g (1.03 mmol, 57%) of **10a** (Z:E = 96:4) as a colorless liquid: ^{1}H (C$_6$D$_6$) δ 6.54 (1 H, dd of septet, $J = 11.0$, 1.1 and 2.8 Hz), 6.21 (1 H, td, $J = 11.0$ and 1 Hz), 5.18 (1 H, ddd, $J = 10.5$, 2.4, and 1 Hz), 2.91 (1 H, dd, $J = 2.4$ and 1 Hz), 1.48 (6 H, d, $J = 2.8$ Hz); ^{13}C (C$_6$D$_6$) δ 207.68, 139.60, 106.75, 96.85, 90.86, 84.09, 80.66, 20.01; MS *m/e* 118 (M$^+$), 103, 91, 77.

Cycloaromatization of 10a. A mixture of 0.122 g (1.03 mmol) of **10a** in 5 mL of 1,4-cyclohexadiene was kept under an N$_2$ atmosphere at 37 °C for 15 h. The reaction products were analyzed by GC and were found to contain 43% of cumene (**12**), 2% of 1,2-dimethyl-1,2-diphenylethane (**13**), and 15% of the combination products **14a** and **14b** (1:1).

The rate of the reaction was measured by conducting cycloaromatization of **10a** (ca. 0.2 M) in C$_6$D$_6$ in the presence of an excess of 1,4-cyclohexadiene (1.2 M) under an N$_2$ atmosphere at 37 °C. The rate of disappearance of **10a** was monitored by the ^{1}H NMR using 1,4-dibromobenzene as an internal standard. The half-life of the reaction at 37 °C was determined to be ca. 70 min.

(*Z*)-8,8-Dimethyl-7-(1,1-dimethylethyl)-3,5,6-nonatrien-1-yne (10b). To a dispersion of 0.72 g (18 mmol) of KH in 30 mL of a 1:1 mixture of pentane and diethyl ether at 0 °C was added 1.71 g (4.21 mmol) of **8b**. After 4 h of stirring, KH was removed by filtration, and the filtrate was treated with 2 g of NaOEt in 20 mL of EtOH. After 12 h of stirring, the reaction mixture was extracted with pentane, washed with water, and concentrated. The residue was purified by column chromatography (silica gel/hexanes) to furnish 0.713 g (3.53 mmol, 84%) of **10b** (Z:E > 99:1) as a colorless liquid: IR (neat) 3312, 1919, 1683 cm^{-1}; ^{1}H (CDCl$_3$) δ 6.34 (1 H, d, $J = 10.8$ Hz), 6.28 (1 H, td, $J = 11.0$ and 0.9 Hz), 5.26 (1 H, dd, $J = 9.3$ and 2.7 Hz), 3.24 (1 H, dd, $J = 2.4$ and 0.7 Hz), 1.19 (18 H, s); ^{13}C (CDCl$_3$) δ 208.72, 140.62, 123.15, 104.61, 93.63, 83.01, 80.86, 35.22, 32.12; MS *m/e* 202 (M$^+$), 187, 159, 145, 117, 91, 77.

Cycloaromatization of 10b. A mixture of 0.202 g (1.00 mmol) of **10b** and 0.8 g (10 mmol) of 1,4-cyclohexadiene in 20 mL of benzene under an N$_2$ atmosphere was heated to reflux for 5 h. The reaction mixture was concentrated, and the residue was purified by column chromatography (silica gel/hexanes) to furnish 0.119 g (0.58 mmol, 58%) of **16** as a colorless liquid: IR (neat) 1393, 1367, 740, 706 cm^{-1}; ^{1}H (CDCl$_3$) δ 7.48−7.07 (5 H, m), 2.42 (1 H, s), 1.11 (18 H, s); ^{13}C (CDCl$_3$) δ 144.66, 133.36, 128.25, 127.25, 126.70, 125.39, 65.97, 35.97, 32.07; MS *m/e* 148 (M$^+$ − 56), 131, 117, 105, 91, 57.

The rate of cycloaromatization of **10b** was also measured by conducting the reaction in C$_6$D$_6$ in the presence of an excess of 1,4-cyclohexadiene. The rate of disappearance of **10b** and the appearance of **16** were monitored by ^{1}H NMR at 76 °C. The half-life of the reaction was determined to be ca. 60 min.

(*Z*)-6-Methyl-2,4,5-heptatrienenitrile (18a). To a solution of 0.446 g (2.9 mmol) of **17** in 6 mL of THF was added dropwise 1.15 mL of a 2.5 M solution of *n*-butyllithium (2.9 mmol) in hexanes at −78 °C. After 10 min, a solution of 0.553 g (0.67 mL, 2.9 mmol) of triisopropyl borate in 1.5 mL of THF was added. After an additional 10 min, 0.28 g (2.9 mmol) of the conjugated allenic aldehyde **7a** was introduced, and the reaction mixture was allowed to stir at rt for 12 h. Hexanes (10 mL) was added, and the reaction mixture was washed with water, dried over Na$_2$SO$_4$, and concentrated. The residue was purified by column chromatography (silica gel/2.5% ethyl acetate in hexanes) to furnish 0.235 g (1.97 mmol, 68%) of **18a** (Z:E = 9:1) as a light yellow liquid: IR (neat) 2214, 1949, 1592, 1232, 743 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 6.69 (1 H, t, $J = 10.9$ Hz), 6.14 (1 H, dd of septet, $J = 11.2$, 0.9, and 2.8 Hz), 5.08 (1 H, dd, $J = 10.6$ and 0.9 Hz), 1.75 (6 H, d, $J = 2.8$ Hz); ^{13}C NMR (CDCl$_3$) δ 209.82, 148.29, 116.32, 98.17, 94.75, 90.07, 19.68; MS *m/e* 119 (M$^+$), 118, 104, 91, 77. A minor set of the ^{1}H NMR signals at 6.86 (l H, dd, $J = 15.9$ and 10.8 Hz), 5.75 (1 H, dd of septet, $J = 10.8$, 0.7 and 2.8 Hz), and 5.26 (1 H, dd, $J = 16.0$ and 10.6 Hz) attributable to the presence of the *E* isomer were also observed.

(*Z*)-7,7-Dimethyl-6-(1,1-dimethylethyl)-2,4,5-octatrienenitrile (18b). To a solution of 0.31 g (2.0 mmol) of **17** in 20 mL of THF was added 0.80 mL of a 2.5 M solution of *n*-butyllithium (2.0 mmol) in hexanes at −78 °C. After 20 min, 0.30 mL (0.27 g, 2.6 mmol) of trimethyl borate was added. After an additional 20 min at −78 °C, 0.36 g (2.0 mmol) of **7b** in 5 mL of THF was introduced, and the reaction mixture was stirred at −78 °C for 1 h before 6 mL of water was added. The organic layer was separated, and the aqueous layer was extracted with diethyl ether (3 × 20 mL). The combined organic layers were dried over MgSO$_4$ and concentrated. The residue was purified by column chromatography (silica gel/hexanes) to furnish 0.35 g (1.74 mmol, 87%) of **18b** (Z:E = 98:2) as a light yellow liquid: IR (neat) 2214, 1916, 1585, 1471, 1083, 736, 700, 679 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 6.67 (1 H, dd, $J = 11.2$ and 10.6 Hz), 6.29 (1 H, dd, $J = 11.3$ and 1.0 Hz), 5.03 (1 H, dd, $J = 10.6$ and 0.9 Hz), 1.20 (18 H, s); ^{13}C NMR (CDCl$_3$) δ 211.11, 148.70, 124.37, 116.51, 93.65, 93.51, 35.17, 31.81; MS *m/e* 203 (M$^+$), 188, 147, 146, 132, 91, 77, 57.

Acknowledgment. The financial support of the National Science Foundation (CHE-9307994) to K.K.W. and sabbatical leave and a Research Development Grant of the Pennsylvania State University to P.D.S. are gratefully acknowledged.

Supporting Information Available: ^{1}H and ^{13}C NMR spectra of **7b**, **8a**, **8b**, **9a**, **10a**, **10b**, **16**, **18a**, and **18b** (18 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO9517149