Stereoselective Synthesis of Enediynes and Enyne–Allenes Having a Tetrasubstituted Central Carbon–Carbon Double Bond

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The trimethyltin-substituted alkenylborane **2** was prepared by simply treating lithium 1-alkynyltrialkylborate **1**, readily obtained from the corresponding trialkylborane and 1-lithio-1-alkyne, with trimethyltin chloride. The transformation is stereoselective with the boron and tin appendages cis to each other. Sequential treatment of **2** generated in situ with *n*-butyllithium, $CuBr{\cdot}SMe_2$, 1-bromo-1-alkyne, and iodine furnished the corresponding enynyl iodide **3** in a single operation. Similarly, ene-allenic iodide **7a** was produced by coupling with methanesulfonate **6**. The subsequent $Pd(PPh_3)_4$-catalyzed cross-coupling between **3** or **7a** with 1-alkynylzinc chloride or with 1-alkyne in the presence of $CuI/n\text{-}BuNH_2$ produced enediyne **4** or enyne–allene **8** having a tetrasubstituted central double bond. The use of propargyl alcohol for coupling with **7a** resulted in the formation of **10**, presumably because a facile cycloaromatization reaction of the anticipated enyne–allene **9** occurred.

Recent interest in enediyne and enyne–allene chemistry has focused mainly on the use of these chemical structures in generating biradicals as potential DNA-cleaving agents.[1] The possibility of using the resulting biradical species for synthetic applications has received much less attention. It can be imagined that the high reactivities of the radical centers could promote many interesting chemical transformations.[2] One such example involves capturing the radical centers intramolecularly by properly situated carbon–carbon double or triple bonds to furnish multiring structures.[3] It is also apparent that the versatility of this approach could be greatly enhanced if enediynes[4] and enyne–allenes[3a,b,5] with diverse chemical structures could be readily synthesized. To this end, we have thus developed a facile route to both enediynes and enyne–allenes having a tetrasubstituted central double bond.

We reported earlier that the different reactivities of the boron and tin appendages in the trimethyltin-substituted alkenylborane **2** can be independently exploited.[6] This strategy was successfully utilized for sequential coupling with alkyl halides, leading to the tetrasubstituted alkenes. We now have extended this approach to the synthesis of a variety of enediynes and enyne–allenes.

Treatment of lithium 1-alkynyltriethylborate **1**, readily obtained from triethylborane and the corresponding 1-lithio-1-alkyne, with trimethyltin chloride furnished the trimethyltin-substituted alkenylborane **2** with the boron and tin substituents cis to each other (Scheme 1).[7] The chemical reactivity of the boron functionality was then first exploited by adding *n*-butyllithium to form the corresponding borate complex without interference from the adjacent trimethyltin group. The reaction mixture was then treated with a solution containing $CuBr{\cdot}SMe_2$[8] to promote cross-coupling with 1-bromo-1-alkyne.[9] Direct treatment of the resulting enynylstannane with iodine provided enynyl iodide **3** in a single operation from triethylborane without isolation of any reaction intermediates (Table 1). A straightforward $Pd(PPh_3)_4$-catalyzed cross-coupling of **3** with 1-alkynylzinc chloride[10] or with 1-alkyne in the presence of $CuI/n\text{-}BuNH_2$[4b] produced enediyne **4** in good yields (Table 2).

The enediynes listed in Table 2 were found to contain essentially only one geometric isomer. The geometry of the central carbon–carbon double bond was assigned on the basis of earlier reports that the two cross-coupling steps[4b,9,10] as well as iodination of alkenylstannanes[6] are stereospecific with retention of the geometry of the

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(1) Nicolaou, K. C.; Dai, W.-M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1387–1416 and refs cited therein.

(2) Curran, D. P. *Synthesis* **1988**, 417–439 and 489–513.

(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. (c) Bharucha, K. N.; Marsh, R. M.; Minto, R. E.; Bergman, R. G. *J. Am. Chem. Soc.* **1992**, *114*, 3120–3121. (d) Grissom, J. W.; Calkins, T. L.; Egan, M. *J. Am. Chem. Soc.* **1993**, *115*, 11744–11752. (e) Grissom, J. W.; Calkins, T. L.; McMillen, H. A. *J. Org. Chem.* **1993**, *58*, 6556–6558. (f) Xu, S. L.; Taing, M.; Moore, H. W. *J. Org. Chem.* **1991**, *56*, 6104–6109.

(4) (a) Wang, K. K.; Wang, Z.; Gu, Y. G. *Tetrahedron Lett.* **1993**, *34*, 8391–8394. (b) Vollhardt, K. P. C.; Winn, L. S. *Tetrahedron Lett.* **1985**, *26*, 709–712. (c) Stracker, E. C.; Zweifel, G. *Tetrahedron Lett.* **1991**, *32*, 3329–3332. (d) Magnus, P.; Lewis, R. T.; Huffman, J. C. *J. Am. Chem. Soc.* **1988**, *110*, 6921–6923. (e) Magnus, P.; Annoura, H.; Harling, J. *J. Org. Chem.* **1990**, 55, 1709–1711. (f) Magriotis, P. A.; Kim, K. D. *J. Am. Chem. Soc.* **1993**, *115*, 2972–2973. (g) Petasis, N. A.; Teets, K. A. *Tetrahedron Lett.* **1993**, *34*, 805–808. (h) Myers, A. G.; Dragovich, P. S. *J. Am. Chem. Soc.* **1992**, *114*, 5859–5860. (i) Semmelhack, M. F.; Gallagher, J. *Tetrahedron Lett.* **1993**, *34*, 4121–4124. (j) Schreiber, S. L.; Kiessling, L. L. *J. Am. Chem. Soc.* **1988**, *110*, 631–633. (k) Danishefsky, S. J.; Mantlo, N. B.; Yamashita, D. S. *J. Am. Chem. Soc.* **1988**, *110*, 6890–6891. (l) Lockhart, T. P.; Comita, P. B.; Bergman, R. G. *J. Am. Chem. Soc.* **1981**, *103*, 4082–4090.

(5) (a) Myers, A. G.; Kuo, E. Y.; Finney, N. S. *J. Am. Chem. Soc.* **1989**, *111*, 8057–8059. (b) Myers, A. G.; Dragovich, P. S. *J. Am. Chem. Soc.* **1989**, *111*, 9130–9132. (c) Nagata, R.; Yamanaka, H.; Okazaki, E.; Saito, I. *Tetrahedron Lett.* **1989**, *30*, 4995–4998. (d) Nagata, R.; Yamanaka, H.; Murahashi, E.; Saito, I. *Tetrahedron Lett.* **1990**, *31*, 2907–2910. (e) Wang, K. K.; Wang, Z. *Tetrahedron Lett.* **1994**, *35*, 1829–1832.

(6) (a) Wang, K. K.; Chu, K.-H.; Lin, Y.; Chen, J.-H. *Tetrahedron* **1989**, *45*, 1105–1118. (b) Chu, K.-H.; Wang, K. K. *J. Org. Chem.* **1986**, *51*, 767–768.

(7) (a) Hooz, J.; Mortimer, R. *Tetrahedron Lett.* **1976**, 805–808. (b) Wrackmeyer, B.; Bihlmayer, C.; Schilling, M. *Chem. Ber.* **1983**, *116*, 3182–3191. (c) Zweifel, G.; Backlund, S. J. *J. Organomet. Chem.* **1978**, *156*, 159–170. (d) Wang, K K.; Chu, K.-H. *J. Org. Chem.* **1984**, *49*, 5175–5178.

(8) (a) Campbell, J. B., Jr.; Brown, H. C. *J. Org. Chem.* **1980**, *45*, 549–550. (b) Yamamoto, Y.; Yatagai, H.; Maruyama, K.; Sonoda, A.; Murahashi, S.-I. *J. Am. Chem. Soc.* **1977**, *99*, 5652–5656.

(9) (a) Brown, H. C.; Molander, G. A. *J. Org. Chem.* **1981**, *46*, 645–647. (b) Magriotis, P. A.; Scott, M. E.; Kim, K. D. *Tetrahedron Lett.* **1991**, *32*, 6085–6088.

(10) (a) King, A. O.; Okukado, N.; Negishi, E.-i. *J. Chem. Soc., Chem. Commun.* **1977**, 683–684. (b) Satoh, Y.; Serizawa, H.; Miyaura, N.; Hara, S.; Suzuki, A. *Tetrahedron Lett.* **1988**, *29*, 1811–1814.

0022-3263/94/1959-4738$04.50/0

Scheme 1

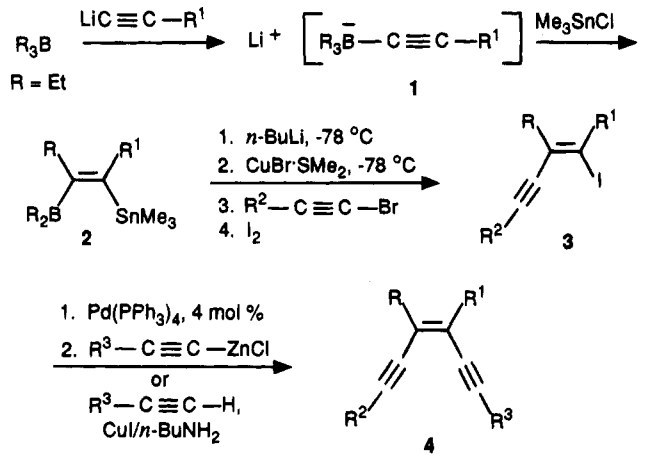
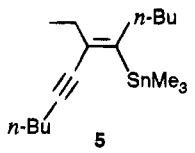


Table 1. Stereoselective Synthesis of Enynyl Iodide 3

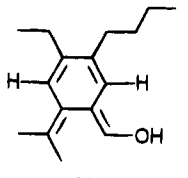
enynyl iodide	R^1	R^2	isolated yield, %
3a	*n*-Bu	*n*-Bu	71
3b	*n*-Bu	Ph	74
3c	Ph	*n*-Bu	63

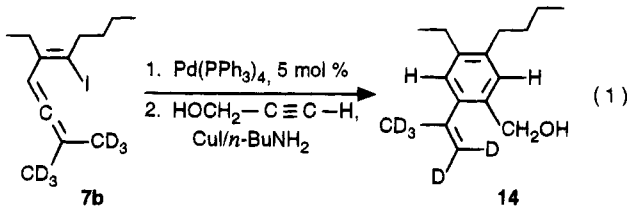
alkenyl group. The four substituents on the enediyne system were easily assembled from triethylborane and a variety of terminal alkynes, including 1-hexyne, phenylacetylene, (trimethylsilyl)acetylene, 1-ethynylcyclohexene, propargyl alcohol, and 2-methyl-3-butyn-2-ol. It was also possible to isolate enynylstannane **5** (70% yield) from **2a**, providing opportunities to use the chemical reactivities of alkenylstannane for subsequent synthetic elaborations.[11]



By using methanesulfonate **6** derived from 2-methyl-3-butyn-2-ol for cross-coupling with **2a**,[12] ene-allenic iodide **7a** was obtained in 50% yield from triethylborane (Scheme 2). The subsequent $Pd(PPh_3)_4$-catalyzed cross-coupling with phenylacetylene in the presence of CuI/*n*-$BuNH_2$ proceeded smoothly to produce enyne–allene **8** in 59% yield. Enyne-allene **8** was stable enough to allow purification and isolation by column chromatography.

Interestingly, the use of $Pd(PPh_3)_4$ to promote cross-coupling between ene-allenic iodide **7a** and propargyl alcohol resulted in the formation of the cycloaromatized adduct **10** in 58% yield (Scheme 3). Although it appears that a facile Myers cycloaromatization reaction[3a,b,5] of the initially formed enyne–allene **9** to produce α,3-dehydrotoluene biradical **11** followed by two hydrogen-transfer steps through **12** could account for the formation of **10** (Scheme 4), it is not at all certain that this is the actual reaction pathway. Instead, one normally would expect the hydrogen atoms at C-3 carbon of the butyl group to undergo a faster 1,5-hydrogen shift to the benzenoid radical center because the methylene C–H bond (ca. 95 kcal/mol) is weaker than the O–H bond of alcohols (ca. 110 kcal/mol).[13] The possibility of a 1,3-hydrogen shift to produce *o*-quinodimethane **13** was also ruled out because of a lack of deuterium incorporation to the benzylic carbon bearing the hydroxyl group as shown in **14** when deuterated ene-allenic iodide **7b** was utilized (eq 1). It is also unlikely that disproportionation occurred intermolecularly because of the extreme low concentrations of the radical species.





(1)

Perhaps an alternative reaction mechanism involving a cationic pathway could better account for the formation of **10** (Scheme 5). Protonation of the carbon–carbon triple bond with the help of the adjacent hydroxyl group could trigger the cycloaromatization reaction, leading to benzylic cation **15** and consequently **10**. The possibility of having the palladium catalyst serve as a Lewis acid in forming a complex with the carbon–carbon triple bond and thus promote the cycloaromatization reaction is also an attractive alternative. Further studies will be needed to determine the actual reaction mechanism.

In conclusion, the reaction sequences summarized in Schemes 1 and 2 provide facile synthetic routes to enediynes and enyne–allenes having a tetrasubstituted central carbon–carbon double bond. The ability to place a variety of substituents at different positions of the enediyne and enyne–allene systems is an especially attractive feature and creates pathways to highly functionalized derivatives for subsequent synthetic elaborations.

Experimental Section

General procedures for manipulation of organoboranes and other organometallic reagents were described previously.[14] All reactions were conducted in oven-dried (120 °C) glassware under a nitrogen atmosphere. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were distilled from sodium benzophenone ketyl prior to use. *N,N*-Dimethylformamide (DMF), *n*-butylamine, and hexamethylphosphoramide (HMPA) were distilled from CaH_2 and stored under a nitrogen atmosphere. The following reagents were purchased from Aldrich Chemical Co., Inc., and were used without further purification: 1-alkynes, $Pd(PPh_3)_4$, trimethyltin chloride (1.0 M in THF), *n*-butyllithium (2.5 M in hexanes), triethylborane (1.0 M in THF), $CuBr{\cdot}SMe_2$, CuI, and methanesulfonyl chloride. 1-Bromo-1-hexyne and 1-bromo-2-phenylacetylene were prepared according to the reported procedures.[15] Silica gel (70–230 mesh) for column chromatography was also obtained from Aldrich. ^1H (270 MHz) and ^{13}C (67.9 MHz) NMR spectra were recorded in

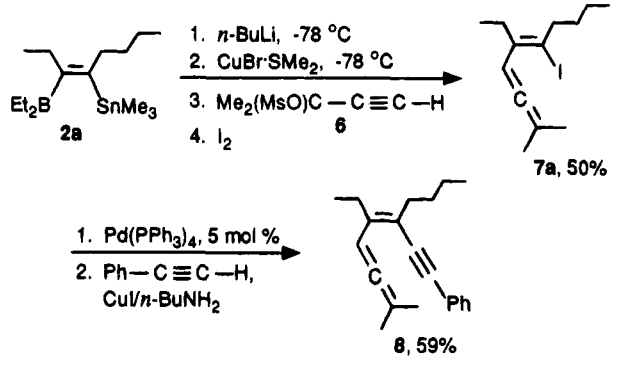
(11) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508–524.
(12) Westmijze, H.; Ruitenberg, K.; Meijer, J.; Vermeer, P. *Tetrahedron Lett.* **1982**, *23*, 2797–2798.
(13) March, J. *Advanced Organic Chemistry*, 3rd ed.; Wiley-Interscience: New York, 1985; p 23 and p 166.
(14) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. *Organic Syntheses via Boranes*; Wiley-Interscience: New York, 1975.
(15) Brandsma, L. *Preparative Acetylenic Chemistry*, 2nd ed.; Elsevier: Amsterdam, 1988; pp 149–151.

Table 2. Stereoselective Synthesis of Enediyne 4

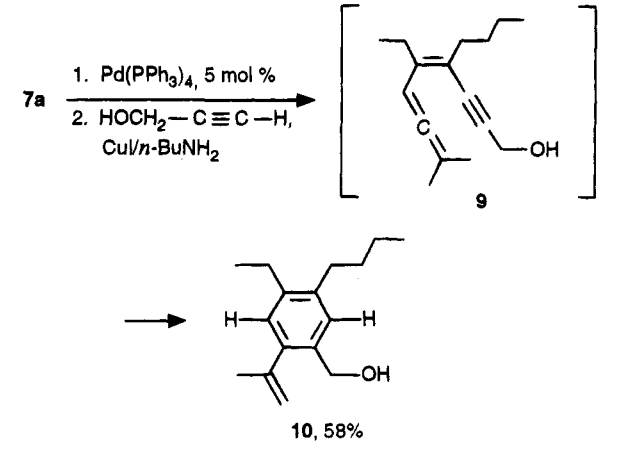
enynyl iodide	cross-coupling method[a]	enediyne	R^1	R^2	R^3	reaction temp, °C	reaction time, h	isolated yield, %
3a	A	**4a**	*n*-Bu	*n*-Bu	Ph	40	4	51
3a	A	**4b**	*n*-Bu	*n*-Bu	Me_3Si	rt	15	61
3a	A	**4c**	*n*-Bu	*n*-Bu	1-cyclohexenyl	40	4	50
3a	B	**4d**	*n*-Bu	*n*-Bu	hydroxymethyl	40	4	70
3a	B	**4e**	*n*-Bu	*n*-Bu	1-hydroxy-1-methylethyl	40	4	77
3b	A	**4f**	*n*-Bu	Ph	*n*-Bu	rt	20	90
3b	B	**4g**	*n*-Bu	Ph	hydroxymethyl	40	4	53
3c	B	**4h**	Ph	*n*-Bu	hydroxymethyl	40	4	57

[a] Method A utilized 1-alkynylzinc chloride for cross-coupling with enynyl iodide **3**, whereas method B utilized 1-alkyne in the presence of CuI and *n*-$BuNH_2$ for cross-coupling.

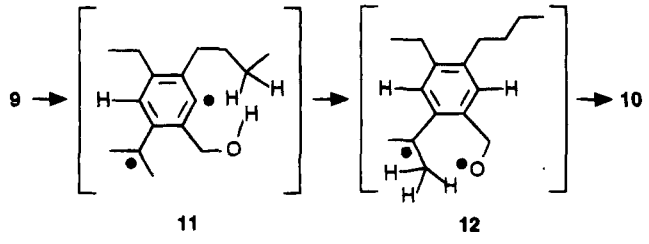
Scheme 2



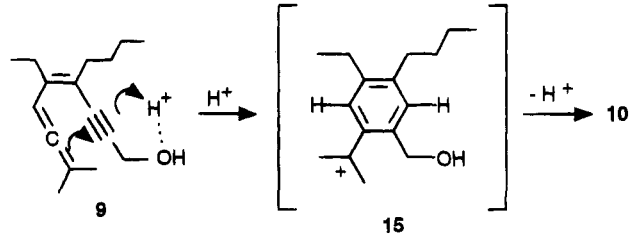
Scheme 3



Scheme 4



Scheme 5



$CDCl_3$ or C_6D_6 using Me_4Si, $CHCl_3$ (^1H δ 7.26), $CDCl_3$ (^{13}C δ 77.02), C_6D_5H (^1H δ 7.15), or C_6D_6 (^{13}C δ 128.00), as internal standard. Mass spectra were obtained at 70 eV, and the fragments containing ^{120}Sn are indicated with an asterisk.

(Z)-6-Ethyl-5-iodo-5-dodecen-7-yne (3a). The following procedure for the preparation of **3a** is representative. To a flask equipped with a low-temperature thermometer were successively added by syringes 5 mL of THF and 0.58 mL of 1-hexyne (0.41 g, 5.0 mmol). *n*-Butyllithium (2.5 M in hexanes, 2.0 mL, 5.0 mmol) was then introduced dropwise at 0 °C. After 15 min of stirring, triethylborane (5.0 mL, 1.0 M in THF, 5.0 mmol) was slowly introduced and the reaction mixture was then allowed to warm to rt and stirred for 1 h followed by the addition of 5.0 mL of a 1.0 M solution of trimethyltin chloride (5.0 mmol) in THF. After 1 h at rt, the reaction mixture was cooled to −78 °C and treated with 2.0 mL of a 2.5 M solution of *n*-butyllithium (5.0 mmol) in hexanes. After 15 min, the reaction mixture was transferred via cannula to a second flask containing 1.03 g of $CuBr·SMe_2$ (5.0 mmol) in 10 mL of THF maintained at −78 °C. After an additional 1 h at −78 °C, 1-bromo-1-hexyne (1.0 g, 6.2 mmol) was introduced dropwise and the reaction mixture was stirred for 1 h at −78 °C before allowing to warm slowly to rt. The reaction mixture was treated with 5 mL of a 6 N NaOH solution and 5 mL of a 30% H_2O_2 solution. The organic layer was then separated, washed with water, dried over $MgSO_4$, and concentrated to give the corresponding crude enynylstannane derivative. A solution of I_2 (1.3 g, 5.0 mmol) in 10 mL of Et_2O was added to the crude enynylstannane derivative in 20 mL of Et_2O. The resulting mixture was stirred for 1 h at rt followed by the addition of a saturated $Na_2S_2O_3$ solution to destroy excess I_2. An additional 40 mL of water and 50 mL of Et_2O were added and the organic layer was then separated, washed with a saturated NaCl solution, dried over $MgSO_4$, and concentrated. The residue was purified by column chromatography (silica gel/hexanes) to furnish 1.13 g of **3a** (71% yield) as a yellow liquid: IR (neat) 2217 (w), 1594 (w), 1464 (s), 1114 (m) cm^{-1}; ^1H ($CDCl_3$) δ 2.56 (2 H, t, J = 7.4 Hz), 2.36 (2 H, t, J = 6.8 Hz), 2.25 (2 H, t, J = 7.5 Hz), 1.6−1.4 (6 H, m), 1.38−1.25 (2 H, m), 1.09 (3 H, t, J = 7.5 Hz), 0.92 (3 H, t, J = 7.1 Hz), 0.91 (3 H, t, J = 7.2 Hz); ^{13}C ($CDCl_3$) δ 132.70, 110.90, 93.59, 85.23, 40.30, 31.82, 30.67, 26.66, 22.02, 21.72, 19.24, 13.97, 13.63, 13.56; MS *m/e* 318 (M^+), 275, 191; HRMS calcd for $C_{14}H_{23}I$ 318.0846, found 318.0849.

(Z)-3-Ethyl-4-iodo-1-phenyl-3-octen-1-yne (3b): IR (neat) 2203 (w), 1660 (w), 1600 (s), 1488 (s), 754 (s), 689 (s) cm^{-1}; ^1H ($CDCl_3$) δ 7.54−7.51 (2 H, m), 7.35−7.30 (3 H, m), 2.65 (2 H, t, J = 7.4 Hz), 2.38 (2 H, q, J = 7.5 Hz), 1.56 (2 H, quintet), 1.37 (2 H, sextet), 1.20 (3 H, t, J = 7.5 Hz), 0.95 (3 H, t, J = 7.2 Hz); ^{13}C ($CDCl_3$) δ 132.30, 131.45, 128.24, 128.21, 123.37, 113.36, 94.23, 91.97, 40.51, 31.87, 26.43, 21.73, 13.98, 13.62; MS *m/e* 338 (M^+), 295, 211.

(Z)-2-Ethyl-1-iodo-1-phenyl-1-octen-3-yne (3c): IR (neat) 2216 (s), 1601 (m), 1486 (s), 765 (s), 695 (s) cm^{-1}; ^1H ($CDCl_3$, Me_4Si) δ 7.33−7.20 (5 H, m), 2.45 (2 H, t, J = 6.8 Hz), 2.12 (2 H, q, J = 7.5 Hz), 1.62−1.48 (4 H, m), 1.06 (3 H, t, J = 7.5 Hz), 0.95 (3 H, t, J = 7.1 Hz); ^{13}C ($CDCl_3$) δ 143.00, 135.26, 128.40, 128.12, 127.90, 102.07, 96.36, 84.59, 30.61, 27.87, 22.03, 19.34, 13.69, 13.63; MS *m/e* 338 (M^+), 295, 211.

(Z)-3-Butyl-4-ethyl-1-phenyl-3-decene-1,5-diyne (4a). The following procedure for the preparation of **4a** is representative for the cases using 1-alkynylzinc chloride for cross-

coupling. A solution of 0.638 g of **3a** (2.00 mmol) and 0.088 g of $Pd(PPh_3)_4$ (0.076 mmol) in 5 mL of THF was degassed by three cycles of freeze-thaw and stirred at rt for 30 min. In a second flask, 0.255 g of phenylacetylene (2.50 mmol) was dissolved in 5 mL of THF and was then treated with 1.0 mL of a 2.5 M solution of *n*-butyllithium (2.5 mmol) in hexanes at 0 °C followed by the addition of a degassed solution of anhydrous zinc chloride (0.34 g, 2.5 mmol) in 5 mL of THF. After 5 min, the reaction mixture containing **3a** was transferred via cannula to the second reaction flask followed by the addition of 2 mL of HMPA. The resulting solution was stirred at 40 °C for 4 h followed by the addition of 20 mL of water and 40 mL of pentane. The organic layer was separated, washed with a saturated NaCl solution, dried over $MgSO_4$, and concentrated. The residue was purified by column chromatography (silica gel/hexanes) to afford 0.298 g of **4a** (51% yield) as a pale yellow liquid: IR (neat) 2213 (w), 2193 (w), 1598 (m), 1489 (s), 1465 (s), 755 (s), 690 (s) cm^{-1}; ^1H ($CDCl_3$, Me_4Si) δ 7.47–7.43 (2 H, m), 7.33–7.25 (3 H, m), 2.44 (2 H, t, J = 6.8 Hz), 2.28 (2 H, t, J = 7.6 Hz), 2.26 (2 H, q, J = 7.6 Hz), 1.63–1.31 (8 H, m), 1.12 (3 H, t, J = 7.5 Hz), 0.93 (3 H, t, J = 7.3 Hz), 0.86 (3 H, t, J = 7.2 Hz); ^{13}C ($CDCl_3$) δ 131.52, 131.27, 128.11, 127.72, 126.99, 124.01, 95.45, 92.64, 91.18, 81.48, 31.52, 31.06, 30.95, 25.62, 22.42, 22.00, 19.49, 13.99, 13.63, 13.23; MS *m/e* 292 (M^+), 249, 235, 221.

(*Z*)-3-Butyl-4-ethyl-1-(trimethylsilyl)-3-decene-1,5-diyne (4b): IR (neat) 2214 (w), 2140 (s), 1465 (m), 1249 (s), 842 (s) cm^{-1}; ^1H ($CDCl_3$) δ 2.39 (2 H, t, J = 7.0 Hz), 2.18 (2 H, q, J = 7.5 Hz), 2.17 (2 H, t, J = 7.5 Hz), 1.6–1.4 (6 H, m), 1.4–1.25 (2 H, m), 1.06 (3 H, t, J = 7.5 Hz), 0.91 (3 H, t, J = 7.1 Hz), 0.90 (3 H, t, J = 7.2 Hz), 0.19 (9 H, s); ^{13}C ($CDCl_3$) δ 132.18, 126.97, 106.49, 97.32, 95.47, 81.21, 31.25, 30.99, 30.75, 25.50, 22.34, 22.04, 19.40, 13.93, 13.66, 13.07, 0.10; MS *m/e* 288 (M^+), 273, 245, 215, 73.

(*Z*)-3-Butyl-1-(1-cyclohexenyl)-4-ethyl-3-decene-1,5-diyne (4c): IR (neat) 2215 (w), 2182 (w), 1628 (w), 1458 (s) cm^{-1}; ^1H ($CDCl_3$) δ 6.10 (1 H, tt, J = 4.1 and 1.9 Hz), 2.40 (2 H, t, J = 6.8 Hz), 2.20 (2 H, q, J = 7.5 Hz), 2.18 (2 H, t, J = 7.3 Hz), 2.2 (2 H, m), 2.1 (2 H, m), 1.7–1.4 (10 H, m), 1.4–1.25 (2 H, m), 1.07 (3 H, t, J = 7.5 Hz), 0.91 (3 H, t, J = 7.1 Hz), 0.90 (3 H, t, J = 7.2 Hz); ^{13}C ($CDCl_3$) δ 134.26, 129.95, 127.34, 121.17, 94.83, 94.71, 88.53, 81.55, 31.56, 31.08, 30.89, 29.35, 25.76, 25.50, 22.38 (2 carbons), 22.02, 21.57, 19.46, 13.97, 13.71, 13.24; MS *m/e* 296 (M^+), 281, 267, 253, 240, 239.

(*Z*)-4-Butyl-5-ethyl-4-undecene-2,6-diyn-1-ol (4d). The following procedure for the preparation of **4d** is representative for the cases using 1-alkyne in the presence of CuI/*n*-$BuNH_2$ for cross-coupling. A solution of 0.636 g of **3a** (2.00 mmol), 0.088 g of $Pd(PPh_3)_4$ (0.076 mmol), and 0.060 g of CuI (0.32 mmol) in 10 mL of THF was degassed by three cycles of freeze-thaw. *n*-Butylamine (0.44 g, 0.60 mL, 6.0 mmol) and propargyl alcohol (0.14 g, 0.15 mL, 2.5 mmol) were introduced and the resulting solution was stirred at 40 °C for 4 h before 20 mL of water and 40 mL of Et_2O were added. The organic layer was then separated, washed with a saturated NaCl solution, dried over $MgSO_4$, and concentrated. The residue was purified by column chromatography (silica gel/ethyl acetate:hexanes = 1:9) to afford 0.343 g of **4d** (70% yield) as a pale yellow liquid: IR (neat) 3330 (br, OH), 2212 (w), 1462 (m), 1019 (m) cm^{-1}; ^1H ($CDCl_3$) δ 4.43 (2 H, s), 2.39 (2 H, t, J = 6.7 Hz), 2.18 (2 H, q, J = 7.7 Hz), 2.17 (2 H, t, J = 8.6 Hz), 1.85 (1 H, br s, OH), 1.55–1.4 (6 H, m), 1.30 (2 H, sextet, J = 7.5 Hz), 1.06 (3 H, t, J = 7.5 Hz), 0.91 (3 H, t, J = 7.0 Hz), 0.89 (3 H, t, J = 7.3 Hz); ^{13}C ($CDCl_3$) δ 131.60, 126.16, 95.17, 90.24, 87.07, 81.20, 51.75, 31.46, 30.86, 30.79, 25.50, 22.36, 21.85, 19.33, 13.91, 13.60, 13.11; MS *m/e* 246 (M^+), 217, 187; HRMS calcd for $C_{17}H_{26}O$ 246.1985, found 246.1964.

(*Z*)-5-Butyl-6-ethyl-2-methyl-5-dodecene-3,7-diyn-2-ol (4e): IR (neat) 3419 (br, OH), 2244 (w), 2208 (w), 1463 (s), 1164 (s) cm^{-1}; ^1H (C_6D_6) δ 2.29 (2 H, t, J = 6.8 Hz), 2.15 (2 H, q, J = 7.5 Hz), 2.14 (2 H, t, J = 7.7 Hz), 2.05 (1 H, OH), 1.55 (6 H, s), 1.57–1.30 (6 H, m), 1.24 (2 H, sextet, J = 7.5 Hz), 1.11 (3 H, t, J = 7.5 Hz), 0.84 (3 H, t, J = 7.3 Hz), 0.81 (3 H, t, J = 7.1 Hz); ^{13}C (C_6D_6) δ 131.26, 126.90, 98.00, 94.74, 84.00, 82.26, 65.53, 31.90, 31.79, 31.36, 31.23, 25.90, 22.59, 22.29, 19.68, 14.14, 13.76, 13.50; MS *m/e* 274 (M^+), 259, 245, 217.

(*Z*)-4-Butyl-3-ethyl-1-phenyl-3-decene-1,5-diyne (4f): IR (neat) 2211 (w), 2195 (w), 1598 (m), 1570 (w), 1489 (s), 1464 (s), 754 (s), 690 (s) cm^{-1}; ^1H ($CDCl_3$, Me_4Si) δ 7.40–7.36 (2 H, m), 7.26–7.18 (3 H, m), 2.36 (2 H, t, J = 6.8 Hz), 2.23 (2 H, q, J = 7.6 Hz), 2.16 (2 H, t, J = 7.9 Hz), 1.52–1.35 (6 H, m), 1.28 (2 H, sextet, J = 7 Hz), 1.08 (3 H, t, J = 7.5 Hz), 0.85 (3 H, t, J = 7.3 Hz), 0.79 (3 H, t, J = 7.2 Hz); ^{13}C ($CDCl_3$) δ 131.54, 129.64, 128.65, 128.13, 127.75, 123.95, 95.23, 92.90, 90.85, 81.79, 32.06, 31.03, 30.85, 25.12, 22.44, 21.99, 19.47, 14.00, 13.63, 13.34; MS *m/e* 292(M^+), 277, 263, 249, 235.

(*Z*)-4-Butyl-5-ethyl-7-phenyl-4-heptene-2,6-diyn-1-ol (4g): IR (neat) 3386 (br, OH), 2236 (w), 2210 (w), 1598 (m), 1489 (s), 1025 (s), 755 (s), 690 (s) cm^{-1}; ^1H ($CDCl_3$, Me_4Si) δ 7.49–7.45 (2 H, m), 7.32–7.28 (3 H, m), 4.48 (2 H, s), 2.32 (2 H, q, J = 7.6 Hz), 2.25 (2 H, t, J = 7.9 Hz), 1.99 (1 H, br s, OH), 1.58–1.47 (2 H, m), 1.35 (2 H, sextet, J = 7.5 Hz), 1.17 (3 H, t, J = 7.5 Hz), 0.92 (3 H, t, J = 7.2 Hz); ^{13}C ($CDCl_3$) δ 131.54, 130.86, 128.25, 128.16, 128.04, 123.51, 93.86, 91.61, 90.29, 86.86, 51.72, 31.59, 30.77, 25.11, 22.37, 13.92, 13.20; MS *m/e* 266 (M^+), 237, 223, 209, 207.

(*E*)-5-Ethyl-4-phenyl-4-undecene-2,6-diyn-1-ol (4h): IR (neat) 3362 (br, OH), 2210 (m), 1599 (m), 1014 (s), 771 (s), 700 (s) cm^{-1}; ^1H ($CDCl_3$, Me_4Si) δ 7.35-7.25 (5 H, m), 4.40 (2 H, s), 2.47 (2 H, t, J = 6.8 Hz), 2.25 (1 H, br s, OH), 2.21 (2 H, q, J = 7.5 Hz), 1.6–1.45 (4 H, m), 1.09 (3 H, t, J = 7.5 Hz), 0.94 (3 H, t, J = 7.2 Hz); ^{13}C ($CDCl_3$) δ 137.63, 133.59, 128.54, 128.10, 127.46, 126.04, 98.05, 91.29, 86.76, 80.95, 51.52, 30.69, 26.42, 21.79, 19.37, 13.53, 13.26; MS *m/e* 266 (M^+), 237, 223.

(*Z*)-6-Ethyl-5-(trimethylstannyl)-5-dodecen-7-yne (5). Purification by distillation (94–95 °C, 0.05 torr) of the crude enynylstannane, starting from 20.0 mmol of triethylborane, as described for **3a** afforded 4.943 g of **5** (70% yield) as a colorless liquid: IR (neat) 2213 (w), 1717 (w), 1459 (s), 767 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.31–2.20 (4 H, m), 2.20 (2 H, q, J = 7.5 Hz), 1.55–1.15 (8 H, m), 1.06 (3 H, t, J = 7.5 Hz), 0.91 (3 H, t, J = 7.1 Hz), 0.89 (3 H, t, J = 7.1 Hz), 0.16 (9 H, s); ^{13}C NMR ($CDCl_3$) δ 151.52, 134.66, 88.27, 83.92, 33.38, 32.37, 30.91, 25.12, 22.67, 22.12, 19.14, 14.11, 13.77, 13.63, −8.41; MS *m/e* 341* (M^+ − 15), 231*, 165*.

(*Z*)-5-Ethyl-6-iodo-2-methyl-2,3,5-decatriene (7a). A similar procedure as described for **3a** by starting from triethylborane (10.0 mmol) was utilized. A solution of 15.0 mmol of methanesulfonate **6** was prepared in situ by treating 1.26 g of 2-methyl-3-butyn-2-ol (15.0 mmol) in 10 mL of THF at −70 °C with 6.0 mL of a 2.5 M solution of *n*-butyllithium in hexanes for 15 min followed by 1.16 mL of methanesulfonyl chloride (1.72 g, 15.0 mmol) for 15 min. Methanesulfonate **6** was used to replace 1-bromo-1-hexyne for cross-coupling at −78 °C. The resulting crude alkenylstannane was treated with an I_2 solution in diethyl ether until the color of I_2 persisted (ca. 7 mmol). Purification by column chromatography (silica gel/hexanes) afforded 1.522 g of **7a** (50% yield) as a yellow liquid: IR (neat) 1948 (m), 1678 (w), 1630 (w), 1595 (m), 1455 (s) cm^{-1}; ^1H ($CDCl_3$) δ 6.13 (1 H, septet, J = 2.9 Hz), 2.61 (2 H, t, J = 7.6 Hz), 2.27 (2 H, q, J = 7.4 Hz), 1.73 (6 H, d, J = 2.9 Hz), 1.54 (2 H, quintet, J = 8 Hz), 1.34 (2 H, sextet, J = 7.5 Hz), 0.97 (3 H, t, J = 7.5 Hz), 0.93 (3 H, t, J = 7.3 Hz); ^{13}C ($CDCl_3$) δ 205.41, 139.67, 105.51, 100.10, 97.97, 41.63, 32.02, 23.83, 21.87, 20.20, 14.07, 14.06; MS *m/e* 304 (M^+), 261, 177, 135.

(*Z*)-5-Ethyl-6-iodo-2-[($^2H_3$)methyl]-(1,1,1-$^2H_3$)-2,3,5-decatriene (7b). The same procedure was repeated as described for **7a** except that deuterated 2-methyl-3-butyn-2-ol, derived from acetone-d_6 and lithium acetylide,[16] was used to prepare the corresponding methanesulfonate for cross-coupling with **2a** to afford 1.536 g of **7b** (50% yield) as a yellow liquid: IR (neat) 2234 (m), 2197 (m), 2121 (w), 2063 (m), 1949 (m), 1464 (s) cm^{-1}; ^1H ($CDCl_3$) δ 6.12 (1 H, s), 2.61 (2 H, t, J = 7.6 Hz), 2.27 (2 H, q, J = 7.5 Hz), 1.60–1.48 (2 H, m), 1.35 (2 H, sextet, J = 7.2 Hz), 0.97 (3 H, t, J = 7.5 Hz), 0.93 (3 H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 205.42, 139.69, 105.47, 100.06, 41.63, 32.02, 23.83, 21.88, 14.07, 14.06; MS *m/e* 310 (M^+), 267, 183, 141.

(*Z*)-3-Butyl-4-ethyl-7-methyl-1-phenyl-3,5,6-octatrien-1-yne (8). A solution of 0.608 g of **7a** (2.00 mmol), 0.060 g of

(16) Midland, M. M. *J. Org. Chem.* **1975**, *40*, 2250–2252.

CuI (0.32 mmol), and 0.110 g of $Pd(PPh_3)_4$ (0.095 mmol) in 10 mL of DMF was degassed by three cycles of freeze-thaw followed by the addition of 0.60 mL of *n*-butylamine (0.44 g, 6.0 mmol) and 0.25 mL of phenylacetylene (0.23 g, 2.3 mmol). The resulting solution was stirred at rt for 3 h before a saturated NH_4Cl solution (20 mL) was added and the reaction mixture was exposed to air. After 1 h, an additional 40 mL of pentane and 20 mL of water were added. The organic layer was separated, washed with a saturated NaCl solution, dried over $MgSO_4$, and concentrated. The residue was purified by column chromatography (silica gel/hexanes) to afford 0.328 g of **8** (59% yield) as a pale yellow liquid: IR (neat) 2189 (m), 1946 (m), 1598 (m), 1488 (s), 754 (s), 735 (s), 689 (s) cm^{-1}; ^1H ($CDCl_3$, Me_4Si) δ 7.46–7.42 (2 H, m), 7.31–7.24 (3 H, m), 6.57 (1 H, septet, J = 2.9 Hz), 2.30 (2 H, t, J = 7.5 Hz), 2.25 (2 H, q, J = 7.3 Hz), 1.76 (6 H, d, J = 2.9 Hz), 1.65–1.58 (2 H, m), 1.46–1.33 (2 H, sextet), 1.01 (3 H, t, J = 7.5 Hz), 0.95 (3 H, t, J = 7.2 Hz); ^{13}C ($CDCl_3$) δ 204.52, 143.80, 131.22, 128.19, 127.59, 124.09, 118.46, 97.75, 93.78, 90.06, 31.96, 31.23, 22.68, 22.55, 20.28, 14.10, 13.98; MS *m/e* 278 (M^+), 263, 249, 235, 221, 207; HRMS calcd for $C_{21}H_{26}$ 278.2036, found 278.2035. A minor set of signals in the ^1H NMR spectra attributable to a cycloaromatized adduct as in the case of **10** was also detected.

1-Butyl-2-ethyl-5-(hydroxymethyl)-4-(1-methylethenyl)-benzene (10). The same procedure was repeated as described for **8** except that 0.14 g of propargyl alcohol (2.5 mmol) was used for cross-coupling with **7a** to afford, after purification by column chromatography (silica gel/9:1 hexanes:ethyl acetate), 0.269 g of **10** (58% yield) as a colorless liquid: IR (neat) 3333 (br s, OH), 1639 (m), 1458 (s), 1020 (s), 896 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.21 (1 H, s), 6.98 (1 H, s), 5.21 (1 H, dq, J = 2.2 and 1.7 Hz), 4.91 (1 H, dq, J = 2.1 and 1.0 Hz), 4.65 (2 H, s), 2.64 (2 H, q, J = 7.5 Hz), 2.61 (2 H, t, J = 7.7 Hz), 2.09 (3 H, dd, J = 1.5 and 1.1 Hz), 1.69 (1 H, br, OH), 1.65–1.53 (2 H, m), 1.42 (2 H, sextet, J = 7.4 Hz), 1.22 (3 H, t, J = 7.6 Hz), 0.96 (3 H, t, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 144.94, 141.18, 140.56, 139.50, 134.59, 129.20, 128.04, 115.12, 63.26, 33.44, 32.11, 25.25, 25.20, 22.94, 15.36, 14.04; MS *m/e* 232 (M^+), 217, 203, 189, 175.

1-Butyl-2-ethyl-5-(hydroxymethyl)-4-[1-($^2H_3$)methyl-(2,2-$^2H_2$)ethenyl]benzene (14). The same procedure was repeated as described for **10** to afford 0.261 g of **14** (55% yield) as a colorless liquid: IR (neat) 3318 (br s, OH), 2226 (m), 1594 (m), 1462 (s), 1027 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.21 (1 H, s), 6.98 (1 H, s), 4.65 (2 H, s), 2.64 (2 H, q, J = 7.5 Hz), 2.61 (2 H, t, J = 7.2 Hz), 1.70 (1 H, br s, OH), 1.64–1.53 (2 H, m), 1.42 (2 H, sextet, J = 7.3 Hz), 1.22 (3 H, t, J = 7.5 Hz), 0.96 (3 H, t, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 141.17, 139.49, 134.59, 129.21, 128.04, 63.26, 33.44, 32.11, 25.25, 22.94, 15.36, 14.04; MS *m/e* 237 (M^+), 220, 219, 208, 207, 194, 180.

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Supplementary Material Available: ^1H and ^{13}C spectra of **3a–c**, **4a–h**, **5**, **7a,b**, **8**, **10**, and **14** (34 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.