Efficient and Stereoselective Synthesis of Freelingyne *via* Pd-Catalyzed Cross Coupling and Lactonization[1]

Fang Liu[1] and Ei-ichi Negishi*

Department of Chemistry, Purdue University, West Lafayette, Indiana 47907-1393

Received July 24, 1997

Freelingyne (**1**), a sesquiterpene from *Eremophila freelingii*,[2] features several synthetically interesting structural subunits, such as a methyl-substituted (*E*)-alkene and a (*Z*)-γ-alkylidenebutenolide. Although it has been synthesized twice in the past,[3] a mixture of the *Z* and *E* isomers of **1** was obtained in either case as a consequence of nonstereoselective olefination, the reported *Z*/*E* ratio in one case[3a] being 40/60. Herein, we report an efficient synthesis of freelingyne[4] with essentially full control of the alkene geometries, employing the synthetic strategy outlined in Scheme 1.

The *E* and *Z* methyl-substituted alkene units were prepared by the Zr-catalyzed carboalumination with Me_3Al[5] and the Cu-catalyzed methylmagnesation,[6] respectively, of propargyl alcohol, followed by iodinolysis. The stereoselectivity in either case was ≥99%. The yield of (*E*)-3-iodo-2-methyl-2-propen-1-ol (**2**) was 53% and relatively constant. On the other hand, the yield of the *Z* isomer **3** obtained via methylmagnesation ranged from 30 to 75%. At this point, it is not very clear what factor is responsible for the observed yield fluctuation, but efficient and vigorous mechanical stirring of the reaction mixture appears to be essential to obtaining **3** in high yields. Conversion of **3** into (*Z*)-3-iodo-2-methylpropenoic acid (**4**) was achieved by oxidation first with PCC (2 equiv) and Celite in CH_2Cl_2[7] and then with $NaClO_2-H_2O_2$ in the presence of NaH_2PO_3 in MeCN[8] in 57% overall yield.

After protection of **2** with 3,4-dihydro-2*H*-pyran in 84% yield, the Pd-catalyzed cross coupling with commercially available ethynylmagnesium chloride[9] in THF in the presence of 5 mol % of $Pd(PPh_3)_4$ afforded enyne **5** in 94% yield. The direct synthesis of terminal alkynes such as **5** using ethynylzinc or ethynylmagnesium derivatives in the Pd-catalyzed cross coupling[9] offers a distinct advantage over the Sonogashira protocol[10] which is known to require protection−deprotection of the ethynyl group. In this case, HC≡CMgCl was as satisfactory as HC≡CZnBr. However, cross coupling of **5** with 3-iodofuran in the presence of 5 mol % of $Pd(PPh_3)_4$ was best achieved by in situ conversion of **5** into the bromozinc derivatives via sequential treatment with *n*-BuLi and freshly dried $ZnBr_2$. The desired cross-coupling product **6** was obtained in 82% yield along with **5** recovered in 16%. 3-Iodofuran was prepared by treatment of commercially available 3-bromofuran with *n*-BuLi followed by iodinolysis. After removal of the THP group in 97% yields with *p*-TsOH in MeOH, oxidation with Dess−Martin periodinane[11] in CH_2Cl_2 gave the corresponding aldehyde **7** in essentially quantitative yield. Corey-Fuchs olefination[12] of **7** with CBr_4 (3 equiv) and PPh_3 (6 equiv) in the presence of K_2CO_3 afforded the desired dibromide **8** in 95% yield. Its sequential treatment with $NaN(SiMe_3)_2$ (1.5 equiv) in THF, *n*-BuLi (3 equiv), and MeOH provided **9** in 86% yield.

With **4** and **9** in hand, the stage was set for the crucial Pd-catalyzed cross coupling−lactonization tandem process developed recently[13−15] on the basis of an earlier report[16] on an application of the Sonogashira coupling[10] to effect the above-mentioned tandem process. Despite repeated successes observed by ourselves in the synthesis of rubrolides[13] and (+)-goniobutenolide A,[14] our initial attempt to convert **4** and **9** into **1** using 5 mol % each of $Pd(PPh_3)_4$ and CuI in the presence of NEt_3 (4 equiv) in MeCN at 23 °C produced mainly the homo coupling dimer of **9** (68% based on **9**) along with only a trace, if any, of **1**. Formation of the alkyne dimer was, in fact, observed to the extent of 27% in the synthesis of (+)-goniobutenolide A in 55% yield.[14] To probe the main cause for the failure mentioned above, the reaction of phenylethyne with **4** and its bromo analogue **4a** was examined under otherwise the same conditions. To our surprise, this reaction too gave only a trace (<1%) of the desired lactone **11** along with a 26% yield of 1,4-diphenyl-1,3-butadiyne. These results, vis-à-vis our earlier success[13−15] in converting PhC≡CH into **12** and **13** in 75−95% yields using **14** and **15**, respectively, as the halides, led us to suspect **4** and/or other more subtle factors, such as radical sources present in the reaction mixture, as possible causes for the observed failure. Accordingly, the reactions of PhC≡CH with **4** and **14a** as well as their bromo analogues **4a** and **14b** in a nearly 1:1 reactant ratio using the standardized conditions mentioned above were examined. As indicated by the results summarized in Table 1, the observed difficulty has indeed turned out to be subtle and not yet fully clarified. Nonetheless, it may now be largely alleviated by either degassing via several freeze−thaw cycles[17] or addition of an antioxidant, such as *2,6*-di-*tert*-butyl-4-methylphenol (BHT) and Galvinoxyl. The observed difficulty may therefore be tentatively attributed to some radical sources. Additionally,

† Presented at the 213th National Meeting of the American Chemical Society, San Francisco, April 13−17, 1997; Abstract ORGN 1.

(1) Purdue Research Foundation Graduate Research Fellow (1996−97).

(2) Massy-Westropp, R. A.; Reynolds, G. D.; Spotswood, T. M. *Tetrahedron Lett.* **1966**, *18*, 1939.

(3) (a) Knight, D. W.; Pattenden, G. *J. Chem. Soc., Chem. Commun.* **1974**, 188. (b) Ingham, C. F. *Aust. J. Chem.* **1974**, *27*, 1477.

(4) Recently, we were informed about another total synthesis of freelingyne. See: Mori, H.; Kubo, H.; Hara, H.: Katsumura, S. *Tetrahedron Lett.* **1997**, *38*, 5311.

(5) (a) Van Horn, D. E.; Negishi, E. *J. Am. Chem. Soc.* **1978**, *100*, 2252. (b) Negishi, E.; Van Horn, D. E.; King, A. O.; Okukado, N. *Synthesis* **1979**, 501. (c) Negishi, E.; Van Horn, D. E.; Yoshida, T. *J. Am. Chem. Soc.* **1985**, *107*, 6639.

(6) Duboudin, J. G.; Jousseaume, B. *J. Organomet. Chem.* **1979**, *168*, 1.

(7) Corey, E. J.; Kim, C. U.; Takeda, M. *Tetrahedron Lett.* **1972**, 4339.

(8) Dalcanale, E.; Montanari, F. *J. Org. Chem.* **1986**, *51*, 567.

(9) Negishi, E.; Kotora, M.; Xu, C. *J. Org. Chem.* In press.

(10) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467.

(11) (a) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *43*, 4155. (b) Ireland, R. E.; Liu, L. *J. Org. Chem.* **1993**, *58*, 2899.

(12) (a) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769. (b) Lin, N. H.; Overman, L. E.; Rabinson, L. A.; Sharp, M. J.; Zablocki, J. *J. Am. Chem. Soc.* **1996**, *118*, 9062.

(13) Kotora, M.; Negishi, E. *Synthesis* **1997**, 121.

(14) Kotora, M.; Negishi, E. *Tetrahedron Lett.* **1996**, *37*, 9041.

(15) Negishi, E.; Kotora, M. *Tetrahedron* **1997**, *53*, 6707.

(16) Lu, X.; Huang, X.; Ma, S. *Tetrahedron Lett.* **1993**, *34*, 5963.

(17) (a) Magnus, P.; Carter, P.; Elliott, J.; Lewis, R.; Harling, J.; Pitterna, T.; Bauta, W. E.; Fortt, S. *J. Am. Chem. Soc.* **1992**, *114*, 2544. (b) Jacobi, P.; Guo, J.; Rajeswari, S.; Zheng, W. *J. Org. Chem.* **1997**, *62*, 2907.

S0022-3263(97)01360-1 CCC: $14.00

Scheme 1

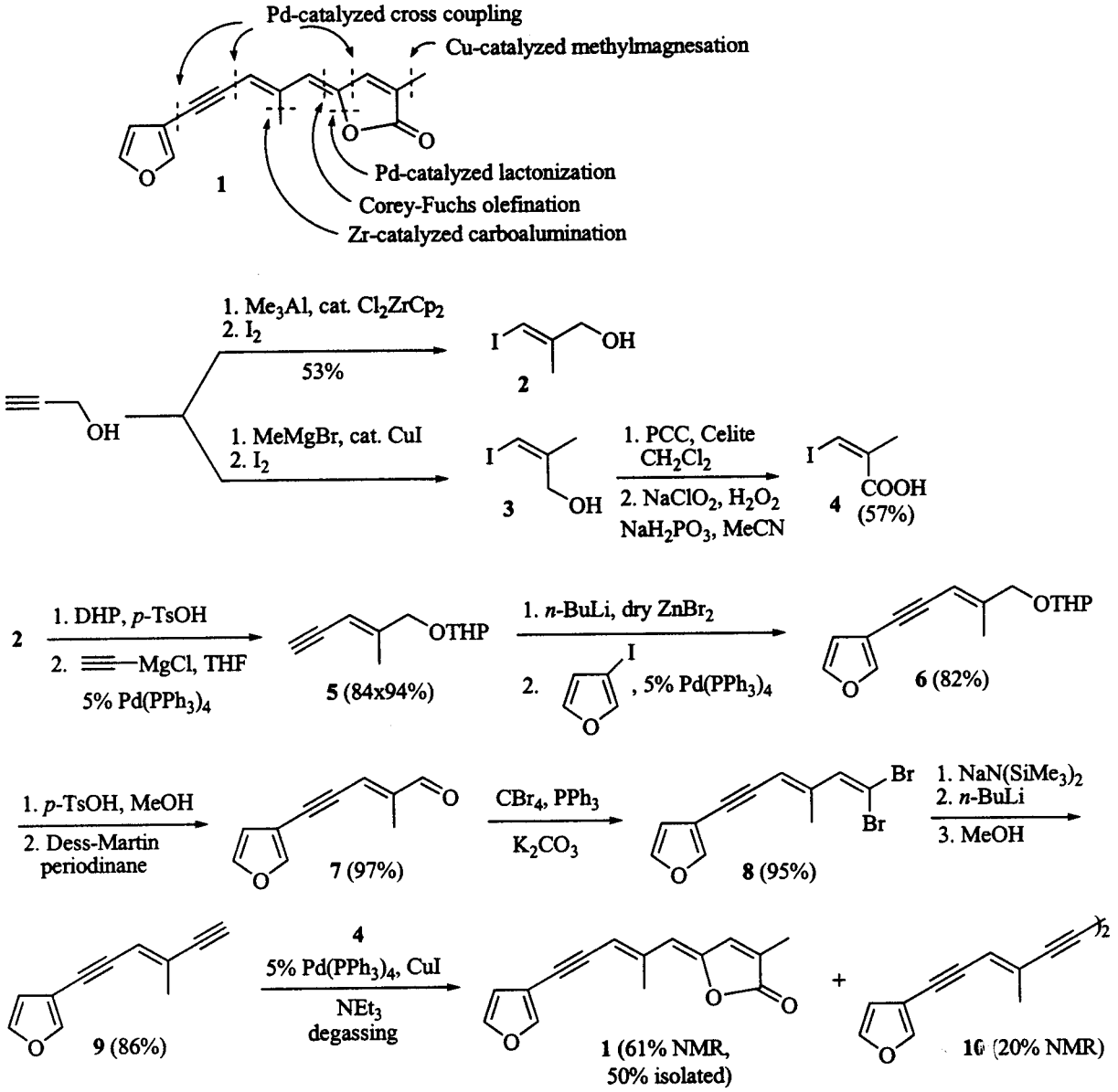
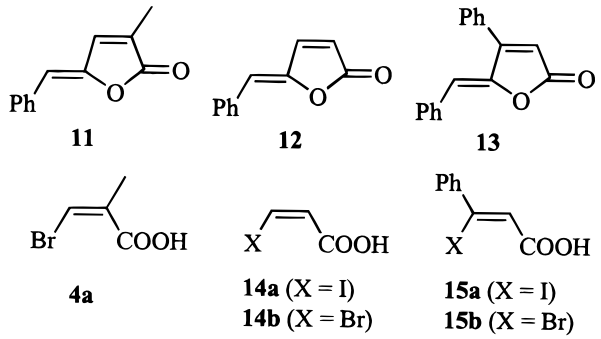


Table 1. Pd-Catalyzed Cross-Coupling−Lactonization Reaction of Phenylethyne with (*Z*)-β-Halomethacrylic Acids and (*Z*)-β-Haloacrylic Acids[a]

		yield,[b] %	
β-halo acid	modification	lactone	PhC≡C−)$_2$
(*Z*)-ICH=C(Me)COOH (**4**)[c]	none	5	50
4	degassing	78	16
4	Galvinoxyl	66	23
(*Z*)-BrCH=C(Me)COOH (**4a**)	none	50	34
4a	degassing	74	20
4a	BHT	77	13
(*Z*)-ICH=CHCOOH (**14a**)	none	trace (≤2)	26
14a	BHT	51	11
(*Z*)-BrCH=CHCOOH (**14b**)[c]	none	50	26

[a] The reaction was carried out at 23 °C in MeCN using 5 mol % each of $Pd(PPh_3)_4$ and CuI as catalysts in the presence of NEt_3 (4 equiv). The ratio of PhC≡CH to β-halo acid was 1.1 unless otherwise stated. [b] By GLC or NMR. [c] 1.5 equiv of PhC≡CH was used.

the following generalizations may be made as tentative guides for future investigation. First, the presence of the α-methyl group in the β-halo acids is not detrimental. The lower yields of **12** observed in this study relative to those reported earlier[13] may be largely attributable to the nearly 1:1 reactant ratio used in this study. Second, β-iodo acids must be much more prone to the observed difficulty than the corresponding β-bromo acids. However, they can give comparably satisfactory results under the modified conditions. Third, degassing and addition of an antioxidant appear to be comparably effective. Even under the modified conditions, however, the formation of 1,4-diphenyl-1,3-butadiyne occurs to the extent of roughly 10−20%.



As expected, the reaction of **4** with **9** run after five freeze−thaw cycles under otherwise the same conditions as mentioned earlier indeed produced freelingyne (**1**) in 61% NMR yield along with the alkyne dimer **10** formed in 20% yield based on **9**. The stereoisomeric purity of **1** was >98%. Further improvement of the Pd-catalyzed cross-coupling−lactonization tandem process and its application to the synthesis of other γ-alkylidenebutenolides are under investigation.

Experimental Section

General Procedures. All reactions involving organometallic reagents were conducted under dry Ar atmosphere. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a 300 MHz spectrometer. NMR yields were determined using CH_2Br_2 as an internal standard. GLC analysis was performed with a column packed with SE-30 Chromosorb W using a TC detector. Unless otherwise mentioned, commercially available reagents were used as received. THF was distilled from sodium benzophenone ketyl.

(*E*)-3-Iodo-2-methyl-1-[(tetrahydropyranyl)oxy]-2-propene. To a mixture of (*E*)-3-iodo-2-methyl-2-propen-1-ol[5b] (1.98 g, 10 mmol) and 3,4-dihydro-2*H*-pyran (1.9 mL, 20 mmol) in CH_2Cl_2 (20 mL) at 0 °C was added *p*-TsOH (190 mg, 1 mmol). The resulting mixture was stirred for 1 h at 23 °C, diluted with ether, washed with aqueous $NaHCO_3$ and NaCl, dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (95:5 pentane−ether) afforded 2.36 g (84%) of the title compound: ^{1}H NMR δ 1.4−2.0 (m, 6 H), 1.85 (s, 3 H), 3.4−3.6 (m, 1 H), 3.75−3.9 (m, 1 H), 3.9−4.05 (m, 1 H), 4.1−4.25 (m, 1 H), 4.60 (d, J = 2.6 Hz, 1 H), 6.25 (s, 1 H); ^{13}C NMR δ 19.15, 21.63, 25.31, 30.36, 61.98, 70.47, 78.14, 97.44, 144.49; IR (neat) 3058, 2942, 1622, 1440, 1282, 1022 cm^{-1}.

(*E*)-2-Methyl-1-[(tetrahydropyranyl)oxy]-2-penten-4-yne (5). To a solution of (*E*)-3-iodo-2-methyl-1-[(tetrahydropyranyl)oxy]-2-propene (5.31 g, 18.8 mmol) in THF (20 mL) at 23 °C was added ethynylmagnesium chloride (0.5 *M* in THF, 56.5 mL, 28.2 mmol) followed by $Pd(PPh_3)_4$ (1.09 g, 0.94 mmol).[9] After stirring for 1 h, the mixture was diluted with ether, washed with aqueous NH_4Cl and NaCl, dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (95:5 pentane−ether) afforded 3.18 g (94%) of **5**: ^{1}H NMR δ 1.4−2.0 (m, 6 H), 1.87 (s, 3 H), 3.04 (d, J = 1.1 Hz, 1 H), 3.4−3.55 (m, 1 H), 3.75−3.85 (m, 1 H), 3.89 (d, J = 14.2 Hz, 1 H), 4.14 (d, J = 14.2 Hz, 1 H), 4.57 (t, J = 3.2 Hz, 1 H), 5.53 (s, 1 H); ^{13}C NMR δ 16.63, 19.06, 25.26, 30.30, 61.81, 69.88, 80.82, 97.57, 104.32, 149.45; IR (neat) 3292, 2944, 2102, 1638, 1442, 1202, 1036 cm^{-1}; MS (CI, 70 eV) *m*/*z* (relative intensity) 181 ($M^+ + 1$, 28), 85 (100); HRMS (CI) calcd for $C_{11}H_{16}O_2$ ($M^+ + 1$) 181.1229, found 181.1223.

(*E*)-5-(3-Furanyl)-2-methyl-1-[(tetrahydropyranyl)oxy]-2-penten-4-yne (6). To a solution of **5** (3.288 g, 18.3 mmol) in THF were added sequentially *n*-BuLi (2.5 *M* in hexane, 7.6 mL, 19 mmol, −78 °C, 20 min), a solution of dry $ZnBr_2$ (4.28 g, 19 mmol) in THF (10 mL) (−78 to 23 °C), 3-iodofuran (1.7 M in THF, prepared by treatment of 3-bromofuran with 1.1 equiv of *n*-BuLi in THF followed by iodinolysis with I_2 in THF, 14.0 mL, 23.8 mmol), and $Pd(PPh_3)_4$ (1.06 g, 0.92 mmol).[18] The resulting mixture was stirred for 1 h at 23 °C, quenched with aqueous NH_4Cl, diluted with ether, washed with aqueous NaCl, dried over $MgSO_4$, filtered, and concentrated. NMR examination indicated the formation of **6** in 82% yield along with unreacted **5** (16%). Chromatographic purification (95:5 pentane−ether) afforded its pure sample: ^{1}H NMR δ 1.4−2.0 (m, 6 H), 1.92 (s, 3 H), 3.4−3.55 (m, 1 H), 3.75−3.9 (m, 1 H), 3.96 (d, J = 14.0 Hz, 1 H), 4.20 (d, J = 14.0 Hz, 1 H), 4.62 (t, J = 3.2 Hz, 1 H), 5.74 (s, 1 H) 6.42 (d, J = 0.7 Hz, 1 H), 7.35 (s, 1 H), 7.58 (s, 1 H); ^{13}C NMR δ 16.84, 19.16, 25.33, 30.40, 61.91, 70.16, 83.89, 97.57, 105.53, 107.90, 112.39, 142.66, 144.87, 147.26; IR (neat) 3146, 2942, 1442, 1350, 1202, 1022 cm^{-1}; MS (EI, 70 eV) *m*/*z* (relative intensity) 246 (M^+, 2), 162 (6), 145 (16), 85 (100); HRMS (EI) calcd for $C_{15}H_{18}O_3$ (M^+) 246.1256, found 246.1257.

(*E*)-5-(3-Furanyl)-2-methyl-2-penten-4-yn-1-ol.[3a] A solution of **6** (3.05 g, 12.4 mmol) in MeOH (40 mL) in the presence of *p*-TsOH (30 mg, 0.16 mmol) was stirred at 23 °C for 1 h. The mixture was diluted with ether, washed with aqueous $NaHCO_3$ and NaCl, dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (75:25 pentane−ether) afforded 1.95 g (97%) of the title compound: ^{1}H NMR δ 1.91 (s, 3 H), 2.7−3.0 (m, 1 H), 4.10 (s, 2 H), 5.72 (s, 1 H), 6.4−6.5 (m, 1 H), 7.3−7.4 (m, 1 H), 7.59 (s, 1 H); ^{13}C NMR δ 16.40, 66.45, 84.02, 88.24, 104.32, 107.79, 112.35, 142.69, 144.91, 149.76; IR (neat) 3356, 3150, 2912, 2198, 1506, 1442, 1350, 1162 cm^{-1}; MS (EI, 70 eV) *m*/*z* (relative intensity) 162 (M^+, 58), 147 (38), 105 (80), 91 (100), 77 (75).

(*E*)-5-(3-Furanyl)-2-methyl-2-penten-4-ynal (7). To a solution of (*E*)-5-(3-furanyl)-2-methyl-2-penten-4-yn-1-ol (630 mg, 3.9 mmol) in CH_2Cl_2 (25 mL) at 0 °C was added Dess−Martin periodinane (5.1 g, 12 mmol).[11] After 1 h at 23 °C, silica gel (5 g) was added, and the solvent was removed in vacuo. Flash chromatography (CH_2Cl_2) afforded 621 mg (100%) of **7**: ^{1}H NMR δ 1.95 (s, 3 H), 6.45−6.5 (m, 1 H), 6.49 (s, 1 H), 7.40 (s, 1 H), 7.69 (s, 1 H), 9.45 (s, 1 H); ^{13}C NMR δ 11.57, 87.36, 98.07, 106.99, 112.09, 128.56, 143.27, 146.36, 147.16, 193.63; IR (neat) 3150, 2818, 2716, 2206, 1686, 1380, 1200 cm^{-1}; MS (EI, 70 eV) *m*/*z* (relative intensity) 160 (M^+, 75), 131 (77), 103 (70), 92 (100), 77 (72).

(3*E*)-1,1-Dibromo-6-(3-furanyl)-3-methyl-1,3-hexadien-5-yne (8). A mixture of Ph_3P (6.14 g, 23.4 mmol), CBr_4 (3.88 g, 11.7 mmol), and K_2CO_3 (540 mg, 3.9 mmol) in CH_2Cl_2 was stirred at 23 °C for 30 min.[12] To this was added **7** (621 mg, 3.9 mmol) in CH_2Cl_2 (8 mL). After 20 min, silica gel (1 g) was added, and the solvent was removed in vacuo. Flash chromatography (pentane) afforded 1.17 g (95%) of **8**: ^{1}H NMR δ 2.24 (s, 3 H), 5.88 (s, 1 H), 6,47 (d, J = 0.8 Hz, 1 H), 7.06 (s, 1 H), 7.39 (s, 1 H), 7.65 (s, 1 H); ^{13}C NMR δ 18.25, 88.65, 88.88, 89.63, 107.72, 112.26, 113.91, 138.64, 142.94, 143.80, 145.31; IR (neat) 3150, 2200, 1772, 1094 cm^{-1}; MS (EI, 70 eV) *m*/*z* (relative intensity) 316 (M^+, 7), 234 (9), 128 (91), 51 (100); HRMS (EI) calcd for $C_{11}H_8Br_2O$ (M^+) 314.9020, found 314.9008.

(*E*)-6-(3-Furanyl)-3-methyl-3-hexene-1,5-diyne (9). To a solution of **8** (1.58 g, 5.0 mmol) in THF (20 mL) was added $NaN(SiMe_3)_2$ (1.0 M in THF, 11.0 mL, 11.0 mmol, −100 °C, 10 min) followed by *n*-BuLi (2.5 *M* in hexanes, 8.8 mL, 22.0 mmol, −100 °C, 10 min).[19] The reaction mixture was quenched at −100 °C with MeOH, warmed to 23 °C, diluted with ether, washed with aqueous NH_4Cl and NaCl, dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (pentane) afforded 713 mg (91%) of **9**: ^{1}H NMR δ 2.08 (s, 3 H), 3.17 (s, 1 H), 6.05 (s, 1 H), 6.45 (d, J = 1.8 Hz, 1 H), 7.39 (t, J = 1.6 Hz, 1 H), 7.64 (s, 1 H) ppm; ^{13}C NMR δ 20.14, 80.29, 85.19, 87.77, 90.00, 107.55, 112.26, 117.00, 129.37, 142.94, 145.38 ppm; IR (neat) 3314, 2178, 1164 cm^{-1}; MS (EI, 70 eV) *m*/*z* (relative intensity) 156 (M^+, 100), 139 (5), 127 (49), 102 (25); HRMS (EI) calcd for $C_{11}H_8O$ (M^+) 156.0575, found 156.0577.

(*Z*)-3-Iodo-2-methylpropenoic Acid (4).[20] To a solution of **3**[6] (490 mg, 2.47 mmol) in CH_2Cl_2 (20 mL) at 0 °C were added Celite (1.1 g) and PCC (1.07 g, 4.8 mmol). The resulting mixture was stirred at 0 °C for 4 h, filtered, washed with aqueous $NaHCO_3$ and NaCl, dried over $MgSO_4$, filtered, and concentrated to afford crude (*Z*)-3-iodo-2-methylpropenal. This compound was not characterized due to its rapid decomposition. To a mixture of crude (*Z*)-3-iodo-2-methylpropenal in CH_3CN (3 mL), $NaH_2PO_4 \cdot H_2O$ (104 mg, 0.75 mmol) in H_2O (2 mL), and H_2O_2 (30%, 3.5 mL, 30 mmol) at 0 °C was added dropwise a solution of $NaClO_2$ (80%, 390 mg, 3.5 mmol) in H_2O (4 mL). The reaction mixture was extracted with ether. The aqueous layer was acidified with 3 M HCl and extracted with ether. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was chromatographed (50:50 pentane−ether) to afford 298 mg (57%, two steps) of **4**: ^{1}H NMR δ 2.03 (d, J = 1.1 Hz, 3 H), 8.01 (d, J = 1.1 Hz, 1 H), 11.63 (br s, 1 H); ^{13}C NMR δ 22.21, 86.08, 137.52, 171.11.

(*Z*)-5-Benzylidene-3-methyl-5*H*-furan-2-one (11).[21] A mixture of PhC≡CH (23 mg, 0.22 mmol), **4** (42 mg, 0.2 mmol), $Pd(PPh_3)_4$ (12 mg, 0.01 mmol), CuI (2 mg, 0.01 mmol), and Et_3N (0.11 mL, 0.8 mmol) in CH_3CN (5 mL) was degassed via five

(18) Negishi, E. In *Aspects of Mechanism and Organometallic Chemistry*; Brewster, J. H., Ed.; Plenum Press: New York, 1978; p 285.

(19) Grandjean, D.; Pale, P.; Chuche, J. *Tetrahedron Lett.* **1994**, *35*, 3529.

(20) Larock, R. C.; Zenner, J. M. *J. Org. Chem.* **1995**, *60*, 482.

(21) Scheeren, J. W.; Lange, J. *Tetrahedron Lett.* **1984**, *25*, 1609.

freeze−thaw cycles, warmed to 23 °C, and stirred for 29 h at 23 °C. After removal of the solvent in vacuo, the residue was analyzed by NMR spectrometry which indicated the formation of **11** in 78% yield. GC analysis using mesitylene as an internal standard indicated the formation of 1,4-diphenylbutadiyne in 16% (based on PhC≡CH).

Freelingyne (1). A mixture of **9** (34 mg, 0.22 mmol), **4** (42 mg, 0.2 mmol), $Pd(PPh_3)_4$ (12 mg, 0.01 mmol), CuI (2 mg, 0.01 mmol), and Et_3N (0.11 mL, 0.8 mmol) in CH_3CN (5 mL) was degassed via five freeze−thaw cycles, warmed to 23 °C, and stirred for 23 h. The mixture was diluted with ether, washed with aqueous $NaHCO_3$ and NaCl, dried over $MgSO_4$, filtered, and concentrated. The residue was analyzed by NMR spectrometry which indicated the formation of freelingyne (**1**) in 61% yield (>98% *Z*) and (3*E*,8*E*)-1,11-bis(3-furanyl)-4,8-dimethyl-3,8-dodecadiene-1,5,7,10-tetrayne (**10**) in 20% yield (based on the starting alkyne). Flash chromatography (90:10 pentane−ether) afforded freelingyne in 50% yield. Its ^{1}H NMR spectral data are in good agreement with those reported:[2] δ 2.04 (d, J = 1.2 Hz, 3 H), 2.35 (d, J = 1.0 Hz, 3 H), 5.64 (s, 1 H), 5.90 (s, 1 H), 6.48 (t, J = 1.8 Hz, 1 H), 7.04 (d, J = 1.5 Hz, 1 H), 7.40 (t, J = 1.7 Hz, 1 H), 7.66 (d, J = 0.6 Hz, 1 H) ppm; ^{13}C NMR δ 10.66, 18.24, 89.88, 90.61, 108.38, 112.36, 114.42, 115.03, 128.91, 138.92, 143.03, 143.94, 145.50, 147.39, 171.02 ppm; IR (neat) 2926, 1770, 1560 cm^{-1}; MS (EI, 70 eV) *m*/*z* (relative intensity) 240 (M^+, 18), 211 (4), 172 (12), 115 (100). (3*E*,8*E*)-1,11-Bis(3-furanyl)-4,8-dimethyl-3,8-dodecadiene-1,5,7,10-tetrayne (**10**) gave the following spectral data: ^{1}H NMR δ 2.09 (d, J = 1.2 Hz, 6 H), 6.10 (s, 2 H), 6.45 (d, J = 1.8 Hz, 2 H), 7.40 (t, J = 1.5 Hz, 2 H), 7.64 (s, 2 H); ^{13}C NMR δ 19.84, 77.08, 85.30, 88.20, 92.07, 107.56, 112.27, 118.70, 128.90, 143.08, 145.58; MS (EI, 70 eV) *m*/*z* (relative intensity) 310 (M^+, 100), 279 (11), 252 (53), 226 (21); HRMS (EI) calcd for $C_{22}H_{14}O_2$ (M^+) 310.0994, found 310.1003.

Acknowledgment. We thank the National Institutes of Health (GM 36792) for support of this research. Purdue Research Foundation has provided a PRF Graduate Research Fellowship to Ms. F. Liu, and Johnson Matthey has provided Pd compounds.

JO971360G