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Bulky Trialkylsilyl Acetylenes in the Cadiot−Chodkiewicz Cross-Coupling Reaction

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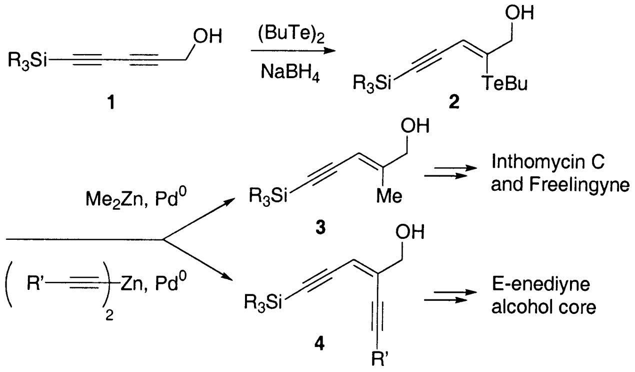
Abstract: Bulky trialkylsilyl-protected alkynes such as triethylsilyl (TES), *tert*-butyldimethylsilyl (TBS), and triisopropylsilyl (TIPS) acetylenes underwent the Cadiot−Chodkiewicz cross-coupling reaction with different bromoalkynes to form a variety of synthetically useful unsymmetrical diynes in good yields. The diyne alcohol **10** was transformed regio- and stereoselectively into enynes by hydrotelluration, carbometalation, and reduction reactions.

Unsymmetrical diynes are not only incorporated in natural products (polyacetylenes,[1] epoxypolyynes,[2] montipori acids,[3] pellynols E−H,[4] panaxydol,[5] and (3*R*,8*S*)-falcarindiol[6]) but they also provide important precursors for the synthesis of enynes via regioselective hydrotelluration,[7] hydroalumination with lithium aluminum hydride,[8] and carbometalation[9] with alkyl[10] and alkynyl[11] Grignard reagents of the propargylic carbon−carbon triple bond. In connection with our efforts to construct the trisubstituted alkene **3** as a precursor of Inthomycin C[12] and Freelingyne,[13] or the *E*-enediyne alcohol core[14] **4** of Kedarcindin chromophore[15] and C-1027 chromophore[16] via a cross-coupling reaction of the vinylic telluride **2** with dialkyl[17] or dialkynyl[18] zinc reagents, we decided to employ the diyne alcohol **1** as a common precursor (Scheme 1). This diyne alcohol **1** had been synthesized in several steps with low overall yields by selective protection of a carbon−carbon triple bond of penta-2,4-diyn-1-ol[19] or reacting the lithium anion of 1-trimethylsilyl-1,3-butadiyne with formaldehyde.[20] However, both penta-2,4-diyn-1-ol and 1-trimethylsilyl-1,3-butadiyne intermediates were synthesized from the volatile and explosive 1,3-butadiyne that rendered these synthetic routes difficult. Conceivably, the diyne alcohol **1** could be made by the acetylenic coupling[21] with palladium−copper catalyst systems[22] or catalytic CuI/pyrrolidine[23] conditions.

SCHEME 1. Approach to Inthomycin C, Freelingyne, and *E*-Enediyne Alcohol Core



We envisioned that the diyne alcohol **1** could come from the copper-catalyzed Cadiot−Chodkiewicz cross-coupling reaction[24−26] of a bromoalkyne **5** or **8** with a terminal alkyne **6** or **7**, respectively (Scheme 2). Walton[27] and

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(1) (a) Jente, R.; Bonnet, P. H.; Bohlmann, F. *Chem. Ber.* **1972**, *105*, 1694. (b) Bohlmann, F.; Thefeld, W.; Zdero, C. *Chem. Ber.* **1970**, *103*, 2245. (c) Bohlmann, F.; Kleine, K. M.; Bornowski, H. *Chem. Ber.* **1965**, *98*, 369. (d) Bohlmann, F.; Hummel, H. C. *Chem. Ber.* **1970**, *103*, 3419.

(2) (a) Rose, A. F.; Butt, B. A.; Jermy, T. *Phytochemistry* **1980**, *19*, 563. (b) Bohlmann, F.; Zdero, C.; Robinson, H.; King, R. M. *Phytochemistry* **1979**, *18*, 1519. (c) Grandjean, D.; Pale, P.; Chuche, J. *Tetrahedron* **1993**, *49*, 5225−5236.

(3) (a) Fusetani, N.; Toyoda, T.; Asai, N.; Matsunaga, S.; Maruyama, T. *J. Nat. Prod.* **1996**, *59*, 796−797. (b) Stefani, H. A.; Costa, I. M.; Zeni, G. *Tetrahedron Lett.* **1999**, *40*, 9215.

(4) Fu, X.; Schmitz, F. J.; Kelly, M. *J. Nat. Prod.* **1999**, *62*, 1336−1338.

(5) (a) Bohlmann, F.; Niedballa, U.; Rode, K. M. *Chem. Ber.* **1966**, *99*, 3552−3558. (b) Bentley, R. K.; Bhattacharjee, D.; Jones, E.; Thaller, V. *J. Chem. Soc. C* **1969**, 685−688. (c) Lemmich, E. *Phytochemistry* **1981**, *20*, 1419−1420. (d) Zheng, G.; Lu, W.; Cai, J. *J. Nat. Prod.* **1999**, *62*, 626−628.

(6) (a) Dabrowski, Z.; Wrobel, J. T.; Wojtasiewicz, K. *Phytochemistry* **1980**, *19*, 2464−2465. (b) Lu, W.; Zheng, G.; Haji; Aisa, A.; Cai, J. *Tetrahedron Lett.* **1998**, *39*, 9521−9522.

(7) Dabdoub, M. J.; Dabdoub, V. B. *Tetrahedron* **1995**, *57*, 9839−9850.

(8) (a) Green, K.; Keeping, J. W.; Thaller, V. *J. Chem. Res. (S)* **1985**, *4*, 103. (b) Rao, A. V. R.; Reddy, S. P.; Reddy, E. R. *J. Org. Chem.* **1986**, *51*, 4158−4159. (c) Rao, A. V. R.; Reddy, E. R. *Tetrahedron Lett.* **1986**, *27*, 2279−2282.

(9) Fallis, A. G.; Forgione, P. *Tetrahedron* **2001**, *57*, 5899−5913.

(10) Doboudin, J. G.; Jousseaume, B. *J. Organomet. Chem.* **1979**, *168*, 1−11.

(11) Forgione, P.; Fallis, A. G. *Tetrahedron Lett.* **2000**, *41*, 11−15.

(12) Henkel, T.; Zeek, A. *Liebigs Ann. Chem.* **1991**, 367−373.

(13) (a) Massy-Westropp, R. A.; Reynolds, G. D.; Spotswood, T. M. *Tetrahedron Lett.* **1966**, 1939. (b) Ingham, C. F.; Massy-Westropp, R. A. *Aust. J. Chem.* **1974**, *27*, 1491. (c) Knight, D. W.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* **1975**, 641.

(14) (a) Dai, W.-M.; Fong, K. C.; Danjo, H.; Nishimoto, S. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 779−781. (b) Dai, W.-M.; Fong, K. C. *Tetrahedron Lett.* **1996**, *37*, 8413−8416. (c) Dai, W.-M.; Lee, M. Y. H. *Tetrahedron Lett.* **1998**, *39*, 8149−8152.

(15) (a) Lam, K. S.; Hesler, G. A.; Gustavson, D. R.; Crosswell, A. R.; Veitch, J. M.; Forenza, S.; Tomita, K. *J. Antibiot.* **1991**, *44*, 472−478. (b) Hofstead, S. J.; Matson, J. A.; Malacko, A. R.; Marquardt, H. *J. Antibiot.* **1992**, *45*, 1250−1254.

(16) (a) Hu, J.; Xue, Y.-C.; Xie, M.-Y.; Zhang, R.; Otani, T.; Minami, Y.; Yamada, Y.; Marunaka, T. *J. Antibiot.* **1988**, *41*, 1575−1579. (b) Minami, Y.; Yoshida, K.-I.; Azuma, R.; Saeki, M.; Otani, T. *Tetrahedron Lett.* **1993**, *34*, 2633−2636. (c) Minami, Y.; Yoshida, K.-I.; Azuma, R.; Saeki, M.; Otani, T. *Tetrahedron Lett.* **1993**, *34*, 2637−2640.

(17) Dabdoub, M. J.; Dabdoub, V. B.; Marino, J. P. *Tetrahedron Lett.* **2000**, *41*, 433−436.

(18) Dabdoub, M. J.; Dabdoub, V. B.; Marino, J. P. *Tetrahedron Lett.* **2000**, *41*, 437−441.

(19) Coles, B. F.; Walton, D. R. M. *Synthesis* **1975**, 390−391.

(20) Jones, G. E.; Holmes, A. B. *Tetrahedron Lett.* **1982**, *23*, 3203−3206.

(21) Siemsen, P.; Livingston, R. C.; Diederich, F. *Angew. Chem., Int. Ed.* **2000**, *39*, 2632−2657.

(22) (a) Wityak, J.; Chan, J. B. *Synth. Commun.* **1991**, *21*, 977−979. (b) Lee, G. C. M.; Tobias, B.; Holmes, J. M.; Harcourt, D. A.; Garst, M. E. *J. Am. Chem. Soc.* **1990**, *112*, 9330−9336.

(23) Alami, M.; Ferri, F. *Tetrahedron Lett.* **1996**, *37*, 2763−2766.

(24) Chodkiewicz, W. *Ann. Chim.* **1957**, *2*, 819−869.

(25) Chodkiewicz, W.; Cadiot, P. *C. R. Hebd. Seances Acad. Sci.* **1955**, *241*, 1055.

(26) Sonogashira, K. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, UK, 1991; Vol. 3, pp 551−561.

(27) (a) Eastmond, R.; Walton, D. R. M. *Tetrahedron* **1972**, *28*, 4591−4599. (b) Johnson, T. R.; Walton, D. R. M. *Tetrahedron* **1972**, *28*, 5221−5236.

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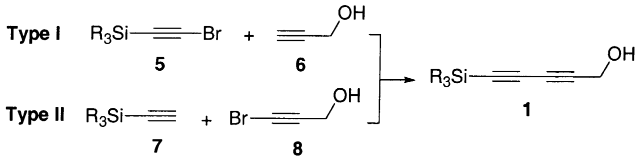
SCHEME 2. Different Approaches to Diyne Alcohol



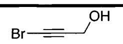
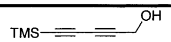
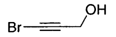
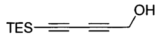
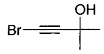
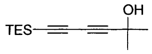
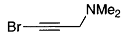
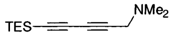
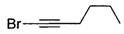
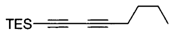
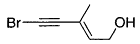
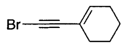
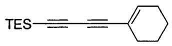
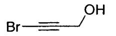
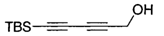
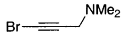
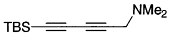
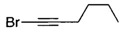
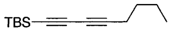
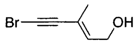
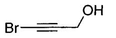
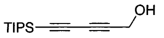
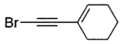
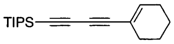
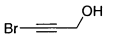
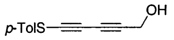
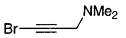
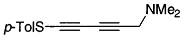
Vollhardt[28] had performed the Cadiot−Chodkiewicz cross-coupling reaction of the Type I using substrates similar to **5** and **6**. Encouraged by these results, we felt that a trialkylsilyl acetylene **7** should undergo a similar cross-coupling reaction with the 3-bromo-prop-2-yn-1-ol (**8**) to afford the desired diyne alcohol **1** (Scheme 2, Type II) under similar Cadiot−Chodkiewicz cross-coupling conditions.

Results and Discussion

We set out to synthesize 5-trialkylsilylpenta-2,4-diyn-1-ol (**1**) by the Cadiot−Chodkiewicz cross-coupling reaction catalyzed by CuCl and $NH_2OH{\cdot}HCl$ in a 30% *n*-butylamine in water solvent (v/v; less basic compared to the commonly used 70% ethylamine in water) between 3-bromo-prop-2-yn-1-ol (**8**), which is a known cross-coupling partner,[24,29,30] and a trialkylsilyl acetylene. When trimethylsilyl acetylene was used, it decomposed possibly via a desilylation path under the conditions studied and no diyne product was obtained (Table 1, entry 1), a result that had been observed by others when using the standard solvent conditions.[27,31] We switched to triethylsilyl acetylene because it was more stable toward hydrolysis (its hydrolysis rate in aqueous methanolic alkali is 277 times slower).[31] We anticipated that the cross-coupling reaction would be much faster than the competing desilylation reaction. As a matter of fact, triethylsilyl acetylene underwent the cross-coupling reaction cleanly with 3-bromoprop-2-yn-1-ol to afford the diyne alcohol **10** in good yield (Table 1, entry 2). It was necessary to maintain a sufficient amount of Cu(I) in the aqueous amine solution.[24,26] If the reaction turned blue or green, immediate addition of hydroxylamine hydrochloride crystals during the reaction was necessary to reduce Cu(II) to Cu(I) to avoid the homocoupling product of the bromoalkyne.

With these results, other bromoalkynes in different combinations with bulky trialkylsilyl-protected alkynes were tested to determine the scope of this cross-coupling reaction. Other bromoalkynes derived from 1,1-dimethylpropargyl alcohol (entry 3), *N*,*N*-dimethylpropargylamine (entry 4), 1-hexyne (entry 5), and enynes (entries 6 and 7) underwent the cross-coupling reaction with triethylsilyl acetylene in good yields. The reactions were completed within 5 min for bromoalkynes containing polar functional groups such as alcohols and amines (entries 2−4 and 6). The insolubility of nonpolar bromoalkynes (entries 5 and 7) in the 30% aqueous *n*-butylamine solution could be the reason the reaction times were longer (20−30 min). A homocoupling product was observed as a minor byproduct (entry 7).[26] Under the condition studied, the cross-coupling reaction between triethylsilyl acetylene and a bromoalkyne derived from ethyl propiolate gave a complex mixture of products.

TABLE 1. Unsymmetrical Diynes Synthesis

Entry	Alkyne	Bromoalkyne	Product[a]		Isolated Yield
1	TMS—≡			(**9**)	0
2	TES—≡			(**10**)	95
3	TES—≡			(**11**)	97
4	TES—≡			(**12**)	92
5	TES—≡			(**13**)	92
6	TES—≡			(**14**)	92
7	TES—≡			(**15**)	87[b]
8	TBS—≡			(**16**)	91
9	TBS—≡			(**17**)	90
10	TBS—≡			(**18**)	92
11	TBS—≡	Br—≡—Ph	TBS—≡—≡—Ph	(**19**)	82[c]
12	TBS—≡			(**20**)	92
13	TIPS—≡			(**21**)	91
14	TIPS—≡			(**22**)	75[d]
15	*p*-TolS—≡			(**23**)	89
16	*p*-TolS—≡			(**24**)	97

[a] All reactions were run using 1.2 equiv of an alkyne, 1 equiv of a bromoalkyne, catalytic amounts of CuCl and hydroxylamine hydrochloride. [b] 12% of 1,4-dicyclohexene-1,3-butadiyne. [c] 14% of 1,4-diphenyl-1,3-butadiyne. [d] 11% of 1,4-dicyclohexene-1,3-butadiyne

Instead of TES, TBS (entries 8−12) and TIPS (entries 13−14) protecting groups were equally successful in the cross-coupling reaction. Analogous to entry 7, homocoupling products were formed in 14% and 11% yields when we used bromoalkynes derived from phenyl acetylene (entry 11) and cyclohexenyl acetylene (entry 14), respectively. It was advantageous to use *tert*-butyldimethylsilyl acetylene (bp 49−51 °C at 55 mmHg)[32] and triethylsilyl acetylene (bp 136−138 °C at 760 mmHg,[33] 51−52 °C at 22 mmHg[34]) over triisopropylsilyl acetylene (bp 100 °C at 20 mmHg)[35] because excess amounts could be removed under a reduced pressure. These high-yielding reactions confirmed that both TBS and TIPS groups were stable during the cross-coupling reaction. In addition to these results, we also found that a thioacetylene, 1-ethylsulfanyl-4-methylbenzene also underwent the cross-coupling reaction with bromoalkynes such as 3-bromoprop-2-yn-1-ol (entry 15) and *N*,*N*-dimethyl(3-bromoprop-2-ynyl)amine (entry 16) in good yields.

The unsymmetrical diyne alcohol **10** could be selectively functionalized at the propargylic carbon−carbon

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(28) Blanco, L.; Helson, H. E.; Mirthammer, M.; Mestdagh, H.; Spyroudis, S.; Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1246−1247.

(29) Godt, A. *J. Org. Chem.* **1997**, *62*, 7471−7474.

(30) Curtis, R. F.; Taylor, J. A. *J. Chem. Soc. C* **1971**, 186−188.

(31) Eaborn, C.; Walton, D. R. M. *J. Organomet. Chem.* **1965**, *4*, 217−228.

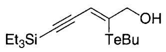
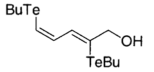
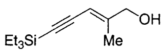
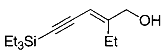
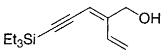
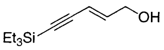
(32) Schaumann, E.; Lindstaedt, J. *Chem. Ber.* **1983**, *116*, 1728−1738 (in German).

(33) (a) Makovetskii, K. L.; Reikhsfel'd, V. O.; Erokhina, L. L. *J. Org. Chem. USSR (Engl. Transl.)* **1966**, *2*, 757−761. (b) Bogatkin, R. A.; Sverdlova, O. V.; Gindin, V. A. *J. Gen. Chem. USSR (Engl. Transl.)* **1971**, *41*, 2245−2248.

(34) Novikova, O. A.; Kuznetsova, V. P.; Kornev, K. A. *J. Gen. Chem. USSR (Engl. Transl.)* **1968**, *38*, 177−179.

(35) Jones, T. K.; Denmark, S. E. *Helv. Chim. Acta* **1983**, *66*, 2397−2411.

TABLE 2. Stereo- and Regioselective Functionalization of Diyne Alcohol 10

Entry	Reactant/Condition	Product		Yield
1	$(BuTe)_2$ (0.5 equiv), $NaBH_4$ (2.5 equiv), EtOH, reflux, 20 min		(**25**)	84%
2	$(BuTe)_2$ (1.5 equiv), $NaBH_4$ (7.5 equiv), EtOH, reflux, 10h		(**26**)	79%
3	MeMgBr (2.5 equiv) CuI (cat.), Et_2O, 0 °C to rt, overnight		(**27**)	84%
4	EtMgBr (2.5 equiv) CuI (cat.), Et_2O, 0 °C to rt, overnight		(**28**)	80%
5	VinylMgBr (2.5 equiv) CuI (cat.), Et_2O, 0 °C to rt, 3hr		(**29**)	84%
6	$LiAlH_4$ (1.5 equiv) Et_2O, 0 °C to rt, 2hr		(**30**)	95%

triple bond. For instance, hydrotelluration of the diyne alcohol **10** with $(BuTe)_2$, and $NaBH_4$ in ethanol afforded three products such as the desired product **25** (7%), the desilylated product of **25** (25%, desilylation of **25** occurred most likely after the hydrotelluration reaction), and the ditellurated product **26** (56%). After several attempts, we found that the desired vinylic telluride **25** could be obtained in high yield if the reaction was stopped after 20 min of reflux (Table 2, entry 1). When excess amounts of $(BuTe)_2$ and $NaBH_4$ were used and with longer reaction times, the ditellurated product **26** was formed predominantly (entry 2). In addition, we were also able to perform the regio- and stereoselective carbometalation[10,36] of the diyne alcohol **10** with 2.5 equiv of methyl-, ethyl-, and vinylmagnesium bromides in the presence of a catalytic amount of CuI to afford enynes **27**, **28**, and **29**, respectively, in good yields (entries 3−5). Furthermore, lithium aluminum hydride reduced the diyne alcohol **10** to enyne **30** regio- and stereoselectively in excellent yield (entry 6).[8]

In summary, our diyne approach utilizing bulky trialkylsilyl protecting groups was very advantageous. First, bulky trialkylsilyl acetylenes were stable under the Cadiot−Chodkiewicz cross-coupling reaction. Second, because of their much higher boiling points, these bulky trialkylsilyl acetylenes were easier to synthesize and handle than the commercially available but expensive and volatile trimethylsilyl acetylene. In addition, both the polar and nonpolar bromoalkynes were readily synthesized from the corresponding alkynes via hypobromide (Strauss method)[24,29,37] or $NBS/AgNO_3$(cat.)[38] conditions. In contrast, the preparation of bromotriethylsilyl acetylene could be difficult because it involved alkyllithium reagents in the deprotonation step. Furthermore, in these diynes having bulky trialkylsilyl protecting groups, the more sterically hindered carbon−carbon triple bonds were inert toward a variety of organometallic and reducing reagents that were very synthetically useful. These silyl groups could be removed with fluoride sources at −80 °C,[39] 0 °C,[40] or room temperature[41] and alkoxide at room temperature.[42]

Experimental Section

General Information. All needles and syringes were oven-dried and cooled to room temperature in a desiccator prior to use. All reactions were carried out under a nitrogen (or argon) atmosphere. Unless otherwise indicated, all starting materials were used as received. *n*-Butyllithium, methylmagnesium bromide, ethylmagnesium bromide, and vinylmagnesium bromide came as a 2.5 M solution in tetrahydrofuran, a 3.0 M solution in diethyl ether, a 3.0 M solution in diethyl ether, and a 1.0 M solution in THF, respectively, and were titrated prior to use.[1] Diethyl ether was dried over 4 Å molecular sieves and distilled over Na/benzophenone. Silica gel, 40 μm, was purchased from Scientific Absorbents Incorporated. TLC monitoring was best with Hex:EtOAc solvent systems. The vinylic tellurides were detected with a UV light, iodine, and a vanillin solution (27 mL of H_2O, 6 mL of concentrated H_2SO_4, 27 mL of MeOH and 1.2 g of vanillin). Alcohols were best observed in a $KMnO_4$ solution (1.5 g of $KMnO_4$, 10 g of K_2CO_3, 2.5 mL of 5% NaOH and 150 mL of water).

Infrared spectra (IR) were recorded on a FT-IR spectrophotometer with internal calibrations. Spectra were recorded either from a neat oil between sodium chloride salt plates or from a potassium bromide pellet. IR data were reported in wavenumbers (cm^{-1}).

Proton nuclear magnetic resonance spectra (^1H NMR) were obtained on 300-, 400-, or 500-MHz FT NMR spectrometers. Spectra were recorded in deuteriochloroform ($CDCl_3$) with residual proteo form as an internal reference or tetramethylsilane (TMS) as the external reference. Data were reported as follows: chemical shift (δ) in ppm (multiplicity, integrated intensity, and coupling constant (J) in hertz (Hz)). Abbreviations to denote the multiplicity of a particular signal were s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sext (sextet), m (multiplet), and br (broad).

Difference nuclear Overhauser effect (NOE) experiments were performed on the 400- and 500-MHz FT NMR spectrometers with automated programs.

Carbon-13 nuclear magnetic resonance spectra (^{13}C NMR) were obtained on 75-, 100-, or 125-MHz FT NMR spectrometers. Spectra were recorded in deuteriochloroform with 77.0 ppm resonance of deuteriochloroform as the internal reference.

High-resolution mass spectra (HRMS) were determined on a VG 70-250S instrument by the University of Michigan, Department of Chemistry Instrument Services Branch. Sample introduction was via direct probe, and ionization was accomplished by electron impact (EI) at 70 eV, by chemical ionization (CI) with methane or ammonia, or by fast atom bombardment (FAB) with sodium. Masses were reported in units of mass over charge (m/z) to four decimal places in conjunction with the relative intensity normalized to 100.

General Procedure for the Diyne Synthesis. CuCl (0.06 mmol, 0.02 equiv) was added to a 30% n-$BuNH_2$ (2.5 mL) aqueous solution at room temperature that resulted in the formation of a blue solution immediately. A few crystals of hydroxylamine hydrochloride were added to discharge the blue

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(36) Henaff, N.; Whiting, A. *Tetrahedron* **2000**, *56*, 5193−5204.

(37) (a) Volkov, A. N.; Skvortsov, Y. M.; Danda, I. I.; Shostakovskii, M. F. *J. Org. Chem. USSR (Engl. Transl.)* **1970**, *6*, 903−907. (b) Brandsma, L. In *Preparative Acetylenic Chemistry*, 2nd ed.; Elsevier: Amsterdam, The Netherlands, 1988; pp 150−151. (c) Saalfrank, R. W.; Welch, A.; Haubner, M.; Bauer, U. *Liebigs Ann.* **1996**, 171−181. (d) Strauss, F.; Follek, L.; Heyn, W. *Berichte* **1930**, *63*, 1868−1885.

(38) (a) Hofmeister, H.; Annen, K.; Laurent, H.; Wiechert, H. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 727−729. (b) Basak, S.; Srivastava, S.; le Noble, W. J. J. *J. Org. Chem.* **1987**, *52*, 5095−5099.

(39) Zapata, A. J.; Gu, Y.; Hammond, G. B. *J. Org. Chem.* **2000**, *65*, 227−234.

(40) (a) Churcher, I.; Hallett, D.; Magnus, P. *Tetrahedron* **1999**, *55*, 1597−1606. (b) Choy, N.; Russell, K. C.; Alvarez, J. C.; Fider, A. *Tetrahedron Lett.* **2000**, *41*, 1515−1518.

(41) (a) Kamikawa, T.; Hayashi, T. *J. Org. Chem.* **1998**, *63*, 8922−8925. (b) Ma, C.; Yu, S.; Liu, X.; Cook, J. M. *Tetrahedron Lett.* **2000**, *41*, 2781−2785.

(42) (a) Nicolaou, K. C.; Murphy, F.; Barluenga, S.; Ohshima, T.; Wei, H.; Xu, J.; Gray, D. L. F.; Baudoin, O. *J. Am. Chem. Soc.* **2000**, *122*, 3830−3838. (b) Raeppel, S.; Raeppel, F.; Suffert, J. *Synlett* **1998**, 794−796.

color. The resulting colorless solution indicated the present of Cu(I) salt. The alkyne (3.6 mmol, 1.2 equiv) was added to the solution at room temperature forming a yellow acetylide suspension that was immediately cooled with an ice−water mixture. The bromoalkyne (3 mmol, 1 equiv) was added at once and the ice bath was removed (a small amount of diethyl ether could be used in the transfer). More crystals of hydroxylamine hydrochloride were added throughout the reaction as necessary to prevent the solution from turning blue or green. After several additions of hydroxylamine hydrochloride crystals, the reaction mixture had a rusty color (normally after 7 to 30 min, depending on alkynyl substrates). At this point, the reaction was complete according to TLC. The product was repeatedly extracted with diethyl ether (3 × 20 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The crude product could be purified further by flash column chromatography on silica gel.

5-Triethylsilylpenta-2,4-diyn-1-ol (10): $C_{11}H_{18}OSi$; FW = 194; $R_f = 0.32$ (90:10 Hex:EtOAc). Column chromatography (90:10 Hex:EtOAc) afforded a light yellow oil that was stored in the freezer; yield 95%. ^1H NMR (400 MHz, $CDCl_3$ with 0.05% v/v TMS) δ 4.30 (d, 2H, $J = 6.2$ Hz), 1.75 (t, 1H, $J = 6.2$ Hz), 0.95 (t, 9H, $J = 8.1$ Hz), 0.58 (q, 6H, $J = 8.1$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$ with 0.05% v/v TMS) δ 88.3, 86.1, 75.2, 71.1, 51.6, 7.5, 4.3; IR (neat) 3326 (br), 2957, 2937, 2877, 2224, 2107, 1458, 1414, 1236, 1018, 974, 798, 728 cm^{-1}; HRMS (CI with NH_3) for $C_{11}H_{18}OSi$ $[M + NH_4]^+$ cacld 212.1471, found 212.1460; CI with NH_3, *m/z* (rel intensity) 120 (40.3), 132 (100), 182 (71.3), 212 (74.5).

Hydrotelluration of Diyne -Alcohol 10. To a solution of $(BuTe)_2$ (185 mg, 0.5 mmol, 0.5 equiv) in EtOH (30 mL) was added solid $NaBH_4$ (95 mg, 2.5 mmol, 2.5 equiv) portionwise under nitrogen. The orange solution became light yellow. Diyne alcohol (194 mg, 1 mmol, 1 equiv) was added to the reaction flask under a nitrogen atmosphere. The reaction mixture was refluxed for 30 min. Careful monitoring of the disappearance of the diyne alcohol and the appearance of the monotelluration product ($R_f = 0.13$ in 90:10 Hex:EtOAc, iodine detection) was required to avoid the formations of the desilylated monotelluration and the ditelluration products. The reaction was cooled to room temperature and quenched with saturated aqueous NH_4Cl. The product was extracted with EtOAc, washed with brine, and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure and the residue was subjected to flash column chromatography on silica gel (90:10 Hex:EtOAc). Yield 84%.

(*Z*)-2-(Butyltelluro)-5-triethylsilylpent-2-en-4-yn-1-ol (25): $C_{15}H_{28}OSiTe$; FW = 382; $R_f = 0.13$ (90:10 Hex:EtOAc). Column chromatography (90:10 Hex:EtOAc) afforded a yellow oil that was stored in the freezer; yield 84%. ^1H NMR (400 MHz, $CDCl_3$ with 0.05% v/v TMS) δ 6.33 (t, 1H, $J = 1.8$ Hz), 4.26 (dd, 2H, $J = 6.2$, 1.5 Hz), 2.86 (t, 2H, $J = 7.7$ Hz), 1.80−1.69 (m, 3H), 2.34 (sext, 2H, $J = 7.3$ Hz), 0.97 (t, 9H, $J = 7.7$ Hz), 0.86 (t, 3H, $J = 7.3$ Hz), 0.60 (t, 6H, $J = 7.7$ Hz); NOE (500 MHz, $CDCl_3$ with 0.05% v/v TMS), the carbinol hydrogens enhanced (2.1%) when the vinylic hydrogen was irradiated; ^{13}C NMR (100 MHz, $CDCl_3$ with 0.05% v/v TMS) δ 136.3, 115.2, 105.1, 100.0, 69.1, 34.4, 25.3, 13.6, 7.8, 5.5, 4.5; IR (neat) 3350 (br), 2956, 2932, 2874, 2181, 2127, 1560, 1457, 1414, 1378, 1237, 1087, 1017, 726 cm^{-1}; HRMS (CI with methane) for $C_{15}H_{28}OSiTe$ $[M + H]^+$ calcd 383.1050, found 383.1062; CI with ammonia, *m/z* (rel intensity) 132.1 (100), 197.1 (32.4), 381.1 (16.7).

General Procedure for the Carbometalations[2] of Diyne Alcohol 10. Methyl-, ethyl-, or vinylmagnesium bromide (7.5 mmol, 2.5 equiv) was added to a suspension of CuI (0.3 mmol, 0.1 equiv) and Et_2O (20 mL) at 0 °C. A dark brown solution formed immediately. To this solution was added a solution of diyne -alcohol **10** (3 mmol, 1 equiv) in 2 mL of Et_2O at 0 °C. The ice-bath was removed and the reaction was stirred overnight. The reaction was quenched slowly at 0 °C with 2 N HCl under nitrogen until the reaction mixture was acidic. The product was extracted with diethyl ether, washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was pure enough for characterizations. Only the *E*-isomer was detected in the crude ^1H NMR.

(*E*)-2-Methyl-5-triethylsilylpent-2-en-4-yn-1-ol (27): $C_{12}H_{22}OSi$; FW = 210; $R_f = 0.26$ (85:15 Hex:EtOAc). Column chromatography (90:10 Hex:EtOAc) afforded a yellow oil that was stored in the freezer; yield 84%. ^1H NMR (500 MHz, $CDCl_3$ with 0.05% v/v TMS) δ 5.63 (s, 1H), 4.11 (d, 2H, $J = 5.1$ Hz), 1.92 (s, 3H), 1.51 (distorted t, 1H), 1.01 (t, 9H, $J = 7.8$ Hz), 0.62 (q, 6H, $J = 8.0$ Hz); NOE (500 MHz, $CDCl_3$ with 0.05% v/v TMS), the carbinol hydrogens enhanced (0.6%) when the vinylic hydrogen was irradiated; ^{13}C NMR (100 MHz, $CDCl_3$ with 0.05% v/v TMS) δ 151.6, 105.2, 103.7, 96.1, 67.0, 16.8, 7.7, 4.7; IR (neat) 3340 (br), 2955, 2913, 2875, 2133, 1635, 1457, 1415, 1377, 1235, 1099, 1017, 723 cm^{-1}; HRMS (EI, 70 eV) for $C_{12}H_{22}O_2Si$ $[M^+]$ calcd 210.1440, found 210.1444; *m/z* (rel intensity) 25 (33.6), 153 (57.2), 181 (100), 205 (21.6).

(*E*)-2-Ethyl-5-triethylsilylpent-2-en-4-yn-1-ol (28): $C_{13}H_{24}OSi$; FW = 224; $R_f = 0.33$ (80:20 Hex:EtOAc); a yellow oil, yield 80%; ^1H NMR (300 MHz, $CDCl_3$ with 0.05% v/v TMS) δ 5.58 (s, 1H), 4.15 (d, 2H, $J = 4.9$ Hz), 2.38 (q, 2H, $J = 7.7$ Hz), 1.82 (br s, 1H), 1.06 (t, 3H, $J = 7.7$ Hz), 1.00 (t, 9H, $J = 8.0$ Hz), 0.62 (q, 6H, $J = 8.0$ Hz); NOE (500 MHz, $CDCl_3$ with 0.05% v/v TMS), the carbinol hydrogens enhanced (0.2%) when the vinylic hydrogen was irradiated; ^{13}C NMR (125 MHz, $CDCl_3$ with 0.05% v/v TMS) δ 157.3, 104.6, 103.5, 96.1, 65.1, 24.3, 12.6, 7.6, 4.7; IR (neat) 3327 (br), 2957, 2913, 2876, 2137, 1634, 1458, 1102, 1017, 724 cm^{-1}; HRMS (DCI with ammonia) for $C_{13}H_{24}OSi$ $[M + H]^+$ calcd 225.1674, found 225.1669; CI with ammonia, *m/z* (rel intensity) 132 (100), 225 (43.2).

(*E*)-5-Triethylsilyl-2-vinylpent-2-en-4-yn-1-ol (29): $C_{13}H_{22}OSi$; FW = 222; $R_f = 0.15$ (90:10 Hex:EtOAc); a yellow oil, yield 89%; ^1H NMR (300 MHz, $CDCl_3$ with 0.05% v/v TMS) δ 6.97 (dd, 1H, $J = 18.1$, 11.3 Hz), 5.78 (m, 1H), 5.38 (d, 1H, $J = 17.9$ Hz), 5.30 (dm, 1H, $J = 11.0$ Hz), 4.35 (m, 2H), 2.16 (br s, 1H), 1.00 (t, 9H, $J = 7.7$ Hz), 0.64 (q, 6H, $J = 7.7$ Hz); NOE (500 MHz, $CDCl_3$ with 0.05% v/v TMS), the carbinol hydrogens enhanced (0.8%) when the vinylic hydrogen was irradiated; ^{13}C NMR (125 MHz, $CDCl_3$ with 0.05% v/v TMS) δ 148.7, 133.0, 116.9, 109.1, 103.1, 100.1, 62.6, 7.7, 4.6; IR (neat) 3336 (br), 3091, 2956, 2912, 2875, 2127, 1458, 1415, 1236, 1094, 1005, 911, 724 cm^{-1}; HRMS (DCI with ammonia) for $C_{13}H_{22}OSi$ $[M + H]^+$ calcd 223.1518, found 223.1509; CI with ammonia, *m/z* (rel intensity) 120 (100), 223 (25.2); EI 70 eV, *m/z* (rel intensity) 45 (38.4), 75 (55.3), 103 (60.3), 137 (68.4), 165 (100), 193 (60.0), 251 (19.3).

Reduction[3] of Diyne Alcohol 10. Powdered $LiAlH_4$ (35.6 mg, 0.9 mmol, 1.5 equiv) was added quickly to a solution of diyne alcohol (121 mg, 0.6 mmol, 1 equiv) in 15 mL of diethyl ether at 0 °C. The reaction was warmed to room temperature and stirred for 2 h. The reaction was cooled with an ice/water bath and quenched with 2 N HCl until acidic. Saturated aqueous Na_2SO_4 was added and the reaction was stirred vigorously until a bilayer was formed. The product was extracted with diethyl ether several times, washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product (95% yield) was pure enough to perform physical characterizations.

(*E*)-5-Triethylsilylpent-2-en-4-yn-1-ol (30): $C_{11}H_{20}OSi$; FW = 196; $R_f = 0.23$ (80:20 Hex:EtOAc); a light yellow oil, 95% yield; ^1H NMR (300 MHz, $CDCl_3$ with 0.05% v/v TMS) δ 6.31 (dt, 1H, $J = 15.9$, 4.9 Hz), 5.79 (dm, 1H, $J = 15.9$ Hz), 4.18 (dd, 2H, $J = 5.2$, 1.9 Hz), 1.83 (br s, 1H), 0.99 (t, 9H, $J = 8.0$ Hz), 0.62 (q, 6H, $J = 8.0$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$ with 0.05% v/v TMS) δ 143.1, 110.8, 104.4, 93.0, 63.1, 7.7, 4.6; IR (neat) 3326 (br), 2955, 2912, 2876, 2175, 2133, 1938, 1630, 1458, 1415, 1378, 1236, 1083, 1008, 954, 724 cm^{-1}; HRMS (DCI with ammonia) for $[M + H]^+$ for $C_{11}H_{20}OSi$ calcd 197.1362, found 197.1355; CI with ammonia, *m/z* (rel intensity) 132 (100), 186 (23.7), 197 (39.1); EI 70 eV, *m/z* (rel intensity) 75 (44.2), 103 (62.8), 139 (85.7), 167 (100), 205 (26.1).

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Supporting Information Available: Sample procedure for the Cadiot−Chodkiewicz cross-coupling reaction, procedures for regio- and stereoselective transformations of diyne alcohol **10**, and characterization data (^1H NMR, ^{13}C NMR, FTIR, and HRMS) for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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