Pergamon

SCIENCE DIRECT®

Tetrahedron 59 (2003) 8913–8917

TETRAHEDRON

Synthesis of skipped enynes via phosphine-promoted couplings of propargylcopper reagents

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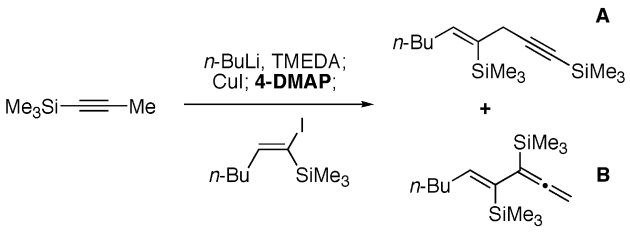
Received 31 March 2003; accepted 8 April 2003

Abstract—An electron-rich phosphine additive is critical and sufficient for propargyl-selective couplings of propargylcopper reagents and alkenyl halides. This method is complementary to those previously described, in which high allenyl selectivity is observed in analogous coupling reactions. While the basis of the phosphine effect requires further investigation, the information gained in these studies enables the synthesis of complex molecules by way of skipped enyne intermediates.

1. Introduction

We recently reported that the only carbon–carbon bond-forming reaction required for the preparation of ladder polyether subunits was a propargylcopper–alkenyl iodide coupling process (Scheme 1).[1] The selectivity for the desired skipped enynes (e.g. **A**) over allenyl-coupled products (**B**) was generally 85:15 when 4-DMAP was used as an additive. Herein we report a full account of our development of an improved process, in which Bu_3P provides maximum yield and selectivity (>95:5 propargyl/allenyl).



Scheme 1.

The development of carbon–carbon bond forming reactions that favor propargyl-coupled products where allenyl-derived adducts are also possible has received much attention. Danheiser demonstrated that high propargyl selectivity is obtained in additions of allenylsilane reagents to carbonyl groups and oxocarbenium ions,[2] and Marshall found that chiral, enantiomerically enriched allenyl-stannanes also undergo propargyl-selective carbonyl addition. In related work, chiral allenylzinc species can be prepared in high ee from chiral propargyl mesylates, and subsequent 1,2-addition to achiral and chiral aldehydes can be effected with high diastereoselectivity.[3]

Prior to these carbonyl addition processes, Corey pioneered propargyl-selective alkylation and allylation of propargyl-copper reagents,[4] and Ganem later reported the first propargyl-selective conjugate additions of these species.[5] Danheiser's allenylsilane reagents generally favor (trimethylsilyl)cyclopentene annulation in analogous reactions,[6] whereas Haruta showed that certain allenyl-stannanes were selective for 1,4-S_E2' addition, affording 4-alkynylcarbonyl compounds.[7]

The development of propargyl-selective cross-coupling methods, however, is much less developed. In a series of recent investigations, Ma observed that Pd-catalyzed cross-coupling of allenylzinc reagents and alkenyl iodides favored the allenyl regioisomer unless the electrophile contained an electron-withdrawing group.[8] Since allenyl coupling was generally favored in cases closest to those for which we required high propargyl selectivity, the starting point for these investigations was a singular example of selective propargyl-sp^2 coupling described by Normant in 1975.[9] Preparation of an organocopper reagent involved deprotonation of 1-(trimethylsilyl)-1-propyne with *n*-BuLi in TMEDA/THF, addition of CuI, removal of the THF in vacuo, and addition of pyridine. An explanation for the solvent switch was not provided, but we reasoned that modification of the organocopper species by interaction with pyridine might be necessary for maximum yield of the propargyl-coupled product. In this vein, we examined a variety of additives with the aim of duplicating this high

Keywords: phosphine; enyne intermediates; organocopper; propargylation.
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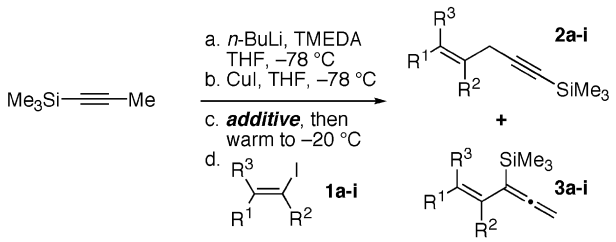
0040–4020/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2003.04.002

propargyl selectivity while simultaneously obviating the solvent exchange.

2. Results and discussion

As summarized in Scheme 2 and Table 1, we found that several additives had dramatically different effects upon both yield and propargyl/allenyl selectivity in our initial investigations with alkenyl iodide **1a**, which was prepared by hydroalumination/iodination (DIBAL-H; I_2). Although propargyl selectivity was high in reactions conducted in THF, they were not of preparative utility (entry 2). Nitrogen- and sulfur-containing additives were either efficacious or selective, but not both (entries 3–6). Organophosphines on the other hand (entries 7–9) displayed very high levels of propargyl selectivity, and of these, tributylphosphine (Bu_3P) also gave the desired product in good yield.



Scheme 2.

Table 1. Effects of additives upon yield and selectivity in coupling reactions of alkenyl iodide **1a**

Entry	Solvent	Additive	**2a**:**3a**[a]	Isolated yield of **2a** (%)
1	Ether	None	n.d.	<5
2	THF	None	>20:1	37
3	THF	Pyridine	10:1	47
4	THF	4-DMAP	7:1	69
5	THF	Et_3N	10:1	39
6	THF	Me_2S	20:1	33
7	THF	Ph_3P	>20:1	41
8	THF	Bu_3P	>20:1	81
9	THF	Cy_3P	>20:1	41

Perfomed on 2 g scale (7.1 mmol of iodide **1a**). See Scheme 2 and Section 4 for details.
[a] Determined by ^{1}H NMR analysis of unpurified product mixture.

Several explanations for the higher yield and selectivity imparted by Bu_3P are possible, including increased solubility and/or thermal stability of the organocopper species, or a change in its aggregation state.[10,11] Since higher yields are observed with the more electron-rich Bu_3P than with Ph_3P (entries 7 and 8), it is possible that oxidative addition into the carbon–iodine bond is accelerated by the former. Nevertheless, the results with Cy_3P (entry 9) might suggest otherwise, unless the increased steric demand of this phosphine is responsible for the reduction in yield.

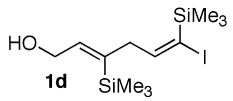
The scope of this transformation with respect to the substitution pattern and nature of the alkenyl iodide was also evaluated (Table 2). In all cases, the desired propargyl-coupled product is formed exclusively (>20:1, ^{1}H NMR). Protected (entry 2) and free hydroxyl groups (entries 3 and 4) are tolerated, and significantly, no π-bond isomerization

Table 2. Propargyl-selective coupling of alkenyl iodides **1a–i**

Entry	Iodide	R^1	R^2	R^3	**2**:**3**[a]	Yield (%)
1	**1a**	*n*-Bu	Me_3Si	H	>20:1	81
2	**1b**	$TBSOCH_2$	Me_3Si	H	>20:1	45
3	**1c**	$HO(CH_2)_3$	Me_3Si	H	>20:1	67
4	**1d**	(see below)	Me_3Si	H	>20:1	67
5	**1e**	H	*n*-Pr	*n*-Pr	n.d.	< 5
6	**1f**	*n*-Pr	*n*-Pr	H	>20:1	33[b]
7	**1g**	Ph	H	Me	>20:1	80
8	**1h**	*n*-Bu	H	H	>20:1	38
9	**1i**	H	H	*n*-Bu	>20:1	52

See Scheme 2 and Section 4 for details.
[a] Determined by ^{1}H NMR analysis of unpurified product mixture.
[b] NMR analysis of the unpurified product mixture indicated a 2:1 mixture of iodide **1f** and product **2f**, i.e. conversion was approximately 33%. The yield reported (33%) is the isolated yield based on a theoretical 100% and therefore is nearly quantitative based on conversion.

is observed in entry 4 with skipped diene **1d**. A trimethylsilyl group geminal to the iodine atom is not required for efficacy or selectivity, as shown by entries 5–9. In one case, subsitution *cis* to the iodide significantly reduces the efficiency of coupling (entry 5). Nevertheless, conjugated alkenyl iodides couple smoothly, as demonstrated by *(E)*-1-iodo-2-phenylpropene (entry 7). Finally, the coupling is stereospecific with respect to olefin geometry (entries 8 and 9).



3. Conclusions

In summary, an electron-rich phosphine additive is critical and sufficient for propargyl-selective couplings of propargylcopper reagents and alkenyl halides. This method is complementary to that reported by Ma, who observed propargyl selectivity in couplings with electron-deficient alkenyl halides and high allenyl selectivity with electron-rich coupling partners, the latter representing those in which we observe high propargyl selectivity. Application of the information gained in these studies to the synthesis of complex molecules and further investigation of the basis of propargyl selectivity are ongoing in our laboratories.

4. Experimental

4.1. General information

Unless otherwise noted, all reactions were performed under an oxygen-free atmosphere of argon with rigid exclusion of moisture from reagents and glassware. Tetrahydrofuran (THF) and Et_2O were distilled from a blue solution of sodium benzophenone ketyl. Dimethylformamide (DMF) was used as supplied by Aldrich (99.8% anhydrous; stored over molecular sieves). Analytical thin layer chromatography (TLC) was performed using EM Science silica gel 60 F_{254} plates. The developed chromatogram was analyzed by UV lamp (254 nm) and ethanolic phosphomolybdic acid

(PMA) or aqueous potassium permanganate ($KMnO_4$). Liquid chromatography was performed using a forced flow (flash chromatography) of the indicated solvent system on Silicycle Silica Gel (230–400 mesh).[12] ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Varian Inova 500 MHz spectrometer. Chemical shifts in ^1H NMR spectra are reported in parts per million (ppm) on the δ scale from an internal standard of residual chloroform (7.27 ppm). Data are reported as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, app=apparent, and br=broad), coupling constant in hertz (Hz), and integration. Chemical shifts of ^{13}C NMR spectra are reported in ppm from the central peak of $CDCl_3$ (77.2 ppm) on the δ scale. Infrared (IR) spectra were recorded on a Perkin–Elmer 2000 FT-IR. High Resolution mass spectra (HR-MS) were obtained on a Bruker Daltonics APEXII 3 Tesla Fourier Transform Mass Spectrometer by Dr Li Li of the Massachusetts Institute of Technology Department of Chemistry Instrumentation Facility.

4.2. Synthesis of Vinyl Iodides 1a–1i

4.2.1. [(1*E*)1-Iodo-hex-1-enyl]-trimethyl-silane (1a). Synthesized according to a reported procedure.[13]

4.2.2. (1*E*)-3-(*tert*-Butyl-dimethyl-silanyloxy)-1-iodo-1-trimethylsilanyl-propene (1b). To a solution of 3-trimethylsilanyl-prop-2-yn-1-ol[6b] (8.0 g, 62.5 mmol) in Et_2O (160 mL) was added a 1 M solution of DIBAL-H in hexane (156 mL). The resulting solution was heated 24 h at reflux. This solution was then cooled to −78°C, diluted with Et_2O (60 mL), and a solution of I_2 (63.5 g, 250 mmol) in Et_2O (200 mL) was added. After stirring for 2 h at −78°C, the reaction was quenched by pouring into 1 M HCl (100 mL) and ice (50 g). The maroon organic layer was separated, and the aqueous layer was extracted with Et_2O (3×150 mL). The combined organic layers were washed with saturated $Na_2S_2O_3$, brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by column chromatography (20% EtOAc in hexane) to yield the vinyl iodide as a pale yellow oil (10.7 g, 67%, >95% E): R_f 0.35 (20% EtOAc in hexane); IR (thin film, NaCl) 3312, 2955, 1250, 1018, 842 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35 (t, J=7.0 Hz, 1H), 4.09 (dd, J=7.0, 6.1 Hz, 2H), 0.29 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.3, 111.6, 63.6, 1.2; HR-MS (ESI) calcd for $C_6H_{13}IOSi$ $(M+Na)^+$ 278.9673, found 278.9681.

To a solution of this vinyl iodide (5.1 g, 20.0 mmol) in DMF (20 mL) was added imidazole (1.9 g, 28.0 mmol), and TBSCl (4.2 g, 28.0 mmol). The reaction mixture was allowed to stir overnight at room temperature and was quenched with water (100 mL). The aqueous layer was extracted with Et_2O (3×50 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo to yield the protected alcohol (6.8 g, 92%) without the need for further purification: R_f 0.45 (5% EtOAc in hexane); IR (thin film, NaCl) 3853, 2955, 2929, 2857, 1251, 1098, 838, 776 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25 (t, J=6.0 Hz, 1H), 4.11 (d, J=6.5 Hz, 2H), 0.90 (s, 9H), 0.27 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.2, 109.0, 64.6, 26.6, 19.0, 1.6, −4.4; HR-MS (ESI) calcd for $C_{12}H_{27}IOSi_2$ $(M+Na)^+$ 393.0537, found 393.0534.

4.2.3. (4*E*)-5-Iodo-5-trimethylsilanyl-pent-4-en-1-ol (1c). To a solution of 5-trimethylsilanyl-pent-4-yn-1-ol[14] (12.2 g, 77.8 mmol) in Et_2O (190 mL) at 0°C was added a 1 M solution of DIBAL-H in hexane (190 mL). The resulting solution was heated 24 h at reflux. This solution was then cooled to −78°C, diluted with Et_2O (60 mL), and a solution of I_2 (79 g, 310 mmol) in Et_2O (175 mL) was added. After stirring for 2 h at −78°C, the reaction was quenched by pouring into 1 M HCl (200 mL) and ice (40 g). The maroon organic layer was separated, and the aqueous layer was extracted with Et_2O (3×200 mL). The combined organic layers were washed with saturated $Na_2S_2O_3$, brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by column chromatography (20% EtOAc in hexane) to yield the vinyl iodide as a pale yellow oil (20.1 g, 91%, >95% E): R_f 0.20 (20% EtOAc in hexane); IR (thin film, NaCl) 3335, 2952, 1588, 1407, 1249, 1059, 841 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.18 (t, J=7.9 Hz, 1H), 3.66 (t, J=6.4 Hz, 2H), 2.18 (dt, J=7.7, 7.6 Hz, 2H), 1.67 (m, 2H), 0.28 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.7, 107.6, 62.2, 32.2, 31.7, 1.4; HR-MS (ESI) calcd for $C_8H_{17}IOSi$ $(M)^+$ 284.0088, found 284.0091.

4.2.4. (2*Z*, 5*E*)-6-Iodo-3,6-bis-trimethylsilanyl-hexa-2,5-dien-1-ol (1d). To a solution of **2b** (see below; 9.6 g, 24.6 mmol) in Et_2O (60 mL) was added a 1 M solution of DIBAL-H in hexane (60 mL). The resulting solution was heated 24 h at reflux. This solution was then cooled to −78°C, diluted with Et_2O (50 mL), and a solution of I_2 (25 g, 98.4 mmol) in Et_2O (150 mL) was added. After stirring for 2 h at −78°C, the reaction mixture was warmed to 0°C and stirred 1 h, warmed to room temperature and stirred 40 min, then quenched by pouring into 1 M HCl (200 mL) and ice (70 g). The maroon organic layer was separated, and the aqueous layer was extracted with Et_2O (3×250 mL). The combined organic layers were washed with saturated $Na_2S_2O_3$, brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by column chromatography (20% EtOAc in hexane) to yield the vinyl iodide as a pale yellow oil (5.6 g, 55%, >95% E): R_f 0.28 (20% EtOAc in hexane); IR (thin film, NaCl) 3324, 2954, 1250, 839 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.10 (t, J=7.6 Hz, 1H), 6.14 (tt, J=7.0, 1.5 Hz, 1H), 4.23 (dd, J=6.7, 5.8 Hz, 2H), 2.87 (dd, J=7.6, 1.5 Hz, 2H), 0.27 (s, 9H), 0.17 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.4, 141.5, 141.4, 108.0, 62.3, 41.9, 1.2, 0.3; HR-MS (ESI) calcd for $C_{12}H_{29}IOSi_2$ $(M+Na)^+$ 391.0381, found 391.0394.

4.2.5. (4*Z*)-4-Iodo-oct-4-ene (1e). Synthesized according to a reported procedure.[15] NMR spectral data were consistent with that reported.[16]

4.2.6. (4*E*)-4-Iodo-oct-4-ene (1f). To a solution of Cp_2-ZrHCl (22.0 g, 87.1 mmol) in CH_2Cl_2 (360 mL) was added 4-octyne (8.0 g, 72.6 mmol) and the reaction mixture stirred overnight. The mixture was cooled to 0°C, iodine (20.3 g, 80.0 mmol) was added and the reaction was warmed to room temperature, stirred 1 h then quenched by pouring into 1 M HCl (200 mL) and ice (50 g). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2

(3×150 mL). The combined organic layers were washed with saturated $Na_2S_2O_3$, brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by column chromatography (hexane) to yield **1f** as a pale yellow oil (9.3 g, 54%, >95% E). NMR spectral data were consistent with that reported.[16]

4.2.7. [(1*E*)-2-Iodo-1-methyl-vinyl]-benzene (1g). Synthesized according to a reported procedure.[17]

4.2.8. (1*Z*)-1-Iodo-hex-1-ene (1h). Synthesized according to a reported procedure.[18] NMR spectral data were consistent with those reported.[19]

4.2.9. (1*E*)-1-Iodo-hex-1-ene (1i). Synthesized according to a reported procedure.[20]

4.3. Representative procedure for the propargyl/allenyl coupling of vinyl iodides 1a–b, 1e–i

A solution of 1-trimethylsilyl-1-propyne (1.5 mL, 10.0 mmol) in THF (21.4 mL) was cooled to −78°C and was treated with a 2.5 M solution of *n*-BuLi (4.6 mL) and TMEDA (1.7 mL, 11.4 mmol). The solution was allowed to warm to 0°C and stirred 45 min. The solution was then transferred via cannula to a −78°C slurry of CuI (2.3 g, 12.1 mmol) in THF (28.6 mL) and stirred at that temperature 30 min. Then the additive (10.0 mmol) was introduced and the solution was allowed to warm to −20°C. At that time the vinyl iodide (7.1 mmol) was added, the reaction mixture was allowed to warm to room temperature gradually and stirred overnight. The reaction was quenched with 1 M HCl (50 mL), and the organic layer was separated. The aqueous layer was extracted with Et_2O (3×200 mL). The combined organic layers were washed with water, brine, dried over $MgSO_4$, and concentrated in vacuo. The allenyl/propargyl ratio of the coupled products was determined by ^1H NMR analysis of the crude material. The crude product was then purified by column chromatography (hexane).

4.3.1. (4*Z*)-1,4-Bis-trimethylsilanyl-non-4-en-1-yne (2a). R_f 0.31 (hexane); IR (thin film, NaCl) 2958, 2859, 2174, 1618, 1466, 1420, 1250, 1054, 1010, 841, 759, 695, 642 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.24 (t, J=7.6 Hz, 1H), 2.98 (s, 2H), 2.14 (app q, J=13.7, 6.4 Hz, 2H), 1.36 (m, 4H), 0.92 (t, J=6.7 Hz, 3H), 0.18 (s, 9H), 0.16 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.4, 132.7, 106.3, 87.6, 32.3, 31.8, 28.9, 22.7, 14.3, 0.4, 0.3; HR-MS (ESI) calcd for $C_{15}H_{30}Si_2$ $(M+Na)^+$ 289.1778, found 289.1773.

4.3.2. (4*Z*)-6-(*tert*-Butyl-dimethyl-silanyloxy)-1,4-bis-trimethylsilanyl-hex-4-en-1-yne (2b). R_f 0.41 (5% EtOAc in hexane); IR (thin film, NaCl) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.36 (tt, J=6.4, 1.5 Hz, 1H), 4.27 (tt, J=6.2, 1.2 Hz, 2H), 3.02 (br d, J=1.5 Hz, 2H), 0.91 (s, 9H), 0.17 (s, 9H), 0.16 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.8, 135.2, 105.7, 88.7, 63.3, 29.1, 26.7, 19.1, 0.8, 0.6, −4.3; HR-MS (ESI) calcd for $C_{18}H_{38}OSi_3$ $(M+Na)^+$ 377.2123, found 377.2124.

4.3.3. Trimethyl-[(4*E*)-4-propyl-oct-4-en-1-ynyl]-silane (2f). R_f 0.39 (hexane); IR (thin film, NaCl) 2960, 2932, 2873, 2176, 1250, 843, 760 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.46 (br t, J=7.3 Hz, 1H), 2.94 (d, J=1.2 Hz, 2H), 2.07 (t, J=7.6 Hz, 2H), 2.01 (app q, J=7.3 Hz, 2H), 1.45–1.34 (m, 4H), 0.91 (app q, J=7.6 Hz, 6H), 0.17 (s, 9H) ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.7, 126.9, 105.3, 87.0, 32.6, 30.1, 27.9, 23.2, 21.6, 14.3, 14.1, 0.3; HR-MS (EI) calcd for $C_{14}H_{26}Si$ $(M)^+$ 222.1798, found 222.1801.

4.3.4. Trimethyl-[(4*E*)-5-phenyl-hex-4-en-1-ynyl]-silane (2g). R_f 0.41 (5% EtOAc in hexane); IR (thin film, NaCl) 2960, 2931, 2873, 2176, 1249, 842, 759 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41–7.24 (m, 5H), 5.80 (tq, J=6.1, 1.2 Hz, 1H), 3.17 (d, J=6.7 Hz, 2H), 2.05 (br s, 3H), 0.17 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.3, 136.9, 128.5, 127.2, 126.0, 122.5, 105.3, 84.7, 26.6, 20.1, 0.4; HR-MS (ESI) calcd for $C_{15}H_{20}Si$ $(M+H)^+$ 229.1407, found 229.1407.

4.3.5. (4*Z*)-Trimethyl-non-4-en-1-ynyl-silane (2h). R_f 0.32 (hexane); IR (thin film, NaCl) 2959, 2929, 2177, 1250, 842, 760 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.51–5.38 (m, 2H), 2.99 (d, J=6.4 Hz, 2H), 2.05 (app q, J=6.4 Hz, 2H), 1.38–1.28 (m, 4H), 0.89 (t, J=7.0 Hz, 3H), 0.16 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 132.2, 124.0, 105.7, 84.2, 31.7, 27.1, 22.6, 18.6, 14.2, 0.3; HR-MS (EI) calcd for $C_{12}H_{22}Si$ $(M-CH_3)^+$ 179.1251, found 179.1252.

4.3.6. (4*E*)-Trimethyl-non-4-en-1-ynyl-silane (2i). R_f 0.24 (hexane); IR (thin film, NaCl) 2959, 2927, 1250, 842, 760 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.68 (dt, J=15.3, 7.0 Hz, 1H), 5.39 (dt, J=15.0, 5.5 Hz, 1H), 2.95 (d, J=5.5 Hz, 2H), 2.03 (app q, J=6.1 Hz, 2H), 1.39–1.29 (m, 4H), 0.90 (t, J=7.0 Hz, 3H), 0.17 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 132.2, 124.0, 105.7, 84.2, 31.7, 27.1, 22.6, 18.6, 14.2, 0.3; HR-MS (EI) calcd for $C_{12}H_{22}Si$ $(M)^+$ 194.1485, found 194.1491.

4.4. Representative procedure for the propargyl/allenyl coupling of vinyl iodides 1c–d

A solution of 1-trimethylsilyl-1-propyne (1.0 mL, 6.5 mmol) in THF (4.3 mL) was cooled to −78°C and was treated with a 2.5 M solution of *n*-BuLi (2.7 mL) and TMEDA (1.0 mL, 6.7 mmol). The solution was allowed to warm to 0°C and stirred 45 min. The solution was then transferred via cannula to a −78°C slurry of CuI (1.4 g, 7.2 mmol) in THF (5.7 mL) and stirred at that temperature 30 min. Then PBu_3 (1.6 mL, 6.5 mmol) was introduced and the solution was allowed to warm to −20°C. At that time the vinyl iodide (1.4 mmol) was added, the reaction mixture was allowed to warm to room temperature gradually and stirred overnight. The reaction was quenched with 1 M HCl (20 mL), and the organic layer was separated. The aqueous layer was extracted with Et_2O (3×20 mL). The combined organic layers were washed with water, brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by column chromatography (20% EtOAc in hexane).

4.4.1. 5,8-Bis-trimethylsilanyl-oct-4-en-7-yn-1-ol (2c). R_f 0.41 (20% EtOAc in hexane); IR (thin film, NaCl) 3314, 2956, 2898, 2173, 1618, 1420, 1249, 1053, 841, 759 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.24 (t, J=7.6 Hz, 1H), 3.68 (t, J=6.4 Hz, 2H), 2.99 (s, 2H), 2.24 (dt, J=7.6, 7.3 Hz, 2H), 1.68 (m, 2H), 0.19 (s, 9H), 0.16 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.6, 134.5, 106.5, 88.3, 63.3, 33.5, 29.4, 28.9, 0.8, 0.7; HR-MS (ESI) calcd for $C_{14}H_{28}OSi_2$ $(M+Na)^+$ 291.1571, found 291.1577.

4.4.2. (2*Z*, 5*Z*)-3,6,9-Tris-trimethylsilanyl-nona-2,5-dien-8-yn-1-ol (2d). R_f 0.42 (20% EtOAc in hexane); IR (thin film, NaCl) 3313, 2956, 2898, 2173, 1249, 839 758 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.23 (tt, J=7.3, 1.5 Hz, 1H), 6.13 (tt, J=7.0, 1.5 Hz, 1H), 4.22 (d, J=7.0 Hz, 2H), 3.02 (d, J=1.2 Hz, 2H), 2.96 (dd, J=7.3, 1.2 Hz, 2H), 0.19 (s, 9H), 0.17 (s, 9H), 0.16 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.1, 141.9, 140.9, 134.5, 105.8, 87.9, 62.4, 39.1, 28.8, 0.49, 0.43, 0.20; HR-MS (ESI) calcd for $C_{18}H_{36}OSi_3$ $(M+Na)^+$ 375.1966, found 375.1964.

Acknowledgements

We thank Johnson and Johnson for a research assistantship to T. P. H. We also thank the National Institute of General Medical Sciences (GM-063755), the NSF (CAREER CHE-0134704), Merck Research Laboratories, Johnson and Johnson, Boehringer-Ingelheim, Pfizer, 3M, The Donors of the Petroleum Research Fund, and MIT for financial support. The NSF (CHE-9809061 and DBI-9729592) and NIH (1S10RR13886-01) provide partial support for the MIT Department of Chemistry Instrumentation Facility.

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