A Facile One-Pot Synthesis of Homopropargylic Alcohols from Terminal Acetylenes

Mark R. Burns and James K. Coward*

Interdepartmental Program in Medicinal Chemistry, College of Pharmacy, and Department of Chemistry, The University of Michigan, Ann Arbor, Michigan 48109

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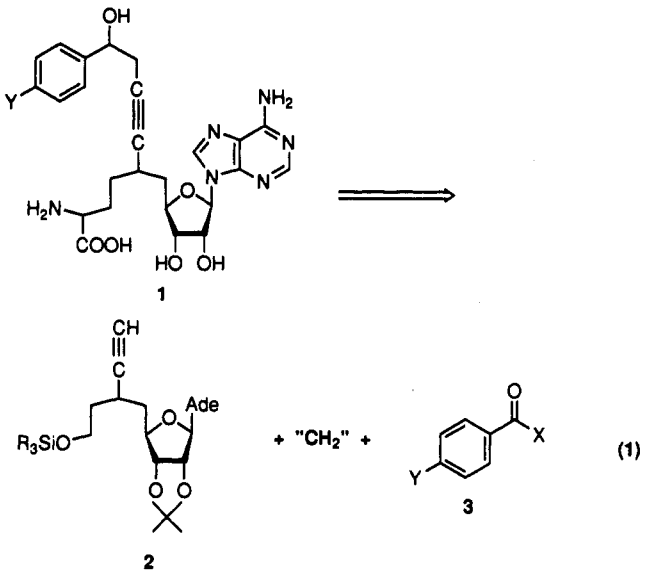
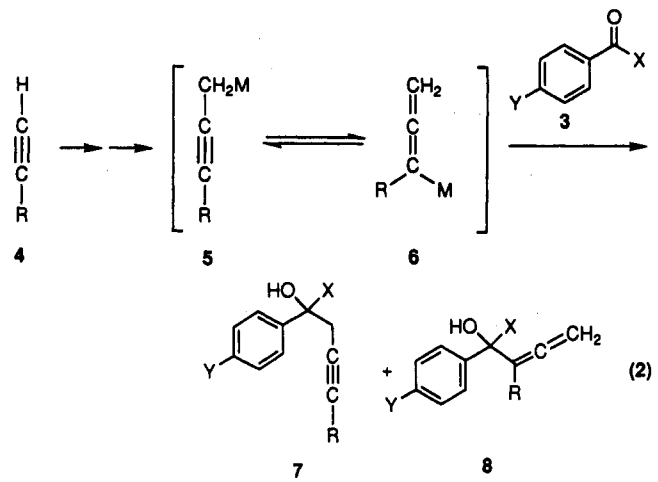
During work toward the synthesis of specific multisubstrate analog inhibitors[1] of the enzyme phenylethanolamine *N*-methyltransferase (PNMT, EC 2.1.1.28), a need arose to construct the homopropargylic alcohol functionality in **1**. Because the terminal acetylenic nucleoside, **2** was available,[2] it was used as the starting point in the present work (eq 1). It was hoped that, through a



two-step process, a suitable propargylic halide could be obtained and transformed into a propargylic organometallic which could then react with an electrophile such as benzaldehyde (**3**, X = Y = H) to give the desired homopropargylic alcohol product (**1**, Y = H). However, due to the ever present propargylic/allenic equilibrium in the organometallic (**5** ⇌ **6**), a mixture of the desired homopropargylic regioisomer **7**, resulting from α-attack, and the allenic regioisomer **8**, resulting from γ-attack, was always obtained (eq 2).[3] This led to a search for a solution of this regiochemical problem.

Several researchers have reported methods to successfully increase the amount of homopropargylic isomer obtained in this reaction, but these methods are restricted by limited substrate versatility and/or starting materials which are difficult to obtain. There is also the concern that these methods[4–7] would be difficult to implement with



a polyfunctional acetylenic nucleoside substrate such as **2**. A much more amenable solution described by both Yamamoto[8] and Noyori[9] entails the use of a "ketone-like" acylsilane as the electrophile in this reaction. The bulky trialkylsilyl group prevents attack at the more sterically congested γ-position, thus reducing or eliminating formation of the allenic regioisomer. The trialkylsilyl group could then be removed either by fluoride treatment or the base-mediated Brook rearrangement discussed below.

Rozema and Knochel recently reported the use of the Simmons–Smith reagent to form a propargylic organometallic directly from an alkynylcopper species.[10] This propargylic organometallic, generated in situ, can then react with various electrophiles already present in the reaction flask to give the coupled products. When this reaction was studied with the α-substituted alkyne **4a**,[2] using benzaldehyde as the electrophile, a 2:1 mixture of the homopropargylic (**7**) and allenic (**8**) alcohols was obtained (Table I, entry 1). The present paper discusses the application of both acylsilane and propargylic organometallic methodologies, used in a combined one-pot process, to form the desired homopropargylic alcohol functionality from a terminal acetylene. A variety of reaction conditions have been studied in order to improve the reaction yield and regioselectivity. The breadth of the reaction was studied with a variety of terminal acetylenes and electrophilic acylsilanes (Table I).

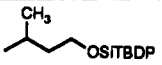
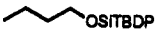
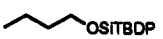
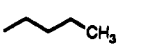
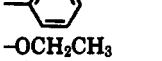
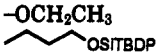
Results and Discussion

As stated above, entry 1 of Table I shows that the in situ generated zinc propargylic organometallic formed from **4a** and the Simmons–Smith reagent, via an alkynyl copper species, reacts with benzaldehyde in a nonregioselective manner to give a 2:1 mixture of **7a** and **8a**.[11] In contrast, the use of a sterically hindered acylsilane, benzoyltriiso-

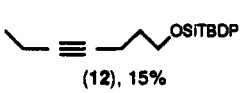
(1) Broom, A. D. *J. Med. Chem.* **1989**, *32*, 2.
(2) Yau, E. K.; Coward, J. K. *J. Org. Chem.* **1990**, *55*, 3147.
(3) (a) Gelin, R.; Gelin, S.; Albrand, M. *Bull. Chem. Soc. Fr.* **1971**, 4546. (b) Epsztein, R. In *Comprehensive Carbanion Chemistry*; Buncel, F., Purst, T., Eds.; Elsevier: New York, 1984; part B, p 107. (c) Klein, J. In *The Chemistry of the Carbon–Carbon Triple Bond*; Patai, S., Ed.; Wiley: New York, 1978; part 1, p 343.
(4) Zweifel, G.; Backlund, S. J.; Leung, T. *J. Am. Chem. Soc.* **1978**, *100*, 5561.
(5) Daniels, R. G.; Paquette, L. A. *Tetrahedron Lett.* **1981**, *22*, 1579.
(6) Furuta, K.; Ishiguro, M.; Haruta, R.; Ikeda, N.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2768.
(7) Danheiser, R. L.; Carini, D. J.; Kwasigroch, C. A. *J. Org. Chem.* **1986**, *51*, 3870.
(8) (a) Yanagisawa, A.; Habaue, S.; Yamamoto, H. *J. Org. Chem.* **1989**, *54*, 5198. (b) Yanagisama, A.; Habaue, S.; Yamamoto, H. *Tetrahedron* **1992**, *48*, 1969.
(9) Suzuki, M.; Morita, Y.; Noyori, R. *J. Org. Chem.* **1990**, *55*, 441.
(10) Rozema, M. J.; Knochel, P. *Tetrahedron Lett.* **1991**, *32*, 1855.
(11) The alkynyl copper species was obtained by transmetalation of the corresponding lithium acetylide. House, H. O.; Umen, M. J. *J. Org. Chem.* **1973**, *38*, 3893.

0022-3263/93/1958-0528$04.00/0

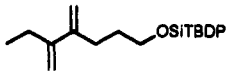
Table I. Reactions Leading to Homopropargylic Alcohols from Terminal Acetylenes

			R'CX			products (%)		
	alkyne	R–	R'	X	condns[a]	7	8	11
1	4a		C_6H_5	H	–78	46	23	
2	4b		C_6H_5	$Si(Pr^i)_3$	–78			29[b]
3	4b		C_6H_5	$SiMe_3$	–78	43		15
4	4b		C_6H_5	$SiMe_3$	–10, ZnI_2	64		22
5	4c		C_6H_5	$SiMe_3$	–10, ZnI_2	63		9
6	4d	$-Si(CH_3)_3$	C_6H_5	$SiMe_3$	–10, ZnI_2	52		8
7	4e		C_6H_5	$SiMe_3$	–10, ZnI_2	79		7
8	4f	$-OCH_2CH_3$	C_6H_5	$SiMe_3$	–10, ZnI_2			c
9	4b		p-$CF_3C_6H_4$	$SiMe_3$	–10, ZnI_2	32[d]		
10	4b		CH_3 (14)	$SiMe_3$	–10, ZnI_2	9 (7g)		12[e] (11g)

[a] Temperature of electrophile (°C) and $Zn(CH_2I)_2$ addition. [b] Also isolated were the following products:



(12), 15%



(13), 17%

[c] n-BuLi addition products: 7c, 15%, and 11c, 5% (see ref 15). [d] p-CF_3 on 7b. [e] Products 7g and 11g arising from acetyltrimethylsilane (14) have CH_3 in place of the phenyl substituent in structures 7 and 11.

propylsilane (3, X = $Si(Pr^i)_3$, Y = H)[12] with acetylene 4b resulted in none of the desired homopropargylic alcohol, 7b, but rather the formation of diene 11b in 29% yield. This product results from the addition of three methylene equivalents (of 3.3 equiv of the Simmons–Smith reagent used in this procedure) to the alkynylcopper reagent (Scheme I). Products of this type were also observed by Rozema and Knochel[10] who noted that diene formation is decreased if the electrophile is placed in the flask before the addition of the Simmons–Smith reagent.[13] In addition, the low reactivity of the hindered acyl silane led to the isolation of products arising from the reaction of ethyl iodide with the anion of 4b (to give 12 (15%)) or 9b (to give 13 (17%)) (Table I, entry 2). The ethyl iodide present in the reaction mixture arises from the generation of the Simmons–Smith reagent from diethylzinc and diiodomethane ($Et_2Zn + CH_2I_2 \rightarrow Zn(CH_2I)_2 + 2\ EtI$).[14]

The use of the less sterically demanding benzoyltrimethylsilane (3, X = TMS, Y = H)[12] was investigated in order to increase the reactivity of the electrophile. As shown in Table I (entry 3), the reaction of this acylsilane with the propargylic organometallic derived from 4b at –78 °C gave a 43% yield of the desired homopropargylic alcohol 7b and 15% of the triple methylene adduct 11b. Finally, the use of this acylsilane with the added electrophilic catalyst, ZnI_2, at the higher temperature of –10 °C led to 7b in an acceptable yield of 64%, together with 22% of the undesired side product 11b (Table I, entry 4). Both the addition of ZnI_2 and the higher temperature at which the Simmons–Smith reagent is added to the reaction solution (alkynylcopper reagent and electrophile) appear to be important modifications. Presumably the reactivity of the acylsilane is increased enough to allow the freshly generated propargylic organometallic to react more readily with the acylsilane to give increased yields of both 7 and 11.

The structural changes allowed in the terminal acetylene substrate were explored next. Entries 5–7 of Table I show that reaction of the simple benzoylsilane 3 (X = TMS, Y = H) with 1-hexyne (4c), (trimethylsilyl)acetylene (4d), or phenylacetylene (4e) gave the desired homopropargylic alcohols 7c–e in 63%, 52%, and 79% yields, respectively, under the now improved conditions. Also isolated were the triple methylenated side products 11c–e, each in less than 10% yield (Table I). In entry 8 the use of ethoxyacetylene (4f) gave only 15% of 7c and 5% of 11c resulting from the addition of n-BuLi to 4f.[15]

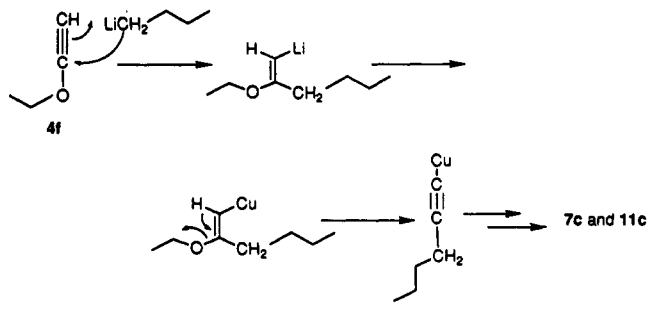
Some structural limitations are imposed on the acylsilane reagent as suggested by entries 9 and 10. The use of the p-CF_3-substituted benzoylacylsilane (3, X = TMS,

(12) Corey, E. J.; Seebach, D.; Freedman, R. *J. Am. Chem. Soc.* **1967**, *89*, 434.

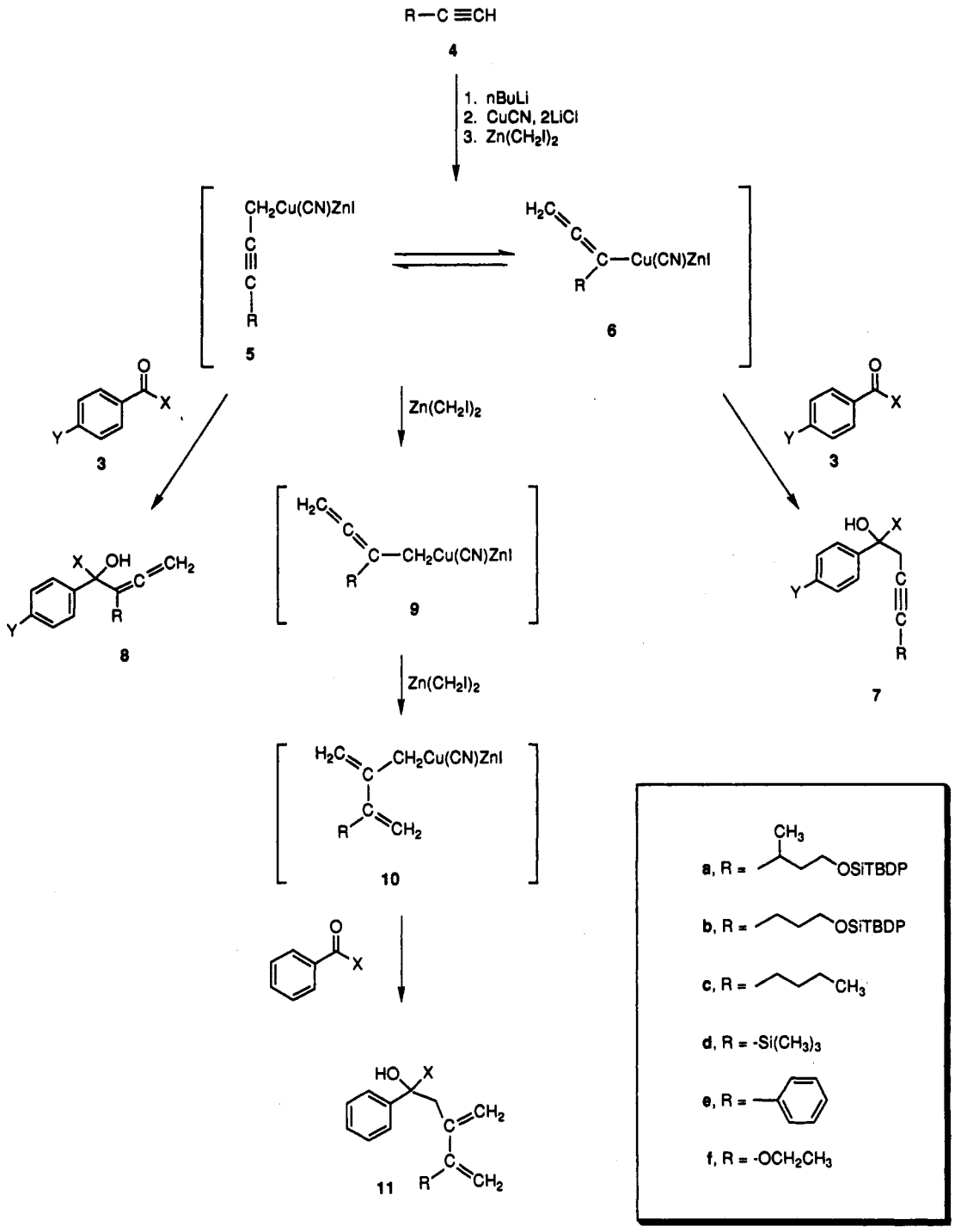
(13) Rozema, M. Ph.D. Thesis, The University of Michigan, Ann Arbor, MI, May, 1992.

(14) Wittig, G.; Wingler, F. *Chem. Ber.* **1964**, *97*, 2139; *Ibid.* 2146.

(15) The formation of 7c and 11c from the reaction of ethoxyacetylene (4f) and n-BuLi under the conditions described is assumed to occur via n-BuLi attack at the electrophilic α-carbon atom followed by elimination of ethanol. The resulting 1-copper hexynyl species can then proceed to give the observed products as before. For a review of chemistry of ethynyl ethers and thioethers, see: Arens, J. F. *Adv. Org. Chem.* **1960**, *2*, 117.



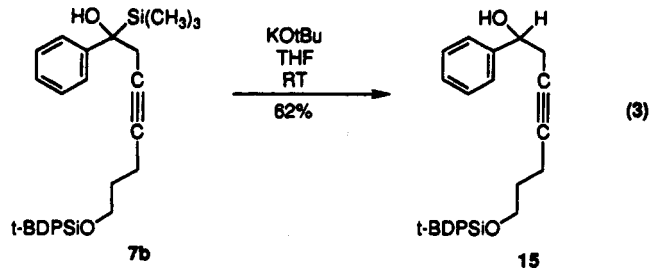
Scheme I



Y = CF_3)[16] gave a lower yield (32%) of the desired homopropargylic alcohol **7b** (X = TMS, Y = CF_3). The use of a nonaryl acylsilane, acetyltrimethylsilane (**14**),[17] also gave a low yield (9%) of the desired homopropargylic alcohol **7g**. In this case a significant amount (12%) of the triple methylenated product **11g** was isolated, thereby suggesting that the alkylacylsilane **14** is not as reactive as the benzoyl silane (**3**, X = TMS, Y = H) under these conditions. The lower yields of product in these two entries clearly shows the sensitivity to changes in the acylsilane portion of the reaction. Further experimentation is required to define the structural limitations of this reaction and to optimize yields.

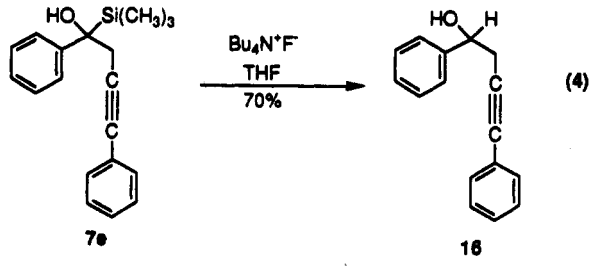
Desilylation of two of the coupled adducts, as depicted in eqs 3 and 4, shows the further synthetic versatility of this approach. Since the ultimate synthetic goal of this research required a method to selectively desilylate a trimethylsilyl group in the presence of a *tert*-butyldiphenylsilyl ether, the Brook rearrangement[18] (eq 3) was explored. Treatment of a THF solution of **7b** with potassium *tert*-butoxide resulted in a Brook rearrangement followed by subsequent Si–O bond cleavage giving a 62% yield of the desired homopropargylic alcohol **15**. No desilylation of the *tert*-butyldiphenylsilyl ether was seen.

(16) Yamamoto, K.; Hayashi, A.; Suzuki, S.; Tsuji, J. *Organometallics* **1987**, *6*, 974.
(17) Brook, A. G.; Duff, J. M.; Jones, P. F.; Davis, N. R. *J. Am. Chem. Soc.* **1967**, *89*, 431.
(18) Brook, A. G. *Acc. Chem. Res.* **1974**, *7*, 77.



7b 15 (3)

However, if no other silyl groups are present in the molecule, the standard fluoride-mediated desilylation can be achieved as shown in eq 4. Desilylation of **7e** with TBAF in THF gave a 70% yield of the desired 1,4-diphenyl-3-butyn-1-ol (**16**).[19]



7e 16 (4)

Work is now underway in our laboratory to optimize the conditions of the procedure described in this paper for the ultimate nucleoside coupling reaction (eq 1). The synthetic and biochemical results will be reported in a subsequent publication.

Conclusions

In this paper we describe the facile synthesis of homopropargylic alcohols from a variety of terminal acetylenes via a one-pot homologation–condensation reaction. The procedure described offers significant advantages over previously described two-step processes described by Yamamoto and colleagues.[8] In addition, use of the acylsilanes in place of free aldehydes as the electrophilic component under the conditions described eliminates formation of the allenic alcohols **8**. The use of an electrophilic catalyst ZnI_2 and a higher temperature greatly reduces the occurrence of products (e.g., **11**) resulting from multiple methylene insertions.[10] In all cases these side products were easily removed from the desired product by silica gel chromatography.

Experimental Section[20]

1-Phenyl-1-(trimethylsilyl)-7-(*tert*-butyldiphenylsiloxy)-hept-3-yn-1-ol (7b). To a solution of 250 mg (0.76 mmol) of terminal acetylene **4b** in 3 mL of THF was added dropwise 0.52 mL (0.84 mmol, 1.1 equiv) of 1.6 M n-BuLi in hexane at −78 °C. After 30 min at −78 °C and 30 min at 0 °C the colorless solution was cooled back to −78 °C. In another flask containing 104 mg (1.16 mmol, 1.5 equiv) of CuCN and 99 mg (2.34 mmol, 3.0 equiv) of LiCl that had been dried at 150 °C under an atmosphere of argon for 2 h was placed 10 mL of THF, and the golden solution was transferred to the flask containing the lithium acetylide at −78 °C. The resulting yellow solution was stirred at −78 °C for 30 min and 0 °C for 30 min while the Simmons–Smith reagent was prepared. To 0.5 mL (6.2 mmol, 2.5 equiv) of CH_2I_2 in 10 mL of THF was added 2.5 mL (2.5 mmol) of a 1 M solution of $ZnEt_2$ in hexane at −78 °C. Diethylzinc is very pyrophoric. Therefore, a gas-tight syringe wrapped tightly with Parafilm was used to make this transfer. The resulting mixture was stirred −78 °C for 30 min and 0 °C for 30 min. The flask containing the alkynylcopper reagent was cooled to −10 °C, and 136 mg (0.76 mmol, 1 equiv) of benzoyl silane **3** (X = TMS, Y = H) and 243 mg (0.76 mmol, 1 equiv) of ZnI_2 in 10 mL of THF was added to this flask. The Simmons–Smith reagent was now introduced dropwise to this flask via a cannula. A red color formed and immediately disappeared in the greenish/yellow solution. The color changed to brown as more of the Simmons–Smith reagent was added. A white ppt was also noticed. The resulting mixture was stirred at −10 °C for 30 min when it was then quenched by addition of saturated NH_4Cl. The mixture was extracted twice with ether, and the ether layers were combined and washed with H_2O and brine. These layers were dried ($MgSO_4$), filtered, and evaporated giving 450 mg crude tan oil. Filtering column chromatography[21] using cyclohexaneCH_2Cl_2 (1:1) gave 250 mg (64%) of **7b** as a clear oil: ^1H NMR ($CDCl_3$) δ 7.66–7.13 (m, 15 H, ArH), 3.55 (t, J = 5.9 Hz, 2 H, H_g), 2.85 (qt (ABX), J_{gem} = 16.6 and J_γ = 2.3 Hz, 2 H, H_b), 2.23 (s, 1 H, D_2O exch, −OH), 2.19 (tt, J = 5.6 and 2.3 Hz, 2 H, H_e), 1.55 (m, 2 H, H_f), 1.04 (s, 9 H, *tert*-butyl), −0.01 (s, 9 H, $Si(CH_3)_3$); ^{13}C NMR ($CDCl_3$) δ 145.6, 135.6, 134.0, 129.6, 127.9, 127.8, 127.7, 125.6, 125.5, 125.4, 124.9 (Ar), 84.1 (C_d), 75.3 (C_c), 70.4 (C_a), 62.3 (C_g), 31.9 (C_e), 28.8 (C_b), 26.9 ($C(CH_3)_3$), 19.2 ($C(CH_3)_3$), 15.2 (C_f), −4.0 ($Si(CH_3)_3$); IR (neat oil, cm^{-1}) 3517 (br, −OH); HRMS (EI) calcd for $C_{32}H_{42}Si_2O_2$ 514.2723, found 514.2690 (M^+, 2.5). Anal. Calcd for $C_{32}H_{42}Si_2O_2$: C, 74.65; H, 8.22. Found: C, 74.58; H, 8.26.

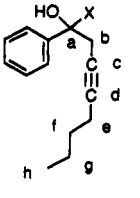
1-Phenyl-1-(trimethylsilyl)-3,4-dimethylene-7-(*tert*-butyldiphenylsiloxy)heptan-1-ol (11b). Also isolated from the reaction of **4b** and **3** (X = TMS and Y = H) was 90 mg (22%) of triple methylenated side product: ^1H-NMR ($CDCl_3$) δ 7.70–7.11 (m, 15 H, ArH), 5.04, 4.90, 4.78, 4.72 (s, 4 H, vinyl H), 3.59 (t, J = 5.3 Hz, 2 H, H_g), 3.00 (q (AB), J_{gem} = 12.1 Hz, 2 H, H_b), 2.23 (t, J = 6.5 Hz, 2 H, H_e), 2.21 (s, 1 H, D_2O exch, −OH), 1.52 (m, 2 H, H_f), 1.07 (s, 9 H, *tert*-butyl), 0.01 (s, 9 H, $Si(CH_3)_3$); ^{13}C NMR ($CDCl_3$) δ 150.8 and 143.4 (C_c and C_d), 135.5, 133.9, 129.5, 128.2, 125.0 (ArC), 116.2 and 112.5 (2 × $=CH_2$), 71.7 (C_a), 63.3 (C_g), 39.6 (C_f), 31.2 and 30.7 (C_b and C_e), 26.8 ($C(CH_3)_3$), 19.2 ($C(CH_3)_3$), −4.1 ($Si(CH_3)_3$); HRMS (CI, NH_3) calcd for $C_{34}H_{46}Si_2O_2H$ 543.3115, found 543.3088 (MH^+, 7.6). Anal. Calcd for $C_{34}H_{46}Si_2O_2 \cdot 0.5\,H_2O$: C, 73.99; H, 8.58. Found: C, 74.16; H, 8.51.

1-(*tert*-Butyldiphenylsiloxy)hept-4-yne (12). From the reaction of **4b** and **3** (X = $Si(Pr^i)_3$, Y = H): ^1H NMR ($CDCl_3$) δ 7.68–7.34 (m, 10 H, ArH), 3.74 (t, J = 6.0 Hz, 2 H, H_g), 2.29 (tt, J = 7.1 and 2.2 Hz, 2 H, H_e), 2.13 (qt (ABX), J_{gem} = 7.5 and J_γ = 2.2 Hz, 2 H, H_b), 1.75 (quin, 2 H, H_f), 1.06 (m, 12 H, *tert*-butyl and H_a); IR (neat oil) showed no −OH absorption; MS (CI, NH_3) 351 (MH^+, 100).

1-(*tert*-Butyldiphenylsiloxy)-4,5-dimethyleneheptane (13). From the reaction of **4b** and **3** (X = $Si(Pr^i)_3$, Y = H): ^1H NMR ($CDCl_3$) δ 7.70–7.34 (m, 10 H, ArH), 5.06 (s, 2 H, vinyl), 4.92 (s, 2 H, vinyl), 3.68 (t, J = 6.3 Hz, 2 H, H_g), 2.36 (t, J = 7.8 Hz, 2 H, H_e), 2.24 (q, J = 7.4 Hz, 2 H, H_b), 1.72 (m, 2 H, H_f), 1.06 (m, 12 H, *tert*-butyl and H_a); IR (neat oil) showed no −OH absorption; MS (CI, NH_3) 379 (MH^+, 13). Anal. Calcd for $C_{25}H_{34}SiO$: C, 79.39; H, 9.06. Found: C, 78.83; H, 9.14.

(19) Padwa, A.; Rodriquez, A.; Tohidi, M.; Kukunaga, T. *J. Am. Chem. Soc.* **1983**, *105*, 933.

(20) For general experimental methods and instrumentation, see ref 2. The methylene protons labeled H_b (see below) are observed as a quartet of triplets (qt) due to geminal coupling (J_{gem}) and γ coupling (J_γ). Other multiplicity abbreviations are tt (triplet of triplets) and td (triplet of doublets). Mass spectral data are reported as m/z (rel intensity). Unless otherwise stated, compounds **7** and **11** described in the Experimental Section have X = TMS and Y = H. The chemical shift assignments in the NMR spectra are according to the following generic structure:



(21) Yau, E. K.; Coward, J. K. *Aldrichim. Acta* **1988**, *21*, 106.

1-Phenyl-1-(trimethylsilyl)-3-octyn-1-ol (7c). This product was synthesized from 1-hexyne (4c) (156 mg, 1.9 mmol) and 3 (X = TMS, Y = H) via the procedure described above. Column chromatography (cyclohexane/CH_2Cl_2 (1:1)) gave 330 mg (63%) of 7c as a clear oil: ^1H NMR ($CDCl_3$) δ 7.31–7.09 (m, 5 H, ArH), 2.82 (qt (ABX), J_{gem} = 16.5 and J_γ = 2.2 Hz, 2 H, H_b), 2.25 (s, 1 H, –OH), 1.98 (tt, J = 6.9 and 2.2 Hz, 2 H, H_e), 1.17 (m, 4 H, H_f and H_g), 0.74 (t, 3 H, H_h), –0.04 (s, 9 H, $Si(CH_3)_3$); ^{13}C NMR ($CDCl_3$) δ 145.6, 127.7, 127.6, 125.4, 125.3, 124.8 (6 × ArC), 84.4 (C_d), 75.0 (C_c), 70.3 (C_a), 30.8 (C_e), 28.8 (C_b), 21.5 and 18.2 (C_f and C_g), 13.4 (C_h), –4.0 ($Si(CH_3)_3$); IR (neat, cm^{-1}) 3515 (br s, OH); HRMS (CI, NH_3) calcd for $C_{17}H_{26}SiONH_4$ 292.2097, found 292.2084 (MNH_4^+, 54).

Also isolated from this reaction was the triple methylenated side product 11c in 9% yield: ^1H NMR ($CDCl_3$) δ 7.31–7.08 (m, 5 H, ArH), 5.02, 4.87, 4.76, and 4.69 (s, 4 H, vinyl), 2.97 (q (AB), 2 H, H_b), 2.22 (s, 1 H, –OH), 2.09 (m, 2 H, H_e), 1.23 (m, 4 H, H_f and H_g), 0.85 (m, 3 H, $-CH_3$), 0.01 (s, 9 H, $Si(CH_3)_3$); ^{13}C NMR ($CDCl_3$) δ 151.5 (ArC), 145.6 and 143.7 (C_c and C_d), 127.5, 125.0, 124.8 (ArC), 116.1 and 112.3 (2 × $=CH_2$), 71.9 (C_a), 39.7, 34.2, 30.4, 22.4 (C_b, C_e, C_f and C_g), 13.9 (C_h), –4.1 ($Si(CH_3)_3$); IR (neat, cm^{-1}) 3526 (–OH), 1591, 1247, 839; HRMS (EI) calcd for $C_{19}H_{30}OSi$ 302.2066, found 302.2066 (M^+, 24).

1-Phenyl-1,4-bis(trimethylsilyl)-3-butyn-1-ol (7d). This product was synthesized from (trimethylsilyl)acetylene (4d) and 3 (X = TMS, Y = H) via the procedure described above for 7b. From 196 mg (2.0 mmol) of 4d was obtained 300 mg (52%) of 7d following purification by column chromatography: ^1H NMR ($CDCl_3$) δ 7.34–7.14 (m, 5 H, ArH), 2.90 (q (AB), 2 H, H_b), 2.27 (s, 1 H, –OH), 0.0 (s, 18 H, 2 X $Si(CH_3)_3$); ^{13}C NMR ($CDCl_3$) δ 145.3, 127.7, 125.4, 124.7 (ArC), 102.6 (C_d), 88.9 (C_c), 70.2 (C_a), 30.2 (C_b), –0.2 and –3.9 (2 X $Si(CH_3)_3$); IR (neat, cm^{-1}) 3550 (–OH), 2171 (–C≡C–), 1249, 842; HRMS (CI, NH_3) calcd for $C_{16}H_{26}OSi_2NH_4$ 308.1866, found 308.1870 (MNH_4^+, 37).

Also isolated from this reaction was the triple methylenated side product 11d in 8% yield: ^1H NMR ($CDCl_3$) δ 7.27–7.07 (m, 5 H, ArH), 5.37 (d, 1 H, vinyl), 5.24 (d, 1 H, vinyl), 4.72 and 4.64 (s, 2 H, vinyl), 3.00 (q (AB), 2 H, H_b), 2.36 (s, 1 H, –OH), 0.06 and 0.00 (2 s, 18 H, 2 X $Si(CH_3)_3$); ^{13}C NMR ($CDCl_3$) δ 156.4 (ArC), 147.4 and 145.5 (C_c and C_d), 133.7, 130.2, 127.8, 127.4, 126.3 ($=CH_2$), 125.3, 124.8, 115.0 ($=CH_2$), 71.0 (C_a), 41.1 (C_b), –0.7 and –4.3 (2 X $Si(CH_3)_3$); IR (neat, cm^{-1}) 3527 (–OH), 1249, 839; HRMS (EI) calcd for $C_{18}H_{30}OSi_2$ 318.1835, found 318.1826 (M^+, 10).

1,4-Diphenyl-1-(trimethylsilyl)-3-butyn-1-ol (7e). This product was synthesized from phenylacetylene (4e) and 3 (X = TMS, Y = H) via the procedure described above for 7b. From 194 mg (1.9 mmol) of 4e was obtained 410 mg (79%) of yellow solid following purification by column chromatography (cyclohexane/CH_2Cl_2 (1:1)): mp 65–67 °C; ^1H NMR ($CDCl_3$) δ 7.42–7.23 (m, 10 H, ArH), 3.17 (q (AB), 2 H, H_b), 2.36 (s, 1 H, –OH), 0.08 (s, 9 H, $Si(CH_3)_3$); ^{13}C NMR ($CDCl_3$) δ 145.5, 131.6, 128.1, 127.9, 127.8, 125.6, 124.8, 123.3 (12 C, ArC), 85.5, 84.2 (C_c and C_d), 70.8 (C_a), 29.7 (C_b), –3.9 ($Si(CH_3)_3$); IR (KBr, cm^{-1}) 3509 (sharp), 3450 (br, –OH), 2960, 1249, 839; HRMS (CI, NH_3) calcd for $C_{19}H_{22}SiONH_4$ 312.1784, found 312.1779 (MNH_4^+, 90). Anal. Calcd for $C_{19}H_{22}SiO$: C, 77.50; H, 7.54. Found C, 77.05; H, 7.46.

1-(4-(Trifluoromethyl)phenyl)-1-(trimethylsilyl)-7-(*tert*-butyldiphenylsiloxy)-3-heptyn-1-ol (7b, X = TMS, Y = CF_3). This product was synthesized from 4b and 3 (X = TMS, Y = CF_3)[16] via the procedure described above for 7b. From 250 mg (0.76 mmol) of acetylene 4b was obtained 140 mg (32%) of 7b (X = TMS, Y = CF_3) by column chromatography (cyclohexane/CH_2Cl_2 (1:1): ^1H NMR ($CDCl_3$) δ 7.68–7.27 (m, 14 H, ArH), 3.55 (t, J = 5.9 Hz, 2 H, H_g), 2.86 (qt (ABX), J_{gem} = 16.8 and J_γ = 2.0 Hz, 2 H, H_b), 2.29 (s, 1 H, –OH), 2.18 (tt, J = 7.1 and 2.0 Hz, 2 H, H_e), 1.52 (m, 2 H, H_f), 1.04 (s, 9 H, *tert*-butyl), 0.00 (s, 9 H, $Si(CH_3)_3$); ^{13}C NMR ($CDCl_3$) δ 150.0, 135.6, 133.8, 129.6, 127.6, 125.2, 124.8 (ArC), 84.5 and 74.6 (C_d and C_c), 70.6 (C_a), 62.1 (C_g), 31.8 (C_e), 28.6 (C_b), 26.8 ($C(CH_3)_3$), 19.2 ($C(CH_3)_3$), 15.1 (C_f), –4.1 ($Si(CH_3)_3$); HRMS (CI, isobutane) calcd for $C_{33}H_{41}F_3O_2Si_2$ 582.2597, found 582.2584 (MH^+, 6). Anal. Calcd for $C_{33}H_{41}F_3O_2Si_2$: C, 68.00; H, 7.09. Found: C, 67.14; H, 7.10.

2-(Trimethylsilyl)-8-(*tert*-butyldiphenylsiloxy)-4-octyn-2-ol (7g). This product was synthesized from acetyltrimethylsilane (14)[17] and 4b via the same procedure as 7b described above. From 777 mg (2.4 mmol) of acetylene 4b was obtained 100 mg (9%) of 7g by column chromatography (hexane/ethyl acetate (96:4)): ^1H NMR ($CDCl_3$) δ 7.70–7.34 (m, 10 H, ArH), 3.73 (t, J = 6.0 Hz, 2 H, H_g), 2.47–2.20 (m, 4 H, H_b and H_e), 1.75 (m, 2 H, H_f), 1.50 (s, 1 H, –OH), 1.20 (s, 3 H, CH_3), 1.04 (s, 9 H, *tert*-butyl), 0.06 (s, 9 H, $-Si(CH_3)_3$); ^{13}C NMR ($CDCl_3$) δ 135.6, 133.9, 129.6, 127.6 (ArC), 83.8 and 75.6 (C_d and C_c), 64.5 (C_a), 62.5 (C_g), 32.0 and 30.3 (C_e and C_b), 26.8 ($C(CH_3)_3$), 24.1 (CH_3), 19.2 ($C(CH_3)_3$), 15.3 (C_f), –4.0 ($Si(CH_3)_3$); HRMS (CI, NH_3) calcd for $C_{27}H_{40}O_2Si_2NH_4$ 453.2645, found 453.2640 (MNH_4^+, 8). Anal. Calcd for $C_{27}H_{40}Si_2O_2$: C, 71.62; H, 8.90. Found: C, 71.15; H, 8.75.

Also isolated from this reaction was the triple methylenated side product 11g isolated in 12% yield: ^1H NMR ($CDCl_3$) δ 7.69–7.34 (m, 10 H, ArH), 5.30, 5.12, 4.95 and 4.89 (s, 4 H, vinyl), 3.68 (t, J = 6.3 Hz, 2 H, H_g), 2.63–2.32 (m, 4 H, H_b and H_e), 1.72 (m, 2 H, H_f), 1.05 (s, 12 H, CH_3 and $C(CH_3)_3$), 0.06 (s, 9 H, $-Si(CH_3)_3$); HRMS (CI, isobutane) calcd for $C_{29}H_{44}O_2Si_2H$ 481.2958, found 481.2935 (MH^+, 39).

1-Phenyl-7-(*tert*-butyldiphenylsiloxy)hept-3-yn-1-ol (15). To a suspension of 157 mg (1.3 mmol, 1.1. equiv) of $KOBu^t$ in 30 mL of THF at rt was added 576 mg (1.12 mmol) of silane 7b in 10 mL of THF. The $KOBu^t$ immediately went into solution forming a brown color. This solution was stirred for 1 h, and then 6 mL of H_2O was added and the THF was evaporated in vacuo. The residue was diluted with CH_2Cl_2 and H_2O, and the organic layer was removed. The aqueous layer was washed again with CH_2Cl_2, and the organic layers were combined. These organic extractions were washed with H_2O and brine, dried, filtered, and evaporated giving 420 mg (85%) of a brown oil. Column chromatography (cyclohexane/CH_2Cl_2 (1:4)) gave 200 mg (40%) of the desired homopropargylic alcohol 15. Also obtained was 130 mg (23%) of the TMS ether intermediate of the Brook rearrangement which could be quantitatively converted to 15 by treatment with HOAc in CH_2Cl_2. Total yield was 310 mg (62%): ^1H NMR ($CDCl_3$) δ 7.71–7.32 (m, 15 H, ArH), 4.76 (m, 1 H, H_a), 3.70 (t, J = 6.0 Hz, 2 H, H_g), 2.57 (m 2 H, H_b), 2.38 (d, 1 H, –OH), 2.33 (tt, J = 7.2 and 2.5 Hz, 2 H, H_e), 1.74 (m, 2 H, H_f), 1.06 (s, 9 H, *tert*-butyl); ^{13}C NMR ($CDCl_3$) δ 142.8, 135.5, 133.8, 129.5, 128.3, 127.6, 125.7, (ArC), 82.9 and 76.2 (C_d and C_c), 72.5 (C_a), 62.4 (C_g), 31.8 (C_e), 30.0 (C_b), 26.8 ($C(CH_3)_3$), 19.2 ($C(CH_3)_3$), 15.2 (C_f); IR (neat, cm^{-1}) 3435 (–OH), 1428, 1111; HR MS (CI, NH_3) calcd for $C_{29}H_{34}Si_2NH_4$ 460.2672, found 460.2668 (MNH_4^+, 21). Anal. Calcd for $C_{29}H_{34}SiO_2$: C, 78.69; H, 7.74. Found: C, 78.20; H, 7.87.

1,4-Diphenyl-3-butyn-1-ol (16).[19] To a solution of 210 mg (0.71 mmol) of 7e in 10 mL of THF was added dropwise at rt 0.71 mL (0.71 mmol, 1.0 equiv) of a 1 M solution of tetrabutylammonium fluoride in THF. The solution was stirred for 5 h, and then it was diluted with CH_2Cl_2 and washed with H_2O, saturated $NaHCO_3$, and brine. Drying with $MgSO_4$, filtration, and evaporation gave 150 mg (95%) crude brown oil. Column chromatography (cyclohexane/CH_2Cl_2 (2:3)) gave 110 mg (70%) of an amorphous off-white solid: ^1H NMR ($CDCl_3$) δ 7.45–7.26 (m, 10 H, ArH), 4.94 (td, 1 H, H_a), 2.85 (d, 2 H, H_b), 2.46 (d, 1 H, –OH); these data are in close agreement with those previously obtained at 60 MHz;[19] ^{13}C NMR ($CDCl_3$) δ 142.7, 131.6, 128.4, 128.2, 128.0, 125.8, 123.2 (ArC), 85.9 and 83.2 (C_c and C_d), 72.6 (C_a), 30.6 (C_b); HRMS (EI) calcd for $C_{16}H_{14}O$ 222.1045, found 222.1031 (M^+, 6).

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Supplementary Material Available: ^1H NMR spectra for all title compounds (11 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.