JOC*Note*

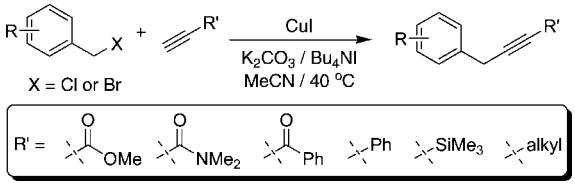
Operationally Simple Copper-Promoted Coupling of Terminal Alkynes with Benzyl Halides

Katherine A. Davies, Ryan C. Abel, and Jeremy E. Wulff*

Department of Chemistry, University of Victoria, Victoria, British Columbia, Canada, V8W 3V6

wulff@uvic.ca

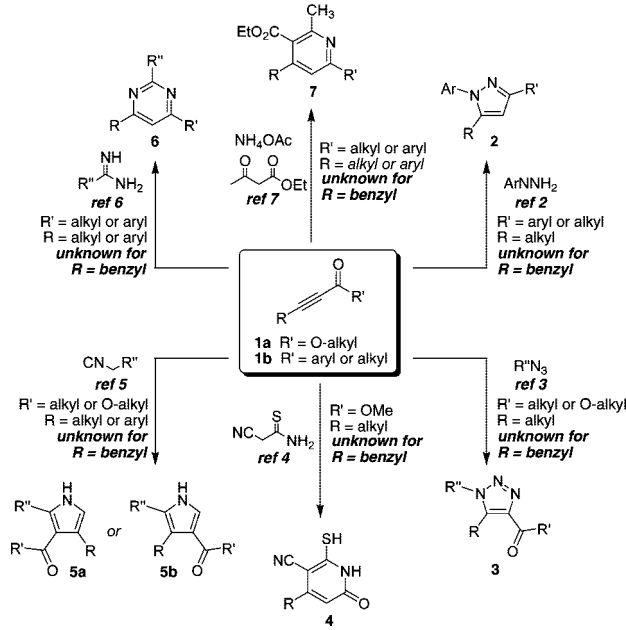
Received February 26, 2009



Benzyl chlorides and bromides are shown to undergo copper-promoted coupling with a variety of terminal alkynes including, for the first time, electron-poor acetylenes such as methyl propiolate. The reaction permits easy access to a wide range of (functionalized) benzyl-substituted propiolates (as well as several related alkynes) from commercially available benzyl halides. These products should in turn function as useful building blocks for the synthesis of previously inaccessible (functionalized) benzyl-substituted heterocycles.

Unsymmetrically substituted alkynes are useful intermediates in the synthesis of natural products, drug candidates, supramolecular constructs, and organic materials.[1] In particular, substituted propiolates (**1a**, Scheme 1) and 2-propynones (**1b**) have proven useful for the synthesis of small-molecule heterocycles for medicinal chemistry programs. Such compounds have been previously used in the preparation of pyrazoles (**2**),[2] 1,2,3-triazoles (**3**),[3] 2-pyridones (**4**),[4] pyrroles (**5**),[5] pyrimidines (**6**),[6] and pyridines (**7**),[7] as illustrated in Scheme 1. Among other useful properties, some of these compounds (and very closely related structures) have been reported as inhibitors of the

SCHEME 1. Synthesis of Heterocycles from Substituted Propiolates and 2-Propynones



$GABA_B$ receptor,[6a] the cholecystokinin-1 receptor,[2b,c] HMG-CoA reductase,[8] D3 dopaminergic and α1 adrenergic G protein-coupled receptors,[9] and the substance P receptor.[10]

Given the utility of substituted propiolates and related compounds in the synthesis of small-molecule heterocycles with useful medicinal properties and taking into account the likelihood of both functionalized and unfunctionalized benzyl substituents acting as rigid lipophilic groups in pharmacophore development, it is surprising that none of the reactions in Scheme 1 have been reported for 4-aryl-2-butynoates (i.e., **1a**, R = benzyl) or the corresponding ketones. This appears to be due to difficulties in preparing the starting compounds; while there exist excellent methods for the synthesis of alkyl- and aryl-substituted propiolates,[11] the benzyl-containing analogues are more troublesome, since they are prone to isomerization to the corresponding allenes.[12] Moreover, benzyl alkynes contain a rather acidic center, which might prove incompatible with the

(1) (a) *Chemistry of Acetylenes*; Viehe, H. G. Ed.; Marcel Dekker: New York, 1969. (b) *Acetylene Chemistry: Chemistry, Biology, and Materials Science*; Diederich, F., Stang, P., Tykwinski, R. R. Eds.; Wiley-VCH GmbH and Co. KGa: Weinheim, 2005.

(2) (a) Bagley, M. C.; Lubinu, M. C.; Mason, C. *Synlett* **2007**, 704–708. (b) Liang, J. T.; Mani, N. S.; Jones, T. K. *J. Org. Chem.* **2007**, *72*, 8243–8250. (c) Gomez, L.; Hack, M. D.; McClure, K.; Sehon, C.; Huang, L.; Morton, M.; Li, L.; Barrett, T. D.; Shankley, N.; Breitenbucher, J. G. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 6493–6498.

(3) Majireck, M. M.; Weinreb, S. M. *J. Org. Chem.* **2006**, *71*, 8680–8683.

(4) Liu, W.; Hickey, E. R.; Cywin, C. L.; Fleck, R. W.; Spero, D. M.; Morwick, T. M.; Proudfoot, J. R. PCT Int. Appl. WO2005035537.

(5) (a) Kamijo, S.; Kanazawa, C.; Yamamoto, Y. *J. Am. Chem. Soc.* **2005**, *127*, 9260–9266. (b) Bhattacharya, A.; Cherukuri, S.; Plata, R. E.; Patel, N.; Tamez, V.; Grosso, J. A.; Peddicord, M.; Palaniswamy, V. A. *Tetrahedron Lett.* **2006**, *47*, 5481–5484. (c) Larionov, O. V.; de Meijere, A. *Angew. Chem., Int. Ed.* **2005**, *44*, 5664–5667.

(6) (a) Verron, J.; Malherbe, P.; Prinssen, E.; Thomas, A. W.; Nock, N.; Masciadri, R. *Tetrahedron Lett.* **2007**, *48*, 377–380. (b) Chen, D.; Banphavichit, V.; Reibenspies, J.; Burgess, K. *Organometallics* **2007**, *26*, 855–859. (c) Bagley, M. C.; Hughes, D. D.; Lubinu, M. C.; Merritt, E. A.; Taylor, P. H.; Tomkinson, N. C. O. *QSAR Comb. Sci.* **2004**, *23*, 859–867. (d) Johns, B. A.; Gudmundsson, K. S.; Turner, E. M.; Allen, S. H.; Jung, D. K.; Sexton, C. J.; Boyd, F. L.; Peel, M. R. *Tetrahedron* **2003**, *59*, 9001–9011.

(7) (a) Xiong, X.; Bagley, M. C.; Chapaneri, K. *Tetrahedron Lett.* **2004**, *45*, 6121–6124. (b) Bohlmann, F.; Rahtz, D. *Chem. Ber.* **1957**, *90*, 2265–2272.

(8) Roth, B. D.; Blankley, C. J.; Chucholowski, A. W.; Ferguson, E.; Hoefle, M. L.; Ortwine, D. F.; Newton, R. S.; Sekerke, C. S.; Sliskovic, D. R.; Wilson, M. *J. Med. Chem.* **1991**, *34*, 357–366.

(9) Loaiza, P. R.; Lber, S.; Hbner, H.; Gmeiner, P. *J. Comb. Chem.* **2006**, *8*, 252–261.

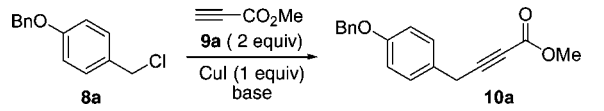
(10) Journet, M.; Cai, D.; Hughes, D. L.; Kowal, J. J.; Larsen, R. D.; Reider, P. J. *Org. Process Res. Dev.* **2005**, *9*, 490–498.

(11) Maezaki, N.; Yagi, S.; Yoshigami, R.; Maeda, J.; Suzuki, T.; Ohsawa, S.; Tsukamoto, K.; Tanaka, T. *J. Org. Chem.* **2003**, *68*, 5550–5558.

(12) For direct access to allenes by coupling benzyl chlorides and terminal alkynes, see ref 19a.

10.1021/jo900444x CCC: $40.75
Published on Web 04/09/2009

TABLE 1. Coupling Reaction Optimization



	base (equiv)	additive	solvent	temp/time	conversion (%)[a,b]
1	Cs_2CO_3 (1.0)	NaI	MeCN	rt, 24 h	25 (23)
2	Cs_2CO_3 (1.0)	NaI	THF	rt, 24 h	<5
3	Cs_2CO_3 (1.0)	NaI	1:1 MeCN:H_2O	rt, 24 h	20
4	Cs_2CO_3 (1.0)	NaI	MeCN	rt, 48 h	36
5	Cs_2CO_3 (1.0)	NaI	MeCN	40 °C, h	80 (75)[c]
6	Na_2CO_3 (1.0)	NaI	MeCN	rt, 24 h	59
7	K_2CO_3 (1.0)	NaI	MeCN	rt, 24 h	88
8	K_2CO_3 (1.0)	NaI + Bu_4NI	MeCN	rt, 24 h	94 (91)[d]
9	K_2CO_3 (1.0)	NaI	MeCN	40 °C, 4 h	98 (96)[d]
10	K_2CO_3 (2.0)	NaI	MeCN	40 °C, 4 h	100 (95)[d]
11	**K_2CO_3 (2.0)**	**none**	**MeCN**	**rt, 24 h**	**99 (99)**
12	K_2CO_3 (2.0)	none	MeCN	rt, 24 h	62[e]
13	K_2CO_3 (2.0)	none	MeCN	40 °C, 24 h	100 (92)

[a] Percent conversion was measured by NMR. [b] Numbers in parentheses refer to isolated yield. [c] The isolated product was contaminated with unidentified impurities. [d] The isolated product was contaminated with traces of allene. [e] Only 1.2 equiv of methyl propiolate were used.

above methods. These factors have substantially limited the development of 4-aryl-2-butynoates and related electron-deficient benzyl alkynes in the synthesis of complex molecules.[13]

The ideal synthesis of 4-aryl-2-butynoates would involve the direct coupling of benzyl chlorides or bromides (>1000 of which are commercially available) with an inexpensive propiolate (e.g., methyl, ethyl, and *tert*-butyl propiolates can all be purchased) under conditions that do not require the use of strong bases, expensive catalyst systems, or high temperatures. Existing 4-aryl-2-butynoate syntheses do not meet these criteria; such preparations require either the use of dilithiated alkyne intermediates[14] or else proceed from arylpropyne starting materials,[15] which are less readily available than benzyl halides.[16]

Inspired by literature reports describing the copper-mediated addition of terminal alkynes to propargyl[17] or allyl halides,[18] we considered whether similar conditions might permit coupling of methyl propiolate with benzyl chlorides or bromides. While previous examples of the direct coupling of terminal alkynes to benzyl halides are known in the literature,[19] these appear to be limited to the use of electron rich alkynes. Our methodology would therefore be the first to afford synthetically valuable 4-aryl-2-butynoates from readily available benzyl halides under mild conditions.

In our initial exploration of this chemistry, we subjected *p*-(benzyloxy)benzyl bromide (**8b**) to reaction with methyl propiolate (**9a**) under Spinella's conditions[17] for the coupling of alkynes with propargyl chlorides (Cs_2CO_3, CuI, NaI, DMF). We observed formation of both the desired 4-aryl-2-butynoate (**10a**) and the corresponding allene in a combined yield of 46%. Changing the solvent to acetonitrile prevented formation of the allene, although the yield remained low (38%). Further experimentation revealed that *p*-(benzyloxy)benzyl chloride (**8a**) was also capable of coupling to **9a**, albeit in poor yield (23%, Table 1, entry 1). We saw this as a significant result (benzyl chlorides are more bench-stable and more readily available commercially than are benzyl bromides) and sought to further optimize the reaction between **8a** and **9a**.

As shown in Table 1, acetonitrile (entry 1) was a better solvent for the reaction than was THF (entry 2). The addition of water (entry 3) did not improve the percent conversion. The use of longer reaction times (entry 4) had less of an impact on the production of **10a** than did the use of a slightly elevated temperature (entry 5), although in the latter case the isolated product was contaminated with uncharacterized byproducts. In contrast to the reaction explored by Caruso and Spinella,[17] sodium carbonate (entry 6) and potassium carbonate (entry 7) were superior bases for our coupling. The addition of tetrabutylammonium iodide as a phase-transfer catalyst (entry 8) improved the percent conversion still further, although under these conditions a small amount of allene could be detected in the isolated product. The use of potassium carbonate at 40 °C (entries 9 and 10) likewise led to high yields of **10a**, contaminated with small amounts of allene.

Finally, we found that removal of the sodium iodide additive from the reaction mixture (entries 11 and 13) permitted the isolation of **10a** in excellent yield with no detectable (by NMR) allenic impurity. Reduction in the amount of alkyne from 2 to 1.2 equiv (entry 12) lowered the percent conversion. We subsequently found (vide infra) that in the absence of sodium iodide and cesium carbonate, higher temperatures and a phase transfer catalyst could be employed to enhance the rate of the reaction, without promoting isomerization.

Having thus optimized the coupling of **8a** and **9a**, we wanted to explore the generality of this potentially useful reaction. We therefore screened a number of benzyl halides (Table 2) and terminal alkynes (Table 3) for their ability to undergo coupling with one another.

We found that several electron-neutral or electron-rich benzyl chlorides and benzyl bromides could be efficiently coupled to **9a** (Table 2, entries 1−7). We generally found benzyl chlorides to give higher yields than benzyl bromides, presumably owing to partial decomposition of the latter under the reaction conditions. For most benzyl halides other than **8a** or **8b**, the best yields were obtained by heating the reaction mixture to 40 °C and adding a phase-transfer catalyst.[20] These conditions also permitted the use of substoichiometric quantities of copper iodide; for example, **10b** was obtained in 75% isolated yield using only 10 mol % CuI (entry 3).[21]

The coupling reaction was tolerant of the presence of both ortho substituents (entry 4) and bulky meta substituents (entry 5) on the benzyl halide. Even a benzyl halide containing a free hydroxyl group (**8g**) was successfully coupled to **9a**, albeit in

(13) Synthesis of benzyl-substituted acetylenic ketones (i.e., **1b**, R = benzyl) appears to be less problematic than synthesis of the corresponding esters. These ketones have been prepared from the appropriate lithiated 3-aryl-1-propyne, by reaction with an aldehyde and subsequent oxidation. Although they have not been extensively used in the preparation of nitrogen-containing heterocycles, they have proven useful for the synthesis of furans. See: (a) Jeevanandam, A.; Narkunan, K.; Ling, Y.-C. *J. Org. Chem.* **2001**, *66*, 6014–6020.

(14) Hooz, J.; Calzada, J. G.; McMaster, D. *Tetrahedron Lett.* **1985**, *26*, 271–274.

(15) (a) Jung, M. E.; Hagenah, J. A. *J. Org. Chem.* **1987**, *52*, 1889–1902. (b) Vasilevsky, S. F.; Trofimov, B. A.; Mal'kina, A. G.; Brandsma, L. *Synth. Commun.* **1994**, *24*, 85–88.

(16) Only the parent 3-phenyl-1-propyne is available from Sigma Aldrich. A few other 3-aryl-1-propynes are available from Anichem LLC, North Brunswick, NJ.

(17) Caruso, T.; Spinella, A. *Tetrahedron* **2003**, *59*, 7787–7790.

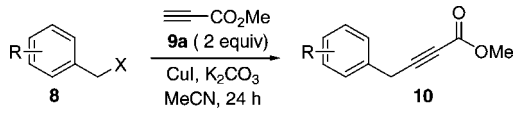
(18) (a) Jeffrey, T. *Tetrahedron Lett.* **1989**, *30*, 2225–2228. (b) Grushin, V. V.; Alper, H. *J. Org. Chem.* **1992**, *57*, 2188–2192. (c) Bieber, L. W.; da Silva, M. F. *Tetrahedron Lett.* **2007**, *48*, 7088–7090.

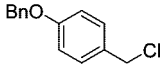
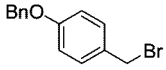
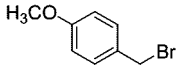
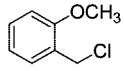
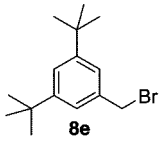
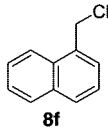
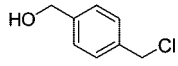
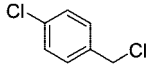
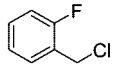
(19) (a) Larsen, C. H.; Anderson, K. W.; Tundel, R. E.; Buchwald, S. L. *Synlett* **2006**, 2941–2946. (b) Takahashi, T.; Li, S.; Huang, W.; Kong, F.; Nakajima, K.; Shen, B.; Ohe, T.; Kanno, K. *J. Org. Chem.* **2006**, *71*, 7967–7977.

(20) Preparation of **10c** (Table 2) using method A gave only 25% conversion.

(21) By comparison, an attempt to prepare **10a** using the conditions of method A with only 10 mol % CuI resulted in only 6% conversion.

TABLE 2. Variation of the Benzyl Halide Coupling Partner



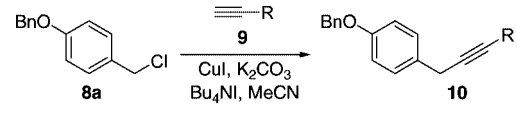
	benzyl halide	method[a,b]	product	allene (%)[c]	isolated yield (%)
1	 **8a**	A	**10a**	< 1	99
2	 **8b**	A	**10a**	< 1	99
3	 **8c**	B	**10b**	< 1	75[d]
4	 **8d**	B	**10c**	< 1	83
5	 **8e**	B	**10d**	1	91
6	 **8f**	B	**10e**	3	90
7	 **8g**	B	**10f**	2	45
8	 **8h**	B	**10g**	13	87
9	 **8i**	A / B	**10h**	n.d.	< 10

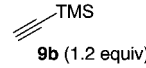
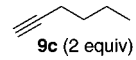
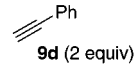
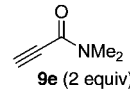
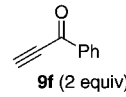
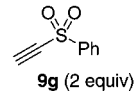
[a] Method A: K_2CO_3 (2 equiv), CuI (1 equiv), rt. [b] Method B: K_2CO_3 (1 equiv), CuI (1 equiv), Bu_4NI (1 equiv), 40 °C. [c] Percentage allene contaminant estimated by ^1H NMR integration. [d] Only 10 mol% of CuI was used.

reduced yield (entry 7). The reaction was less tolerant of electron-withdrawing substituents; alkyne **10g** (entry 8), made by coupling *p*-chlorobenzyl chloride (**8h**) to **9a**, was contaminated with ~13% of the corresponding allene. Similarly, the use of fluorinated benzyl chlorides (*o*-fluorobenzyl chloride, **8i**, and *p*-trifluoromethylbenzyl chloride, not shown) led to complex mixtures of products.

Regarding the use of alkynes other than **9a**, we were surprised to find that more electron-rich alkynes (e.g., **9b** and **9c**) could be efficiently coupled to **8a** (Table 3, entries 1 and 2) using this methodology. The use of representative acetylenic arenes (e.g., **9d**), amides (e.g., **9e**[22]), and ketones (e.g., **9f**[23]) was also explored; these likewise appear to be reasonable substrates for this reaction. For most of these couplings, the use of longer

TABLE 3. Variation of the Alkyne Coupling Partner



	alkyne	conditions[a]	product	allene (%)[b]	isolated yield (%)
1	 **9b** (1.2 equiv)	2 equiv K_2CO_3 40 °C, 24 h	**10i**	< 1	99
2	 **9c** (2 equiv)	2 equiv K_2CO_3 40 °C, 4 d	**10j**	< 1	68
3	 **9d** (2 equiv)	1 equiv K_2CO_3 40 °C, 4 d	**10k**	< 1	83
4	 **9e** (2 equiv)	1 equiv K_2CO_3 40 °C, 4 d	**10l**	< 1	62
5	 **9f** (2 equiv)	1 equiv K_2CO_3 40 °C, 24 h	**10m**	< 1	60
6	 **9g** (2 equiv)	1 equiv K_2CO_3 0 °C, 3 d	**10n**	n.d.	–[c]

[a] CuI (1 equiv) and Bu_4NI (1 equiv) were added to all reactions. [b] Percentage allene contaminant estimated by ^1H NMR integration. [c] A product mixture containing mostly propargyl sulfone was isolated following chromatography over silica gel.

reaction times simplified purification and provided higher yields. Because acetylenic sulfones are particularly useful building blocks for the synthesis of biologically interesting small molecules,[24] and because benzyl-substituted acetylenic sulfones (e.g., **10n**) have not been reported, we attempted to use our methodology to prepare these species as well. In the event, reaction of sulfone **9g**[25] with benzyl halide **8a** under optimized conditions led to the observation (by NMR) of what we believe to be acetylenic sulfone **10n**. However, we were unable to isolate this product in pure form following chromatography over silica gel.[26]

The copper-mediated coupling of commercially available benzyl halides (**8**) to terminal alkynes (**9**) demonstrated here provides a useful methodology for the assembly of 4-aryl-2-butynoates and related synthetic building blocks (**10**). The reaction proceeds under mild conditions (at or below 40 °C), and requires only inexpensive reagents. We have found the reaction to be relatively insensitive to the presence of small quantities of moisture or air, suggesting that this coupling strategy might be useful for parallel-synthesis approaches to libraries of heterocycles (e.g., **2**−**7**, Scheme 1).

(22) Kanner, C. B.; Pandit, U. K. *Tetrahedron* **1982**, *38*, 3597–3604.
(23) Prepared by addition of ethynylmagnesium bromide to benzaldehyde, followed by oxidation with Dess−Martin periodinane. See: Chassaing, S.; Kueny-Stotz, M.; Isorez, G.; Brouillard, R. *Eur. J. Org. Chem.* **2007**, 2438–2448. (b) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155–4156.
(24) For leading references, see: (a) Back, T. G. *Tetrahedron* **2001**, *57*, 5263–5301.
(25) Chen, Z.; Trudell, M. L. *Synth. Commun.* **1994**, *24*, 3149–3155.
(26) Acetylenic sulfones are particularly prone to isomerization. See: Back, T. G.; Parvez, M.; Wulff, J. E. *J. Org. Chem.* **2003**, *68*, 2223–2233.

Experimental Section

General Procedure for the Coupling of Methyl Propiolate with Benzyl Halides: Method A. Methyl propiolate (**9a**, 0.0772 mL, 0.868 mmol) was added via microsyringe to a stirring mixture of 4-benzyloxybenzyl chloride (**8a**, 0.101 g, 0.434 mmol), copper(I) iodide (0.0823 g, 0.432 mmol), and potassium carbonate (0.120 g, 0.868 mmol) in dry acetonitrile (2 mL). The resulting slurry was stirred at room temperature for 24 h. The reaction mixture was then diluted with saturated aqueous ammonium chloride (5 mL) and extracted twice with diethyl ether (20 mL). The combined organic layers were dried using anhydrous sodium sulfate and passed through a filter to remove the drying agent. The filtrate was concentrated in vacuo and purified by flash-column chromatography (hexanes/ethyl acetate, 4:1 to 2:1 gradient), to afford **10a** as a clear, yellow oil (0.120 g, 0.428 mmol, 99% yield). $R_f = 0.72$ (hexanes/ethyl acetate, 2:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45−7.30 (m, 5H), 7.22 (d, $J = 8.6$ Hz, 2H), 6.93 (d, $J = 8.6$ Hz, 2H), 5.04 (s, 2H), 3.76 (s, 3H), 3.66 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.1 (C), 154.3 (C), 137.0 (C), 129.2 (CH), 128.7 (CH), 128.1 (CH), 127.6 (CH), 126.4 (C), 115.3 (CH), 87.3 (C), 74.4 (C), 70.2 (CH_2), 52.8 (CH_3), 24.3 (CH_2). IR (Neat, cm^{-1}) 2237 (m), 1714 (s). MS (EI) *m*/*z* (%) 280 (17), 91 (100), 65 (8). HRMS calcd for $C_{18}H_{16}O_3$ 280.10994, found 280.11003.

Method B. Methyl propiolate (**9a**, 0.124 mL, 1.39 mmol) was added via microsyringe to a stirring mixture of 3,5-di-(*tert*-butyl)benzyl bromide (**8e**, 0.197 g, 0.696 mmol), copper(I) iodide (0.132 g, 0.693 mmol), potassium carbonate (0.0949 g, 0.687 mmol), and tetrabutylammonium iodide (0.255 g, 0.690 mmol) in dry acetonitrile (2 mL). The resulting slurry was stirred at 40 °C for 24 h. The reaction mixture was then diluted with saturated aqueous ammonium chloride (5 mL), and extracted twice with diethyl ether (20 mL). The combined organic layers were dried using anhydrous sodium sulfate and passed through a filter to remove the drying agent. The filtrate was concentrated in vacuo and purified by flash-column chromatography (hexanes/ethyl acetate, 40:1 to 20:1 gradient), to afford **10d** as a clear, yellow-orange oil (0.181 g, 0.632 mmol, 91% yield). $R_f = 0.57$ (hexanes/ethyl acetate, 4:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 (t, $J = 1.8$ Hz, 1H), 7.16 (d, $J = 1.8$ Hz, 2H), 3.78 (s, 3H), 3.73 (s, 2H), 1.34 (s, 18H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.4 (C), 151.5 (C), 133.2 (C), 122.5 (CH), 121.4 (CH), 87.6 (C), 74.5 (C), 52.7 (CH_3), 31.6 (CH_3), 25.6 (CH_2). IR (Neat, cm^{-1}) 2240 (m), 1714 (s). MS (EI) *m*/*z* (%) 286 (40), 271 (100), 215 (76), 203 (32), 57 (89). HRMS calcd for $C_{19}H_{26}O_2$ 286.19328, found 286.19319.

General Procedures for the Coupling of Other Alkynes with Benzyl Halides. Ethynyltrimethylsilane (**9b**, 0.071 mL, 0.51 mmol) was added via microsyringe to a stirring mixture of 4-benzyloxybenzyl chloride (0.100 g, 0.430 mmol), copper(I) iodide (0.0824 g, 0.433 mmol), potassium carbonate (0.119 g, 0.861 mmol), and tetrabutylammonium iodide (0.159 g, 0.430 mmol) in dry acetonitrile (2 mL). The resulting slurry was stirred at 40 °C for 24 h. The reaction mixture was then diluted with saturated aqueous ammonium chloride (5 mL), and extracted twice with diethyl ether (20 mL). The combined organic layers were dried using anhydrous sodium sulfate and passed through a filter to remove the drying agent. The filtrate was concentrated in vacuo and purified by flash-column chromatography (hexanes/ethyl acetate, 4:1 to 2:1 gradient), to afford **10i** as a clear, yellow oil (0.125 g, 0.424 mmol, 99% yield). $R_f = 0.76$ (hexanes/ethyl acetate, 4:1). ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.46−7.42 (m, 5H), 7.29 (d, $J = 8.6$ Hz, 2H), 6.97 (d, $J = 8.6$ Hz, 2H), 5.08 (s, 2H), 3.63 (s, 2H), 0.24 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.5 (C), 137.0 (C), 128.7 (CH), 128.6 (C), 128.5 (CH), 127.8 (CH), 127.3 (CH), 114.8 (CH), 104.7 (C), 86.5 (C), 69.9 (CH_2), 25.2 (CH_2), 0.03 (CH_3). IR (Neat, cm^{-1}) 2175 (m). MS (EI) *m*/*z* (%) 294 (24), 91 (100), 65 (6). HRMS calcd for $C_{19}H_{22}OSi$ 294.14399, found 294.14377.

Acknowledgment. We are grateful to the University of Victoria for startup funds, and to the Canada Foundation for Innovation and the BC Knowledge Development Fund for providing equipment. We further acknowledge NSERC and the Merck Frosst Canadian Academic Development Program for operating funds and also thank Nick Forrester for assistance with the purification of **10b**.

Supporting Information Available: Experimental procedures and full spectroscopic data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO900444X