JOC*Article*

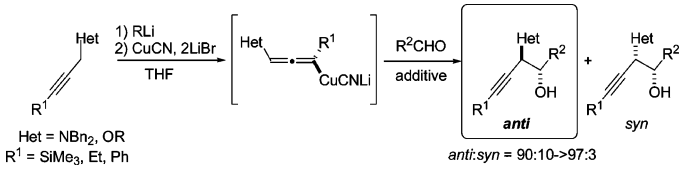
Addition of Hetero Allenyl Copper Reagents to Aldehydes: Scope and Behavior

Emmanuel Vrancken,*[,†] Nacira Alouane,[†] Hélène Gérard,[‡] and Pierre Mangeney*[,†]

Institut Fédératif de Recherche FR 2769, UMR 7611, Université Pierre et Marie Curie, 4 Place Jussieu, F-75252, Paris Cedex, France, and Laboratoire de Chimie Théorique, UMR CNRS 7616, Université Pierre et Marie Curie, 4 Place Jussieu, F-75252, Paris Cedex, France

vrancken@ccr.jussieu.fr

Received November 14, 2006



Cyanocuprates derived from propargylic amines or ethers react with aldehydes to give regioselectively the corresponding *anti*-homopropargylic alcohols with a high level of diastereoselectivity. Such selectivity could be obtained independently of the nature of the heteroatom (amine or ethers) or the acetylenic substituents. Excellent selectivities can be reached regardless of the aldehydes used, remarkably also with vinylic or acetylenic ones. A reactivity scale for the cuprates bearing different acetylenic substituents was established to be: $SiMe_3$ >Ph> Et. The rate of the addition reaction to aldehydes was also found to be slowed down in the presence of HMPA underlining the crucial role of the Li counterion. DFT calculations have shown that the relationship between the rate and the acetylenic substituent is not connected to a possible metallotropic equilibrium but to the stability of the reactive allenic species compared to the less-stable propargylic isomer.

Introduction

Reactions of allenyl metals with aldehydes to give the corresponding homopropargylic alcohols have been studied extensively.[1] Various derivatives such as allenyl lithium,[2] magnesium,[3] aluminum,[4] zinc,[5] boron,[6] cerium,[7] or titanium[8] have been successively tested with poor to high regio- and diastereoselectivity, depending on the nature of the allenyl moiety substituent. Excellent and general results have been reported by Marshall for the use of isolated alkyl-substituted allenyl tin derivatives.[9] This two-step strategy was successfully applied to α-amino[10] and α-alkoxyallenylstannanes.[11,12] Nevertheless, due to the high functional density of homopropargylic

† Institut Fédératif de Recherche FR 2769.

‡ Laboratoire de Chimie Théorique.

(1) (a) Yamamoto, H. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Heathcock, C. H., Eds.; Pergamon Press: Oxford, 1991; Vol. 2, pp 81−98. Marshall, J. A. *Chem. Rev.* **2000**, *100*, 3163−3165. (b) Marshall, J. A.; Gung, B. W.; Grachan, M. L. In *Modern Allene Chemistry*; Krause, N., Hashmi, S. K., Eds.; Willey-VCH: Weinheim, 2004; Vol. 1, Chapter 9, pp 493−592.

(2) Mercier, F.; Epsztein, R.; Holand, S. *Bull. Soc. Chim. Fr.* **1972**, 690−696. Corey, E. J.; Rücker, C. *Tetrahedron Lett.* **1982**, *23*, 719−722. Bour, C.; Suffert, J. *Eur. J. Org. Chem.* **2006**, 1390−1395.

(3) (a) Mercier, F.; Le Goff, N.; Epzstein, R. *C. R. Hebd. Seances Acad. Sci., Ser. C.* **1974**, *279*, 525−528. (b) Mercier, F.; Epzstein, R. *J. Organomet. Chem.* **1976**, *108*, 165−173. (c) Lambert, C.; Schleyer, P. v. R. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1129−1140. (d) Lambert, C.; Schleyer, P. v. R.; Würtwein, E.-U. *J. Org. Chem.* **1993**, *58*, 6377−6389. (e) Shinokubo, H.; Miki, H.; Yokoo, T.; Oshima, K.; Utimoto, K. *Tetrahedron* **1995**, *51*, 11681−11692.

(4) Pearson, N. R.; Hahn, G.; Zweifel, G. *J. Org. Chem.* **1982**, *47*, 3364−3366.

(5) (a) Zweifel, G.; Hahn, G. *J. Org. Chem.* **1984**, *49*, 4565−4567. (b) Poisson, J.-F.; Normant, J. F. *J. Org. Chem.* **2000**, *65*, 6553−6560. (c) Chemla, F.; Ferreira, F.; Hebbe, V.; Stercklen, E. *Eur. J. Org. Chem.* **2002**, 1385−1391. (d) Gung, B. W.; Xue, X.; Knatz, N.; Marshall, J. A. *Organometallics* **2003**, *22*, 3158−3163. (e) Bernaud, F.; Vrancken, E.; Mangeney, P. *Synlett* **2004**, 1080−1082. (f) Marshall, J. A.; Ellis, K. *Tetrahedron Lett.* **2004**, *45*, 1351−1353. (g) Marshall, J. A.; Mulheran, J. J. *Org. Lett.* **2005**, *7*, 1593−1596. (h) Chemla, F.; Ferreira, F. *Synlett* **2006**, 2613−2616.

(6) (a) Wang, K. K.; Nikam, S. S.; Ho, C. D. *J. Org. Chem.* **1983**, *48*, 5376−5377. (b) Ikeda, N.; Arai, I.; Yamamoto, H. *J. Am. Chem. Soc.* **1986**, *108*, 483−486.

(7) Groth, U.; Kesenheimer, C.; Neidhöfer, J. *Synlett* **2006**, 1859−1862.

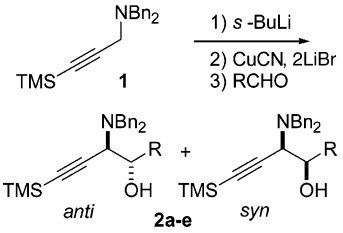
(8) Anies, C.; Lallemand, J.-Y.; Pancrazi, A. *Tetrahedron Lett.* **1996**, *37*, 5519−5522 and references therein.

(9) (a) Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31−47. (b) Marshall, J. A.; Palovich, M. R. *J. Org. Chem.* **1997**, *62*, 6001−6005. (c) Marshall, J. A.; Ellis, K. C. *Org. Lett.* **2003**, *5*, 1729−1732 and references therein.

(10) (a) Ranslow, P. B. D.; Hegedus, L. S.; de los Rios, C. *J. Org. Chem.* **2004**, *69*, 105−111. (b) Amachtowicz, M.; Hegedus, L. S. *J. Org. Chem.* **2004**, *69*, 2229−2234.

10.1021/jo062344z CCC: $37.00
Published on Web 01/26/2007

TABLE 1. Additions of the Copper Derivative of 1 to RCHO



entry	R	product	anti/syn[a]	yield (%)[b]
1	*n*-hexyl	**2a**	>95:5	82
2	*c*-hexyl	**2b**	>95:5	81
3	phenyl	**2c**	>95:5	79
4	propenyl	**2d**	95:5	83
5	heptynyl	**2e**	93:7	74

[a] Determined by ^{1}H NMR of the crude product. [b]Isolated yield.

alcohols, the development of a general and practical access to this important class of compounds is still challenging. Recently, we reported that the copper derivative of the silylated propargylic amine **1** reacts cleanly with aldehydes to give regioselectively the corresponding α-amino-homopropargylic alcohols **2a**−**e** with high anti selectivity (Table 1).[13] This way, a safe, one-pot access to this class of alcohols was open. Furthermore, this methodology was proved to be efficient even with an enantiopure propargylic oxazolidinone.[14]

The excellent regio- and diastereoselectivity of this reaction is surprising. Indeed, such behavior is generally attributed to a cyclic Yamamoto−Chodkiewicz transition state as the result of the complexation of the aldehyde by a Lewis acid allenic metallic species. According to such a transition state, it is difficult to explain why a poorly Lewis acidic cyanocuprate is more anti selective than the much more acidic zinc reagent. Despite a tremendous amount of literature on organocopper chemistry, little is known about copper reagents derived from propargylic substrates[15] and their reactivity toward aldehydes is totally omitted. As their real structure (allenic, propargylic, σ/π-allenic?) is unknown, all attempts of mechanistic rationalization remain uncertain. We have decided to investigate in detail this reaction by studying the influence of several parameters, namely, the nature of the heteroatom (N or O) in the propargylic position, the nature of the acetylenic substituent, the solvent, and the presence of additives.

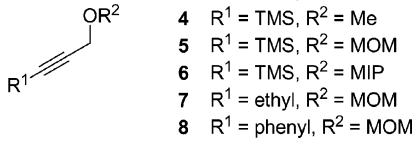
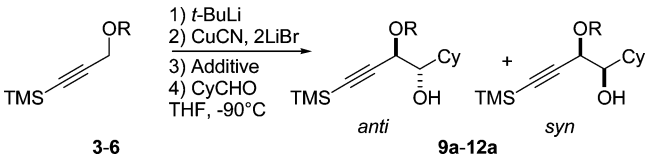


FIGURE 1. Propargylic ethers **3**−**8**.

TABLE 2. Influence of Experimental Conditions and of Oxygen Substituent



entry	propargylic ether	solvent	additive	product	anti/syn[a]	yield (%)[b]
1	**3**	THF	none	**9a**	87:13	68
2	**3**	Et_2O	none	**9a**	36:65	56
3	**3**	THF	none	**9a**	95:5[c]	65
4	**3**	THF	12-crown-4	**9a**	−	0
5	**3**	THF	DBU	**9a**	96:4	70
6	**3**	THF	DMPU	**9a**	95:5	71
7	**3**	THF	HMPA	**9a**	97:3	65
8	**4**	THF	HMPA	**10a**	96:4	69
9	**5**	THF	HMPA	**11a**	94:6	75
10	**6**	THF	HMPA	**12a**	95:5	78

[a] Determined by ^{1}H NMR of the crude product. [b]Isolated yield. [c]Transmetalation with CuCN in place of CuCN−2LiBr, diluted conditions.

Results

We first investigated the influence of the heteroatom by using propargylic ethers instead of amines. The starting ether derivatives **3**−**8** (Figure 1) are prepared with good yields by classical reactions starting from the commercially available propargyl alcohol (see Experimental Section).

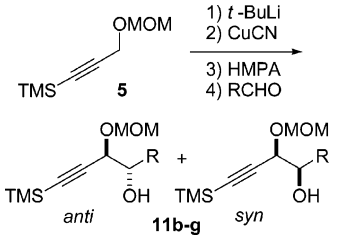
The study on ethers was initiated using the *t*-Bu O-substituted derivative **3** as the model substrate. Its treatment at −90 °C with *s*-BuLi or *t*-BuLi in THF and subsequent transmetalation with the soluble CuCN−2LiBr complex followed by the addition of CyCHO at the same temperature gave regioselectively the homopropargylic alcohol **9a** with an 87:13 anti/syn selectivity (Table 2, entry 1), a slightly lower ratio than what is obtained with an amine derivative[13] (Table 1).

The possible influence of reaction parameters was then checked, and the results are summarized in Table 2 (entries 1−6).

The H−Li exchange, impossible with the amine **1** in Et_2O as solvent, occurs easily when propargylic ethers are used. In this solvent, reversal selectivity is observed, the syn isomer being the major one (Table 2, entry 2). In THF, a dilution two times and a decrease of the amount of lithium salts (transmetalation with CuCN instead of CuCN−2LiBr) result in a significant improvement of the anti/syn ratio (Table 2, entries 1 and 3). These observations led us to examine the effect of lithium-chelating additives such as DBU, DMPU, and HMPA (Table 2, entries 5−7). A beneficial influence of these additives on the diastereoselectivity (anti/syn up to 97:3) is observed. Noteworthy is that no reaction occurs when 12-crown-4 is added to the reaction mixture (Table 2, entry 4). The optimized conditions (HMPA as the additive) were applied with success to the methoxy ether **4** (Table 2, entry 8). Similarly, under these

(11) Savall, B. M.; Powel, N. A.; Roush, W. R. *Org. Lett.* **2001**, *3*, 3057−3060.
(12) Scheidt, K. A.; Bannister, T. D.; Tasaka, A.; Wendt, M. D.; Savall, B. M.; Fegley, G. J.; Roush, W. R. *J. Am. Chem. Soc.* **2002**, *124*, 6981−6990.
(13) Bernaud, F.; Vrancken, E.; Mangeney, P. *Org. Lett.* **2003**, *5*, 2567−2569.
(14) Alouane, N.; Bernaud, F.; Marrot, J.; Vrancken, E.; Mangeney, P. *Org. Lett.* **2005**, *7*, 5797−5800.
(15) For the use of propargyl−allenyl copper(I) reagents, see: (a) Ganem, B. *Tetrahedron Lett*. **1974**, 4467−4470. (b) Commeçron, A.; Normant, J.; Villieras, J. *J. Organomet. Chem.* **1975**, *93*, 415−421. (c) Michelot, D.; Linstrumelle, G. *Tetrahedron Lett*. **1976**, 275−276. (d) Ruitenberg, K.; Kleijn, H.; Meijer, J.; Oostveen, E. A.; Vermeer, P. *J. Organomet. Chem.* **1982**, *224*, 399−405. (e) Ruitenberg, K.; Vermeer, P. *J. Organomet. Chem.* **1983**, *256*, 175−180. de Graaf, W.; Boersma, J.; van Koten, G. *J. Organomet. Chem.* **1989**, *378*, 115−124. (f) Bednarski, P. J.; Nelson, S. D. *J. Med. Chem.* **1989**, *32*, 203−213. (g) Rozema, M. J.; Knochel, P. *Tetrahedron Lett.* **1991**, *32*, 1855−1858. Lam, H. W.; Pattenden, G. *Angew. Chem., Int. Ed.* **2002**, *41*, 508−511.

TABLE 3. Addition of a Copper Derivative of 5 to RCHO[a]



entry	R	product	anti/syn[b]	yield (%)[c]
1	*n*-Pr	**11b**	90:10	79
2	*i*-Pr	**11c**	94:6	78
3	*t*-Bu	**11d**	>97:3	72
4	phenyl	**11e**	97:3	88
5	propenyl	**11f**	>97:3	83
6	heptynyl	**11g**	96:4	79

[a] All reactions are performed during 30 min in THF at −90 °C with HMPA as an additive (see the general procedure in the Experimental Section). [b]Determined by ^{1}H NMR of the crude product. [c]Isolated yield.

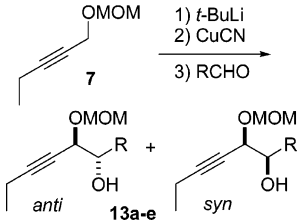
conditions, the MOM and MIP ether derivatives **5** and **6** afford the corresponding homopropargylic alcohols **11a** and **12a**[16] with a diastereomeric ratio close to 95:5 (Table 2, entries 9 and 10). The steric hindrance of the oxygen substituent has poor influence on the diastereoselectivity (Table 2, entries 7−10), although a sterically driven transition state is commonly mentioned to rationalize the anti stereochemistry.[17] Furthermore, the presence of chelating protective groups does not affect the regioselectivity because no trace of allenic products are detected in the crude mixtures.

We next screened the reaction of the MOM ether derivative **5** with a representative set of aldehydes (Table 3).

In all cases, *anti*-ether alcohols **11b**−**g** (Table 3, entries 1−6) are obtained in good yields. The stereoselectivities are in the same range as those reported by Roush when a tin derivative is used[11] (94:6 to >97:3, entries 2−6), except in the case of butyraldehyde which gives a lower 90:10 anti/syn ratio (Table 3, entry 1). Noteworthy are the results obtained with crotonaldehyde and octynal. Indeed, no product arising from a conjugate addition is detected with these unsaturated aldehydes (Table 3, entries 5 and 6). Moreover, these aldehydes give rise to a high level of selectivity despite their small size.

The possible influence of the nature of the triple-bound substituent was studied. Accordingly, the reactivity of the copper derivative of the ethyl-substituted propargylic ether **7** on CyCHO was screened. In the presence of HMPA, no reaction is observed at −90 °C. An increase of the reaction's temperature to −50 °C gives after 5 days only a trace amount of the desired *anti*-homopropargylic alcohol **13a**. This lack of reactivity of the copper derivative of **7** is in good accordance with Roush's observations,[11] no reaction being observed toward aldehydes with the tin derivative of **7**. In our case, a dramatic change is observed when the reaction is performed without HMPA, the attempted product **13a** being obtained in 16 h at −60 °C with a good selectivity (Scheme 1). Its anti stereochemistry is

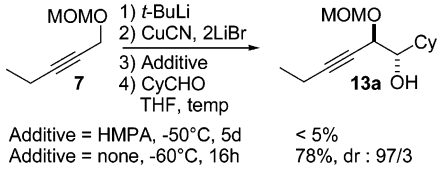
TABLE 4. Addition of the Copper Derivative of 7 to RCHO[a]



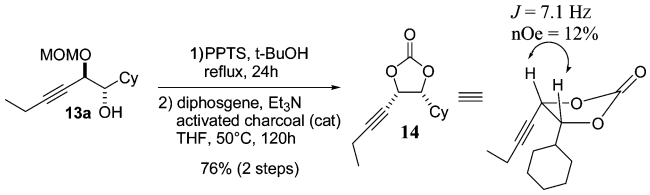
entry	R	product	anti/syn[b]	yield (%)[c]
1	*c*-hexyl	**13a**	97:3	78
2	*n*-Pr	**13b**	90:10	74
3	phenyl	**13c**	96:4	78
4	propenyl	**13d**	>97:3	76
5	heptynyl	**13e**	96:4	76

[a] All reactions are performed during 16 h in THF at −60 °C (see the general procedure in the Experimental Section). [b]Determined by ^{1}H NMR of the crude product. [c]Isolated yield.

SCHEME 1



SCHEME 2



assigned by a nOe analysis of the oxazolidinone **14** obtained by charcoal-promoted ring-closing carbonylation[18] of the corresponding diol (Scheme 2).

Addition of the copper derivative of **7** to various aldehydes occurs with good yields and selectivities (Table 4) notably with unsaturated aldehydes (entries 3−5).

The same study was performed on the phenyl analogue **8**, and the obtained results are reported in Table 5.

As previously observed for analogues **3**−**7**, the addition of aldehydes to the copper derivative of **8** proceeds cleanly to afford regio- and stereoselectively *anti*-propargylic alcohols **15a**−**c**. The kinetics of this reaction (75% conversion after 1 h at −80 °C, 100% at −60 °C after 10 min) stands in between the one of silicon derivative **5** (a few minutes at −90 °C) and the one of ethyl derivative **7** (16 h at −60 °C; compare Table 2 and Scheme 1). Moreover, in this case, the reaction takes place even in the presence of HMPA but is dramatically slowed: 4 h is required to ensure the completion with roughly the same stereoselectivity.

Obviously, the reactivity of copper derivatives depends on the nature of the acetylenic substituent of the starting propargylic ether. To confirm the generality of this observation, the study was extended to the corresponding ethyl and phenyl amine

(16) Noteworthy compound **12a** gives cleanly the corresponding diol **22** after stirring overnight in $CHCl_3$ at room temperature (see Experimental Section).

(17) Epzstein, R. The Formation and Transformations of Allenic and α-Acetylenic Carbanions. In *Comprehensive Carbanions Chemistry*; Buncel, E., Durst, T., Eds.; Elsevier: Amsterdam, 1984; Vol. B, pp 107−175.

(18) Alouane, N.; Boutier, A.; Baron, C.; Vrancken, E.; Mangeney, P. *Synthesis* **2006**, 885−889.

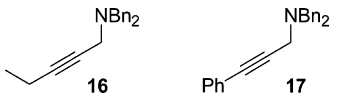
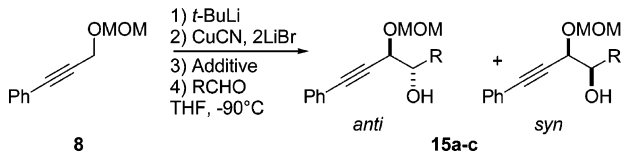


FIGURE 2. Propargylic amines **16** and **17**.

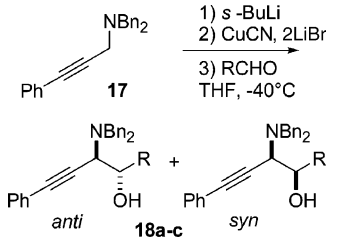
TABLE 5. Addition of a Copper Derivative of 8 to RCHO



entry	R	additive	product	anti/syn[a]	yield (%)[b]
1	*c*-hexyl	HMPA (4 h, −60 °C)	**15a**	>97:3	90
2	*c*-hexyl	none (−60 °C, 10′)	**15a**	>97:3	93
3	phenyl	none (−60 °C, 10′)	**15b**	>97:3	82
4	propenyl	none	**15c**	95:5	95

[a] Determined by ^{1}H NMR of the crude product. [b]Isolated yield

TABLE 6. Addition of a Copper Derivative of 17 to RCHO



entry	R	product	anti/syn[a]	yield (%)[b]
1	cyclohexyl	**18a**	>97:3	91
2	phenyl	**18b**	>97:3	86
3	propenyl	**18c**	95:5	80

[a] Determined by ^{1}H NMR of the crude product. [b]Isolated anti product

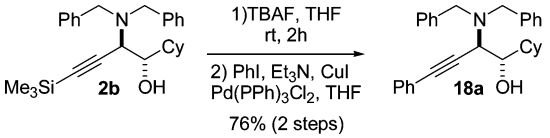
derivatives **16** and **17** (Figure 2). These two compounds are obtained, as their ether analogues, from the propargyl amine (see Experimental Section).

The ethyl derivative **16** was subjected to metalation using several lithium bases. Unfortunately, the deprotonation takes place mainly (*s*-BuLi) or exclusively (*t*-BuLi) on the alkyl-substituted propargylic position, as confirmed by deuteration experiments. With the copper derivative of amine **17**, the addition of representative aldehydes is totally regioselective, affording cleanly aminoalcohols **18a**−**c** with excellent stereoselectivity (Table 6). The anti stereochemistry of **18a** was determined by chemical correlation from **2b** and comparison with the NMR spectra of **18a** (Scheme 3). As already observed for the ether analogue, the kinetics of the reaction is significantly slowed by the presence of the phenyl group (no reaction at −90 °C, 10 min at −40 °C for the phenyl derivative compared to a few minutes at −80 °C for the silicon analogue).

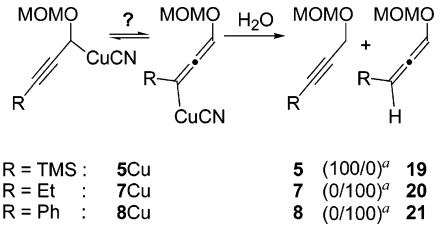
Discussion

Some general features can be brought forward from this study. First of all, the homopropargylic alcohol is exclusively obtained when copper reagents react with aldehydes whichever the experimental conditions (solvents, additives, temperature), the

SCHEME 3. Chemical Correlation of 18a



SCHEME 4. Hydrolysis Experiments



[a] Determined by ^{1}H NMR of the crude mixture.

nature of the heteroatom (N or O), or the nature of the acetylenic substituent ($SiMe_3$, Ph, Et). Such regioselectivity fits well with the existence of an allenyl intermediate, as they are known to react with aldehydes through a S_e'-type mechanism. The acetylenic substituent effect is more surprising. The observed reactivity scale for the ether derivatives **5**, **8**, and **7** toward aldehydes is: $SiMe_3$ > Ph >> Et. Similarly, for the amine analogues, the silicon derivative **1** was found to be much more reactive than the phenyl one (**17**). Thus, the less-stabilized allenyl anions are the less-reactive ones! It could be tempting to correlate this reactivity order with the real structure of the copper reagents in solution, which could depend on the nature of the acetylenic substituent, as reported by Reich for the Li analogues.[19] We reasoned that hydrolysis experiments could give some indications of the structural differences among ether derivatives **5Cu**, **7Cu**, and **8Cu** (Scheme 4).

When treated by H_2O, **5Cu** affords exclusively the initial propargylic ether **5**, as already observed for amine derivatives. In contrast, hydrolysis of the copper derivatives **7Cu** and **8Cu** furnishes exclusively the allenic ethers **20** and **21** (Scheme 4).[20] This behavior toward water is quite surprising, suggesting a structural difference in solution for these three copper species. We thus decided to perform DFT calculations to get insight into the real nature of the reactive organometallic species.

The allenic vs propargylic nature of some ether derivatives in solution is examined for various substituents, R, as described in Table 7.

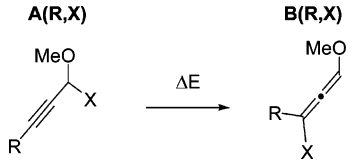
As shown in the second column of Table 7 (X = H), the regioselectivity of hydrolysis reactions can be fully explained on the basis of the stability of the final products. Indeed, the allene **B(R,H)** is found to be the most stable species for R = H or R = CH_3 by 8.0 and 4.1 kcal mol^{-1}, respectively. In opposite, the propargylic form **A(R,H)** is favored for the Si-substituted compounds by 4.1 and 4.2 kcal mol^{-1} for R = SiH_3 or R = $SiMe_3$, respectively (Table 7, column 2).

Because hydrolysis is commonly considered as irreversible, and thus not thermodynamically controlled, the stability of the copper derivatives is also examined (Table 7, columns 3−5). Whatever the nature of the copper reagent (X = Cu, $CuCN^-$,

(19) (a) Reich, H.; Holladay, J. *J. Am. Chem. Soc.* **1995**, *117*, 8470−8471. (b) Reich, H.; Holladay, J.; Mason, E.; Sikorski, W. *J. Am. Chem. Soc.* **1995**, *117*, 12137−12150. (c) Reich, H.; Holladay, J.; Walker, T.; Thompson, J. *J. Am. Chem. Soc.* **1999**, *121*, 9769−9780.

(20) The metalation of propargylic ether **5** was checked by a deuterolysis experiment.

TABLE 7. ΔE (in kcal mol^{-1}) for Various Substituents and Migrating Atoms



X/R	H	Cu	Cu(CN)$^-$	Cu(CN)Li
H	−8.0	−10.7	−13.8	−14.2
CH_3	−4.1	−8.5	−8.4	−10.3
SiH_3	+4.1	−3.0	−5.9	−9.3
$SiMe_3$	+4.2	−1.6	−4.6	−8.4

or CuCNLi) and whatever the nature of the R substituent, the allenic form **B(R,X)** is found to be the most stable structure. Although the preference for the allenic structure is not very pronounced for some neutral complexes **(B(SiMe$_3$,Cu)**, for instance), it becomes clearly favored as soon as a cyano ligand is added on copper **(B(R,CuCN)** or **B(R,CuCNLi)**).

The stability scale observed for the allenyl copper derivatives follows the same trends as the above **B(R,H)** series: R = H > CH_3 > SiH_3 > $SiMe_3$. This trend was investigated on the basis of the geometrical and electronic structure of the allenes, considered as an anionic [R−C═C═CHOMe]$^-$ moiety (R = H, CH_3, SiH_3, and $SiMe_3$; Figure 3). A single minimum is obtained for each allenic moiety, where the R−C−C angle (so-called α(R)) indicates a structure intermediate between an allenic (120°) and a propargylic (180°) form. The following order is found for this angle: α(H) = 118.5° < α(Me) = 124.8° < α(SiH_3) = 135.1° < α($SiMe_3$) = 138.6°. It is thus possible to connect the stability of the organocopper species on the increased allenic character of the organic moiety.

The influence of the nature of the R substituent on the propargylic character as well as of the propargylic proportion on the stability of the copper species was investigated for R = CH_3 and R= SiH_3 on the basis of a topological analysis of the electron localization function (ELF).[21]

The larger propargylic character in the case of SiH_3 compared to CH_3 can be explained by the delocalization of the lone pair on C_1 by the SiH_3 moiety. A monosynaptic basin associated to an electron lone pair on C_1 is located in both [R−C═C═CHOMe]$^-$ moieties (R = CH_3 and SiH_3).[22] Whatever the nature of the substituent, the population on this basin (C_1) is more abundant than that on the C_3 position (see Figure 3). Moreover, a decrease of the electron population is observed for R = SiH_3 (1.70 electrons) compared to CH_3 (2.02 electrons). Coordination of a copper-centered fragment (Cu^+ or CuCN) will thus be favored in the more electron-rich case, namely, for CH_3-substituted species vs SiH_3-substituted ones. This can be confirmed by computation of the Cu−C bonding basin population in B(CH_3−Cu) (1.99 electrons, corresponding to a full single bond) or B(SiH_3−Cu) (1.80 electrons, slightly depopulated). At the same time, the presence of the SiH_3 group leads to an electron transfer from the acetylenic bond in **A(SiH$_3$,Cu)** to the C−Si bond compared to the R = CH_3 case.

As predicted by these calculations, the anionic [R−C═C═CHOMe]$^-$ moieties stand in between an allenic and a propargylic structure, depending on the nature of the acetylenic substituent, the allenic form being preferred in all cases, as shown by the α angle. Clearly, there is a relationship between the observed reactivity scale and the allenic character of these anion moieties, the more propargylic one being the more reactive. Nevertheless, according to the regio- and diastereoselectivity observed in the reaction with aldehydes, as well as the relative calculated stabilities, it seems reasonable to invoke allenes as the reactive species.

The effect of the substituent R on the nucleophilicity of the allenic complex **B(R,Cu)** was further examined by the mean of the Fukui nucleophilicity indexes[23] associated to the atomic basin[24] for C_3 (see Figure 3). It was found to be larger for the SiH_3-substituted species (0.24) than for the CH_3 analogue (0.20, the 0.4 difference being significant because the Fukui indexes over all the molecules sum to 1), in full accordance with the experimental reactivity scale, as measured from reaction time and temperature. The larger nucleophilicity of the silylated allene is thus fully justified from electronic properties as a simple copper adduct, without invoking a metal ancillary ligand, lithium coordination, or solvent, aldehyde, or steric effects (because the SiH_3 entity was used).

The second important and general observation is the inclination for anti selectivity exhibited by all copper reagents. On the basis of the above postulated allenic structure of the reactive species, this selectivity could be rationalized by a classical Yamamoto−Chodkiewicz cyclic transition state, involving the minimization of nonbonding interactions. In our case, a fully sterically driven model is not sufficient to rationalize the selectivity. For example, in the case of propargylic ethers **5** and **7**, the use of unsaturated aldehydes (Table 3, entries 4−6, and Table 4, entries 3−5) gives better selectivities than the more sterically hindered butyraldehyde (Table 3, entry 1, and Table 4, entry 2). In the same manner, it would be difficult to explain the excellent anti selectivity obtained by changing the silyl substituent to an Et or Ph only by steric interactions. In this last case, the main difference lies in their reaction rate, the less-reactive species being the most selective one. Similarly, the use of diluted conditions resulted in a significant improvement of the selectivity (Table 2, entry 3). All this information shows that the diastereoselectivity is also rate dependent, the best selectivities being obtained for slow reactions. The rates of the reactions are dramatically slowed or even stopped in the presence of HMPA (compare reaction rates for Et- or Ph-substituted ether derivatives **7** and **8** in the presence or absence of HMPA; Scheme 1 and Table 5, entries 1 and 2). Apparently, HMPA would act as a rate depletion agent by squeezing the lithium counterion.[25] Therefore, it is now possible to rationalize the solvent effect, the anti selectivity increasing with the lithium complexation ability of the solvent, from Et_2O to a THF/HMPA mixture. Results obtained in the presence of HMPA show that only traces of the lithium counterion are sufficient to promote the reaction, but in this case, the rate is noticeably reduced.

(21) (a) Silvi, B.; Savin, A. *Nature* **1994**, *371*, 683−686. (b) Savin, A.; Silvi, B.; Colonna, F. *Can. J. Chem.* **1996**, *74*, 1088−1096.

(22) The chemical meaning of ELF basins can be obtained from: Noury, S.; Krokidis, X.; Fuster, F.; Silvi, B. *Comput. Chem. (Oxford)* **1999**, *23*, 597−604.

(23) (a) Parr, R. G.; Yang, W. *J. Am. Chem. Soc.* **1984**, *106*, 4049−4050. (b) Yang, W.; Parr, R. G. *Proc. Natl. Acad. Sci. U.S.A.* **1985**, *82*, 6723−6726.

(24) (a) Cioslowski, J.; Martinov, M. *J. Phys. Chem.* **1993**, *97*, 10948−10951. (b) Tiznado, W.; Chamorro, E.; Contreras, R.; Fuentealba, P. *J. Phys. Chem. A* **2005**, *109*, 3220−3224.

(25) For a similar effect, see: (a) Nielsson, K.; Andersson, T.; Ullenius, C.; Gerold, A.; Krause, N. *Chem.−Eur. J.* **1998**, *4*, 2051−2058. (b) Woodward, S. *Chem. Soc. Rev.* **2000**, *29*, 393−401.

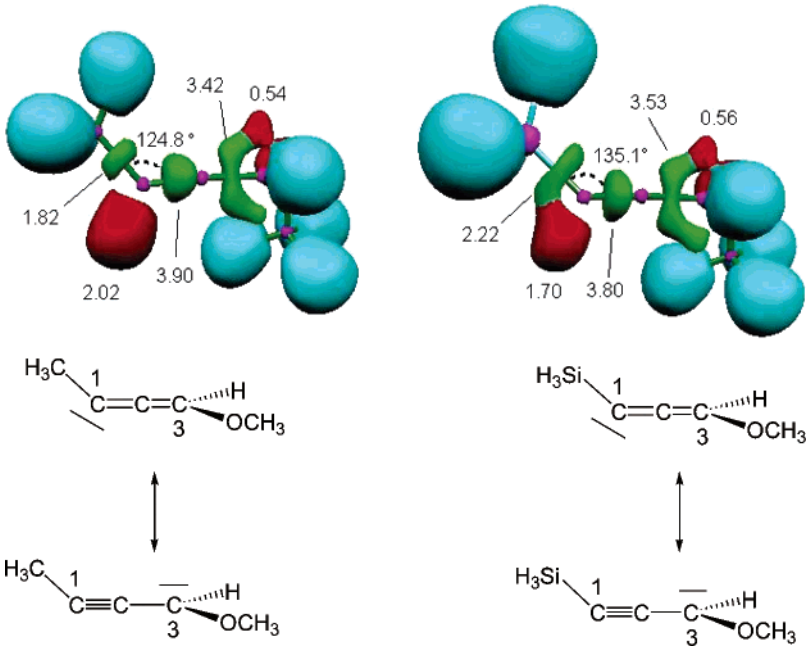


FIGURE 3. ELF isocontours (isosurface = 0.84) for [R−C═C═CHOMe]$^-$ moieties (R = CH_3, left; R = SiH_3, right), basin population (in electrons), and the two mesomeric forms showing the presence of a lone pair basin on both C_1 and C_3.

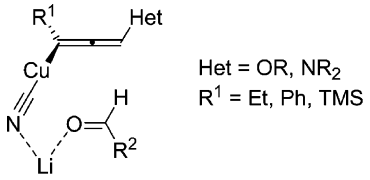


FIGURE 4. Postulated transition state.

This underlines the crucial activating effect of the lithium in these transformations, which is confirmed by the total lack of reactivity observed when 12-crown-4 is used as the additive (entry 4, Table 2). The dramatic role of the lithium counterion does not fit with the Yamamoto−Chodkiewicz cyclic transition state,[17] where the allenic metal ensures the activation of the aldehyde through its own Lewis acidity. When this is not the case, the use of a Lewis acid leads to a change of the transition state from a cyclic to an open one, giving rise to the formation of the syn isomer. In this case, there is no connection between the metal and the Lewis acid, which is distant from the allenic moiety. The allenic copper reagents would thus exhibit an original mode of reaction: in the present case, the lithium would offset the lack of Lewis acidity of the copper, while standing closely associated with it through the CN ligand (Figure 4).[26]

Conclusion

This work represents the first general study on the addition of heterosubstituted allenyl cyanocuprate reagents onto aldehydes. Various copper reagents derived from propargylic ethers or amines and bearing a silyl, an alkyl, or a phenyl group in the acetylenic position have been tested. They all react in a similar fashion, whatever the nature of the heteroatom (amine or ether), yielding exclusively homopropargylic alcohols. In contrast, a strong dependence between the rate and the acetylenic substituent has been underlined. DFT calculations have shown that these differences are not connected to metallotropic equilibrium constants but rather to the inherent stability of the allenic forms, which is therefore the predominant species. The use of additives such as HMPA or 12-crown-4 has pointed out the crucial role of the lithium counterion as the activating agent, even in a catalytic amount.

From a synthetic point of view, hetero allenyl−copper species are promising reagents. Whatever the aldehyde, their addition gives a one-pot, straightforward, and general access to the corresponding *anti*-homopropargylic alcohols with qualitatively similar levels of induction as the tin strategy. Noteworthy is that this methodology allows the efficient preparation of *anti*-alkyl-substituted homopropargylic ether alcohols, which were found to be inaccessible by the tin chemistry.

Experimental Section

Computational Details. Full geometry optimizations were carried out without symmetry constraints using the Gaussian 03 program within the framework of the DFT (B3LYP),[27] using the 6-31+G** basis set for all atoms. Analysis of the electron localization function was carried out using the TopMod Package.[28] The conventional color code is used for the representation of the basins: blue for protonated disynaptic basins, green for bonding pair disynaptic basins, and red for lone pair monosynaptic basins.

General Considerations. Experiments were carried out under a dry argon atmosphere. All glassware was dried at 120 °C and assembled while hot under a stream of argon. All moisture-sensitive reactants were handled under an argon atmosphere. Low-temperature experiments were carried out by cooling a three-necked round-

(26) For the structure of cyanocuprates, see: (a) Bertz, S. *J. Am. Chem. Soc.* **1991**, *113*, 5470−5471. (b) Boche, G.; Boseld, F.; Marsch, M.; Harms, K. *Angew. Chem., Int. Ed.* **1998**, *37*, 1684−1686.

(27) (a) Becke, A. D. *J. Phys. Chem.* **1993**, *98*, 5648−5652. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785−789. (c) Becke, A. D. *Phys. Rev. A: At., Mol., Opt. Phys.* **1988**, *38*, 3098−3100.

(28) Noury, S.; Krokidis, X.; Fuster, F.; Silvi, B. *TopMod Package*, 1997. This package is available on the Web site of the Laboratoire de Chimie Théorique, Université Pierre et Marie Curie (UMR CNRS/UPMC 7616), URL: www.lct.jussieu.fr/silvi.

bottom flask with an ether/acetone (−80/−90 °C) bath, frozen with liquid nitrogen. The flask was equipped with an internal thermometer, a nitrogen inlet, and a septum cap. Tetrahydrofuran was distilled from sodium-benzophenone ketyl. Column chromatographies were performed over silica gel Si 0.040−0.063 mesh. Melting points are uncorrected. ^{1}H NMR spectra were recorded at 400 MHz, and ^{13}C NMR spectra were recorded at 100 MHz, in $CDCl_3$ or C_6D_6 as solvent. Chemical shifts are reported in ppm (reference TMS for ^{1}H NMR and $CDCl_3$ or C_6D_6 for ^{13}C NMR). Compounds **3**, **4**,[29] **5**,[30] **6**,[31]and *anti*-**11c**−**f**[11] have already been described.

1-(Methoxymethoxy)-pent-2-yne (7) and 1-(3-(Methoxymethoxy)prop-1-ynyl)benzene (8). To a stirred solution of propargyl alcohol (11.7 mL, 200 mmol) in dimethoxymethane (200 mL) were added at room temperature lithium bromide (3.5 g, 20 mmol) and toluenesulfonic acid (3.5 g, 20 mmol). Stirring was continued for 24 h. The mixture was treated with water and extracted with ether (2 × 20 mL). The organic layers were combined, dried over sodium sulfate, filtered off, and concentrated in vacuo. Distillation of the residue (82−84 °C, 10 mmHg) gave 15 g (75%) of methoxymethyl ether as a colorless liquid.

A solution of methoxymethyl propargyl ether (15 g, 150 mmol) in THF (150 mL) cooled to −80 °C was treated dropwise with *n*BuLi (2.3 M in hexane, 150 mmol), maintaining the internal temperature below −80 °C. The mixture was stirred for 1 h at −80 °C. EtI (13.5 mL, 165 mmol) was added dropwise at −80 °C. The reaction mixture was then allowed to warm to room temperature and refluxed for 3 h. The reaction was quenched using a saturated aqueous solution of ammonium chloride. The layers were separated. The aqueous phase was extracted with ether, and the combined organic phases were dried over magnesium sulfate and filtered off. The volatiles were removed under reduced pressure, and the residue was purified by fractional distillation under reduced pressure (10 mmHg, 77 °C) to yield 17.1 g (85%) of **7** as a colorless oil. IR (neat) ν = 2938 (br), 2287, 2227, 2714, 1450, 1320, 1148, 1041, 990, 920 cm^{-1}; ^{1}H NMR (400 MHz) δ 4.45 (s, 2H), 3.95 (s, 2H), 3.13 (s, 3H), 2.03−1.99 (m, 2H), 0.93 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz) δ 94.6, 88.3, 74.7, 55.5, 54.7, 13.7,12.4. Elemental anal. calcd for $C_7H_{12}O_2$: C, 65.60; H, 9.44; O, 24.97. Found: C, 65.52; H, 9.48.

The compound **8** was prepared as follows: A solution of methoxymethyl propargyl ether (5 g, 50 mmol), 1-iodobenzene (5.6 mL, 50 mmol), and freshly distilled triethylamine (2 mL) in THF (20 mL) was added dropwise to a solution of CuI (560 mg) and $Pd(PPh_3)_2Cl_2$ (700 mg) in THF (20 mL). The reaction was stirred for 12 h, hydrolyzed with NH_3/NH_4Cl (2:1) solution, and extracted with ether. The combined organic layers were washed with brine, dried over anhydrous magnesium sulfate, filtered off, and concentrated in vacuo. Purification by FC (pentane/Et_2O 95:5) gave 7.6 g (86%) of **8** as a colorless oil. IR (neat) ν = 2850, 1489, 1148, 1099, 1041, 989, 919, 755, 690 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.48−7.32 (m, 5H), 4.80 (s, 2H), 4.47 (s, 2H), 3.44 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 131.8, 128.5, 128.3, 122.6, 94.8, 86.1, 84.6, 55.6, 54.8. Elemental anal. calcd for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86; O, 18.16. Found: C, 74.58; H, 6.69.

General Procedure A for the Addition of Copper Reagents Derived from Propargylic Ethers 3−6 to Aldehydes. A solution of propargylic ether (2 mmol) in THF (15 mL) cooled to −90 °C was treated dropwise with *t*-BuLi (1.5 M in hexane, 2.1 mmol), maintaining the internal temperature below −88 °C. The mixture was stirred for 1 h at −90 °C, during which an orange color developed. A solution of CuCN (270 mg, 3 mmol) and LiBr (521 mg, 6 mmol) in THF (10 mL) was then added dropwise, and the reaction was stirred an additional 30 min at −80 °C. The reaction media turned yellow, and a solution of HMPA (2.8 mL, 16 mmol) in THF (5 mL) was added dropwise at −80 °C, followed by the aldehyde (2.2 mmol). After 30 min at −90 °C, the reaction was quenched by the addition of an aqueous NH_4Cl/NH_3 (2:1) solution and extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with water and brine, dried over magnesium sulfate, and filtered off. The solvents were removed in vacuo, and the product was then subjected to FC (flash chromatography) on SiO_2.

***anti*-2-*tert*-Butoxy-1-cyclohexyl-4-trimethylsilanyl-but-3-yn-1-ol (*anti*-9).** This compound was prepared according to the general procedure A, using (3-*tert*-butoxy-prop-1-ynyl)trimethylsilane **3** (2 mmol, 368 mg) and cyclohexane carboxaldehyde (0.266 mL, 2.2 mmol). Purification by FC (pentane/Et_2O 95:5) gave a mixture of homopropargylic alcohols *anti*-**9** and *syn*-**9** (383 mg, 65%) as a pale yellow oil. The diastereoselectivity of the reaction was determined by ^{1}H NMR to be 97:3. *anti*-**9**: IR (neat) ν = 3550 (br), 2972, 2924, 2852, 1450, 1391, 1366, 1249, 1190, 1057, 840, 759 cm^{-1}; ^{1}H NMR (400 MHz) δ 4.23 (d, J = 4.6 Hz, 1H), 3.32−3.28 (m, 1H), 2.40 (d, J = 3.5 Hz, 1H), 2.01−1.98 (m, 1H), 1.78−1.58 (m, 6H), 1.27 (s, 9H), 1.24−1.04 (m, 4H), 0.17 (s, 9H); ^{13}C NMR (100 MHz) δ 105.0, 90.9, 78.1, 75.7, 64.5, 39.8, 29.4, 28.4, 28.3, 26.6, 23.3, 26.0, 0.0. Elemental anal. calcd for $C_{17}H_{32}O_2Si$: C, 68.86; H, 10.88; O, 10.79. Found: C, 68.91; H, 10.72. *syn*-**9** (only the distinguishable ^{1}H NMR peaks are reported): ^{1}H NMR (400 MHz) δ 4.08 (d, J = 7.8 Hz, 1H), 3.39−3.34 (m, 1H), 2.53 (d, J = 2.3 Hz, 1H), 1.30 (s, 9H).

***anti*-1-Cyclohexyl-2-methoxy-4-trimethylsilanyl-but-3-yn-1-ol (*anti*-10a).** This compound was prepared according to the general procedure A, using (3-methoxy-1-propynyl)trimethylsilane **4** (2 mmol, 284 mg) and cyclohexane carboxaldehyde (0.266 mL, 2.2 mmol). Purification by FC (pentane/Et_2O 85:15) gave pure homopropargylic alcohol *anti*-**10a** (350 mg, 69%) as a pale yellow oil. The diastereoselectivity of the reaction was determined to be 96:4. *anti*-**10a**: IR (neat) ν = 3452 (br), 2924, 2852, 2169, 1738, 1449, 1365, 1249, 1217, 1084, 1021, 840, 760 cm^{-1}; ^{1}H NMR (400 MHz) δ 4.05 (d, J = 4.3 Hz, 1H), 3.48−3.44 (m, 4H), 2.21 (d, J = 4,2 Hz, 1H), 2.02−1.99 (m, 1H), 1.78−1.59 (m, 5H), 1.31−1.04 (m, 5H), 0.21 (s, 9H); ^{13}C NMR (100 MHz) δ 101.0, 93.3, 76.5, 56.9, 40.1, 29.1, 28.5, 26.5, 25.9, 0.0. Elemental anal. calcd for $C_{14}H_{26}O_2Si$: C, 66.09; H, 10.30; O, 12.58. Found: C, 66.13; H, 10.46. *syn*-**10a** (only the distinguishable ^{1}H NMR peaks are reported): ^{1}H NMR (400 MHz) δ 3.93 (d, J = 7.3 Hz, 1H).

***anti*-1-Cyclohexyl-2-methoxymethoxy-4-trimethylsilanyl-but-3-yn-1-ol (*anti*-11a).** This compound was prepared according to the general procedure A, using (3-(methoxymethoxy)-1-propynyl)-trimethylsilane **5** (2 mmol, 344 mg) and cyclohexane carboxaldehyde (0.266 mL, 2.2 mmol). Purification by FC (pentane/Et_2O 85:15) gave pure homopropargylic alcohol *anti*-**11a** (426 mg, 75%) as a pale yellow oil. The diastereoselectivity of the reaction was determined by ^{1}H NMR to be 94:6. *anti*-**11a**: IR (neat) ν = 3490 (br), 2923, 2852, 2181, 1450, 1250, 1152, 1099, 840, 759 cm^{-1}; ^{1}H NMR (400 MHz) δ 4.98 (d, J = 6.8 Hz, 1H), 4.66 (d, J = 6.8 Hz, 1H), 4.47 (d, J = 4.4 Hz, 1H), 3.47 (dt, J = 4.3, 7.1 Hz, 1H), 3.41 (s, 3H), 2.27 (d, J = 4.3 Hz, 1H), 2.05−2.02 (m, 1H), 1.80−1.66 (m, 5H), 1.30−1.06 (m, 5H), 0.20 (s, 9H); ^{13}C NMR (100 MHz) δ 100.7, 94.2, 93.2, 76.9, 68.6, 56.0, 40.2, 29.3, 28.4, 26.5, 26.3, 26.0, 0.0. Elemental anal. calcd for $C_{15}H_{28}O_3Si$: C, 63.33; H, 9.92; O, 16.87. Found: C, 63.21; H, 9.99. *syn*-**11a** (only the distinguishable ^{1}H NMR peaks are reported): ^{1}H NMR (400 MHz) δ 4.98 (d, J = 6.8 Hz, 1H), 4.66 (d, J = 6.8 Hz, 1H), 4.35 (d, J = 6.32 Hz, 1H), 3.39 (s, 3H), 2.49 (d, J = 3.1 Hz, 1H), 0.19 (s, 9H).

***anti*-3-Methoxymethoxy-1-trimethylsilanyl-hept-1-yn-4-ol (*anti*-11b).** This compound was prepared according to the general procedure A, using (3-(methoxymethoxy)-1-propynyl)trimethylsilane **5** (2 mmol, 344 mg) and butyraldehyde (0.200 mL, 2.1 mmol). Purification by FC (pentane/Et_2O 85:15) gave a mixture of homopropargylic alcohols *anti*-**11b** and *syn*-**11b** (386 mg, 79%)

(29) Labaudinière, L.; Hanaizi, J.; Normant, J.-F. *J. Org. Chem.* **1992**, *57*, 6903−6908.
(30) Shikhiev, I. A.; Ibragimov, V. A.; Kraev, S. F. *J. Gen. Chem. USSR* **1971**, *41*, 617−619.
(31) Uchida, K.; Utimoto, K.; Nozaki, H. *Tetrahedron* **1977**, *33*, 2987−2992.

as a pale yellow oil. The diastereoselectivity of the reaction was determined by ^{1}H NMR to be 90:10. *anti*-**11b**: IR (neat) $\nu = 3467$ (br), 2958, 2172, 1250, 1153, 1024, 840, 760 cm^{-1}; ^{1}H NMR (400 MHz) δ 4.98 (d, $J = 6.1$ Hz, 1H), 4.68 (d, $J = 6.1$ Hz, 1H), 4.33 (d, $J = 4.1$ Hz, 1H), 3.77−3.71 (m, 1H), 3.42 (s, 3H), 2.25 (d, $J = 5.6$ Hz, 1H), 1.62−1.41 (m, 4H), 0.97 (t, $J = 7.8$ Hz, 3H), 0.20 (s, 9H); ^{13}C NMR (100 MHz) δ 100.7, 94.5, 93.2, 72.8, 70.9, 56.0, 34.8, 19.0, 14.2, 0.0. Elemental anal. calcd for $C_{12}H_{24}O_3Si$: C, 58.97; H, 9.90; O, 19.64. Found: C, 58.57; H, 9.89. *syn*-**11b** (only the distinguishable ^{1}H NMR peaks are reported): ^{1}H NMR (400 MHz) δ 4.16 (d, $J = 7.1$ Hz, 1H).

***anti*-3-Methoxymethoxy-1-trimethylsilanyl-undeca-1,5-diyn-4-ol (*anti*-11g).** This compound was prepared according to the general procedure A, using (3-(methoxymethoxy)-1-propynyl)-trimethylsilane **5** (2 mmol, 344 mg) and 2-octynal (0.314 mL, 2.1 mmol). Purification by FC (pentane/Et_2O 85:15) gave pure homopropargylic alcohol *anti*-**11g** (480 mg, 79%) as a pale yellow oil. The diastereoselectivity of the reaction was determined by ^{1}H NMR to be 96:4. *anti*-**11g**: IR (neat) $\nu = 3425$ (br), 2932, 2237, 2175, 1249, 1151, 1101, 1026, 840, 760 cm^{-1}; ^{1}H NMR (400 MHz) δ 4.94 (d, $J = 6.8$ Hz, 1H), 4.72 (d, $J = 6.8$ Hz, 1H), 4.50 (ddt, $J = 2.0$, 3.8, 8.1 Hz, 1H), 4.45 (d, $J = 3.8$ Hz, 1H), 3.44 (s, 3H), 2.75 (d, $J = 8.1$ Hz, 1H), 2.24 (dt, $J = 2.0$, 7.1 Hz, 2 H), 1.57−1.50 (m, 2H), 1.44−1.26 (m, 4H), 0.91 (t, $J = 7.1$ Hz, 3H), 0.18 (s, 9H); ^{13}C NMR (100 MHz) δ 100.0, 95.0, 93.3, 87.3, 77.5, 71.4, 65.2, 56.1, 31.2, 28.4, 22.4, 19.0, 14.2, 0.0. Elemental anal. calcd for $C_{16}H_{28}O_3Si$: C, 64.82; H, 9.52; O, 16.19. Found: C, 64.49; H, 9.67. *syn*-**11g** (only the distinguishable ^{1}H NMR peaks are reported): ^{1}H NMR (400 MHz) δ 4.36 (d, $J = 6.3$ Hz, 1H).

***anti*-1-Cyclohexyl-2-(1-methoxy-1-methyl-ethoxy)-4-trimethylsilanyl-but-3-yn-1-ol (*anti*-12a).** This compound was prepared according to the general procedure A, using [3-(1-methoxy-1-methyl-ethoxy)-prop-1-ynyl]trimethylsilane **6** (2 mmol, 400 mg) and cyclohexane carbaldehyde (0.266 mL, 2.2 mmol). Purification by FC (pentane/Et_2O 90:10) gave a mixture of homopropargylic alcohols *anti*-**12a** and *syn*-**12a** (487 mg, 78%) as a pale yellow oil. The diastereoselectivity of the reaction was determined by ^{1}H NMR to be 95:5. *anti*-**12a**: IR (neat) $\nu = 3496$ (br), 2990, 2923, 2852, 2172, 1450, 1374, 1310, 1250, 1210, 1184, 1072, 838, 758 cm^{-1}; ^{1}H NMR (400 MHz) δ 4.50 (d, $J = 3.5$ Hz, 1H), 3.36 (dt, $J = 4.0$, 8.1 Hz, 1H), 3.25 (s, 3H), 2.31 (d, $J = 4.3$ Hz, 1H), 2.10−2.07 (m, 1H), 1.78−1.52 (m, 5H), 1.48 (s, 3H), 1.38 (s, 3H), 1.28−1.01 (m, 5H), 0.18 (s, 9H); ^{13}C NMR (C_6D_6, 100 MHz) δ 105.2, 101.9, 90.8, 78.1, 64.2, 49.3, 40.6, 29.4, 29.3, 27.0, 26.6, 26.4, 25.9, 24.8, 0.0. Elemental anal. calcd for $C_{17}H_{32}O_3Si$: C, 65.33; H, 10.32; O, 15.36. Found: C, 65.53; H, 10.40. *syn*-**12a** (only the distinguishable ^{1}H NMR peaks are reported): ^{1}H NMR (400 MHz) δ 4.32 (d, $J = 7.6$ Hz, 1H), 3.42 (m, 1H), 3.29 (s, 3H), 1.49 (s, 3H), 1.41 (s, 3H).

General Procedure B for the Addition of a Copper Reagent Derived from Propargylic Ether 7 to Aldehydes. A solution of propargylic ether **7** (256 mg, 2 mmol) in THF (15 mL) cooled to −90 °C was treated dropwise with *t*BuLi (1.5 M in hexane, 2.1 mmol), maintaining the internal temperature below −88 °C. The mixture was stirred for 1 h at −90 °C, during which an orange color developed. A solution of CuCN (270 mg, 3 mmol) and LiBr (521 mg, 6 mmol) in THF (10 mL) was then added dropwise, and the reaction was stirred an additional 30 min at −80 °C. The reaction media turned yellow, and the aldehyde (2.2 mmol) was added dropwise. After 16 h at −60 °C, the reaction mixture was quenched by the addition of an aqueous NH_4Cl/NH_3 (2:1) solution and extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with water and brine, dried over magnesium sulfate, and filtered off. The solvents were removed in vacuo, and the product was then subjected to FC (flash chromatography) on SiO_2.

***anti*-1-Cyclohexyl-2-methoxymethoxy-hex-3-yn-1-ol (*anti*-13a).** This compound was prepared according to the general procedure B, using cyclohexane carboxaldehyde (0.266 mL, 2.2 mmol). Purification by FC (pentane/Et_2O 85:15) gave a mixture of homopropargylic alcohols *anti*-**13a** and *syn*-**13a** (375 mg, 78%) as a pale yellow oil. The diastereoselectivity of the reaction was determined by ^{1}H NMR to be 97:3. *anti*-**13a**: IR (neat) $\nu = 3455$ (br), 2922, 2851, 2231, 1450, 1151, 1096, 1021, 918 cm^{-1}; ^{1}H NMR (400 MHz) δ 4.97 (d, $J = 6.7$ Hz, 1H), 4.64 (d, $J = 6.7$ Hz, 1H), 4.64 (dt, $J = 2.0$, 3.8 Hz, 1H), 3.43 (ddd, $J = 3.7$, 4.0, 7.4 Hz, 1H), 3.38 (s, 3H), 2.31 (d, $J = 4$ Hz, 1H), 2.24 (dq, $J = 4.0$, 7.6 Hz, 2H), 2.06−2.02 (m, 1H), 1.71−1.48 (m, 5H), 1.33−1.29 (m, 3H), 1.16 (t, $J = 7.4$ Hz, 3H), 1.39−1.00 (m, 2H); ^{13}C NMR (100 MHz) δ 12.5, 13.9, 25.8, 26.1, 26.4, 28.5, 29.1, 40.0, 55.7, 68.3, 74.0, 77.0, 90.1, 93.8; Elem anal. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.07; O, 19.97. Found: C, 70.11; H, 9.99. *syn*-**13a**: only the distinguishable ^{1}H NMR peaks are reported: ^{1}H NMR (400 MHz) δ 4.98 (d, $J = 6.8$ Hz, 1H), 4.27 (dt, $J = 2.0$, 6.6 Hz, 1H).

***anti*-5-Methoxymethoxy-non-6-yn-4-ol (*anti*-13b).** This compound was prepared according to the general procedure B, using butyraldehyde (0.200 mL, 2.1 mmol). Purification by FC (pentane/Et_2O 80:20) gave pure homopropargylic alcohol *anti*-**13b** (296 mg, 74%) as a pale yellow oil. The diastereoselectivity of the reaction was determined by ^{1}H NMR to be 90:10. *anti*-**13b**: IR (neat) $\nu = 3457$ (br), 2958, 2851, 2205, 1318, 1150, 1098, 1022, 919 cm^{-1}; ^{1}H NMR (400 MHz) δ 4.95 (d, $J = 6.8$ Hz, 1H), 4.65 (d, $J = 6.8$ Hz, 1H), 4.31 (dt, $J = 1.8$, 3.8 Hz, 1H), 3.74−3.68 (m, 1H), 3.39 (s, 3H), 2.33 (d, $J = 5.0$ Hz, 1H), 2.26 (dq, $J = 2.0$, 7.6 Hz, 2H), 1.64−1.32 (m, 4H), 1.15 (t, $J = 7.6$ Hz, 3H), 0.95 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (100 MHz) δ 94.0, 90.1, 74.1, 72.9, 70.5, 55.7, 34.7, 18.9, 14.0, 13.8, 12.4. Elemental anal. calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07; O, 23.97. Found: C, 65.75; H, 10.14. *syn*-**13b** (only the distinguishable ^{1}H NMR peaks are reported): ^{1}H NMR (400 MHz) δ 4.98 (d, $J = 6.8$ Hz, 1H), 4.27 (dt, $J = 2.0$, 6.6 Hz, 1H).

***anti*-2-Methoxymethoxy-1-phenyl-hex-3-yn-1-ol (*anti*-13c).** This compound was prepared according to the general procedure B, using benzaldehyde (0.230 mL, 2.1 mmol). Purification by FC (pentane/Et_2O 80:10) gave a mixture of homopropargylic alcohols *anti*-**13c** and *syn*-**13c** (375 mg, 78%) as a pale yellow oil. The diastereoselectivity of the reaction was determined by ^{1}H NMR to be 96:4. *anti*-**13c**: IR (neat) $\nu = 3449$ (br), 2888, 2231, 1454, 1149, 1097, 1025, 916.7, 751, 699 cm^{-1}; ^{1}H NMR (400 MHz) δ 4.92 (d, $J = 6.7$ Hz, 1H), 4.82 (dd, $J = 4.0$, 4.4 Hz, 1H), 4.61 (d, $J = 6.7$ Hz, 1H), 4.64 (dt, $J = 2.0$, 5.0 Hz, 1H), 3.21 (s, 3H), 2.91 (d, $J = 4.0$ Hz, 1H), 2.24 (dq, $J = 4.0$, 7.6 Hz, 2H), 1.14 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (100 MHz) δ 139.6, 128.0, 126.9, 93.9, 90.8, 75.4, 74.1, 71.6, 55.6, 13.7, 12.5. Elemental anal. calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74; O, 20.49. Found: C, 71.36 H, 8.01. *syn*-**13c** (only the distinguishable ^{1}H NMR peaks are reported): ^{1}H NMR (400 MHz) δ 4.99 (d, $J = 6.0$ Hz, 1H), 4.76 (dd, $J = 2.7$, 7.2 Hz), 4.37 (dt, $J = 1.8$, 7.2 Hz, 1H), 3.33 (s, 3H), 2.16 (dq, $J = 1.8$, 7.3 Hz, 2H), 1.07 (t, $J = 7.3$ Hz, 3H).

***anti*-5-Methoxymethoxy-non-2-en-6-yn-4-ol (*anti*-13d).** This compound was prepared according to the general procedure B, using crotonaldehyde (0.180 mL, 2.1 mmol). Purification by FC (pentane/Et_2O 75:25) gave pure homopropargylic alcohol *anti*-**13d** (299 mg, 76%) as a pale yellow oil. The diastereoselectivity of the reaction was determined by ^{1}H NMR to be >97:3. *anti*-**13d**: IR (neat) $\nu = 3449$ (br), 2287, 2231, 1451, 1318, 1151, 1097, 1023, 964 cm^{-1}; ^{1}H NMR (400 MHz) δ 5.80 (dq, $J = 6.6$, 15.4 Hz, 1H), 5.60 (ddd, $J = 1.8$, 6.8, 15.4 Hz, 1H), 4.93 (d, $J = 6.8$ Hz, 1H), 4.66 (d, $J = 6.8$ Hz, 1H), 4.33 (dt, $J = 2.0$, 3.8 Hz, 1H), 4.17 (m, 1H), 3.38 (s, 3H), 2.55 (d, $J = 5.8$ Hz, 1H), 2.25 (dq, $J = 2.0$, 7.6 Hz, 2H), 1.74 (ddd, $J = 0.8$, 0.8, 6.8 Hz, 3H), 1.15 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (100 MHz) δ 129.4, 128.9, 94.2, 90.2, 74.2, 74.1, 70.7, 55.8, 17.9, 13.8, 12.5. Elemental anal. calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15; O, 24.21. Found: C, 66.97; H, 9.55.

***anti*-5-Methoxymethoxy-trideca-3,7-diyn-6-ol (*anti*-13e).** This compound was prepared according to the general procedure B, using 2-octynal (0.314 mL, 2.1 mmol). Purification by FC (pentane/Et_2O 80:20) gave a mixture of homopropargylic alcohols *anti*-**13e** and *syn*-**13e** (408 mg, 76%) as a pale yellow oil. The diastereoselectivity

of the reaction was determined by ^{1}H NMR to be 96:4. *anti*-**13e**: IR (neat) ν = 3432 (br), 2932, 2235, 1318, 1149, 1100, 1025, 919 cm^{-1}; ^{1}H NMR (400 MHz) δ 4.94 (d, J = 6.8 Hz, 1H), 4.70 (d, J = 6.8 Hz, 1H), 4.48−4.42 (m, 2H), 3.42 (s, 3H), 2.82 (d, J = 7.6 Hz, 1H), 2.29−2.21 (m, 4H), 1.56−1.48 (m, 2H), 1.41−1.28 (m, 4H), 1.16 (t, J = 7.3 Hz, 3H), 0.89 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz) δ 94.5, 90.2, 86.9, 77.30, 73.8, 71.0, 65.3, 55.8, 30.9, 28.2, 22.2, 18.7, 13.9, 13.7, 12.5. Elemental anal. calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59; O, 19.02. Found: C, 70.99; H, 9.58. *syn*-**13e** (only the distinguishable ^{1}H NMR peaks are reported): ^{1}H NMR (400 MHz) δ 4.36 (dt, J = 2.0, 6.0 Hz, 1H).

Structure Determination of *anti*-13a: Preparation of 14. *anti*-**13a** (165 mg, 0.69 mmol) and anhydrous PPTS (1.73 g, 6.9 mmol) in *t*-BuOH (5 mL) were boiled under argon during 24 h. Water was added to the cooled solution, and the aqueous layer was extracted with ether. The ether layer was washed with water, dried, and evaporated. The crude product was then transformed into the corresponding oxazolidinone **14** according to ref 18. IR (neat) ν = 2926 (br), 2854, 2359, 2340, 2243, 1802, 1450, 1350, 1143, 1083, 1000, 769, 726 cm^{-1}; ^{1}H NMR (400 MHz) δ 5.27 (td, J = 2.0, 4.3, 7.1 Hz, 1H), 4.29 (dd, J = 7.1, 8.8 Hz, 1H), 2.29 (dq, J = 2.0, 7.3, 9.6 Hz, 2H), 2.07−1.68 (m, 10H), 1.18 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz) δ 154.2, 93.9, 82.9, 70.7, 70.4, 38.8, 28.6, 28.1, 25.9, 25.3, 25.1, 13.3, 12.5. Elemental anal. calcd for $C_{17}H_{26}O_3$: C, 73.34; H, 9.41; O, 17.24. Found: C, 73.45; H, 9.40.

General Procedure C for the Addition of Copper Reagents Derived from Propargylic Ethers 8 and Amines 17 to Aldehydes. A solution of a propargylic derivative (1 mmol) in THF (20 mL) cooled to −90 °C was treated dropwise with *t*BuLi (1.5 M in hexane, 1.1 mmol), maintaining the internal temperature below −88 °C. The mixture was stirred for 1 h at −90 °C, during which an orange color developed. A solution of CuCN (135 mg, 1.5 mmol) and LiBr (261 mg, 3 mmol) in THF (5 mL) was then added dropwise, and the reaction was stirred an additional 30 min at −80 °C. The reaction media turned yellow, and the aldehyde (1.1 mmol) was added dropwise. After stirring for 45 min at −60 or −40 °C, the reaction mixture was quenched by the addition of an aqueous NH_4Cl/NH_3 (2:1) solution and extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with water and brine, dried over magnesium sulfate, and filtered off. The solvents were removed in vacuo, and the product was then subjected to FC (flash chromatography) on SiO_2.

***anti*-1-Cyclohexyl-2-(methoxymethoxy)-4-phenylbut-3-yn-1-ol (*anti*-15a).** This compound was prepared according to the general procedure C, using cyclohexane carboxaldehyde (0.13 mL, 1.1 mmol). Purification by FC (pentane/Et_2O 80:20) gave pure homopropargylic alcohol *anti*-**15a** (268 mg, 93%) as a yellow oil. The diastereoselectivity of the reaction was determined by ^{1}H NMR to be >97:3. *anti*-**15a**: IR (neat) ν = 3475 (br), 2922, 2850, 1357, 1150, 1097, 1022, 917 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.49−7.28 (m, 5H), 5.07 (d, 1H, J = 6.8 Hz), 4.72 (dd, 2H, J = 6.8, 4.0 Hz), 3.62−3.44 (m, 1H), 3.44 (s, 3H), 2.47 (d, 1H, J = 4.0 Hz), 2.11 (d, 1H, J = 12.9 Hz), 1.80−1.73 (m, 5H), 1.29−1.09 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 131.9, 128.6, 128.3, 122.4, 94.2, 87.7, 84.2, 76.8, 68.6, 55.9, 40.1, 29.1, 28.6, 26.4, 26.1, 25.9. Elemental anal. calcd for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39; O, 16.64. Found: C, 74.61; H, 8.41.

***anti*-(1*S*,2*R*)-2-(Methoxymethoxy)-1,4-diphenylbut-3-yn-1-ol (*anti*-15b).** This compound was prepared according to the general procedure C, using benzaldehyde (0.12 mL, 1.1 mmol). Purification by FC (pentane/Et_2O 70:30) gave pure homopropargylic alcohol *anti*-**15b** (231 mg, 82%) as a yellow oil. The diastereoselectivity of the reaction was determined by ^{1}H NMR to be >97:3. *anti*-**15b**: IR (neat) ν = 3449 (br), 2890, 2360, 1490, 1453, 1149, 1099, 917 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.54−7.28 (m, 5H), 5.02 (d, 1H, J = 6.8 Hz), 4.98 (t, 1H, J = 8.6 Hz), 4.77 (d, 1H, J = 4.8 Hz), 4.71 (d, 1H, J = 6.8 Hz), 3.29 (s, 3H), 3.02 (d, 1H, J = 3.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.4, 131.9, 128.7, 128.3, 128.2, 128.1, 126.9, 122.2, 94.3, 88.3, 84.0, 75.5, 71.9, 55.8. Elemental anal. calcd for $C_{18}H_{18}O_3$: C, 76.57; H, 6.43; O, 17.00. Found: C, 76.33; H, 6.81.

***anti*-(*E*)-3-(Methoxymethoxy)-1-phenylhept-5-en-1-yn-4-ol (*anti*-15c).** This compound was prepared according to the general procedure C, using crotonaldehyde (0.09 mL, 1.1 mmol). Purification by FC (pentane/Et_2O 80:20) gave a mixture of homopropargylic alcohol *anti*-**15c** and *syn*-**15c** (230 mg, 95%) as a yellow oil. The diastereoselectivity of the reaction was determined by ^{1}H NMR to be 95:5. IR (neat) ν = 3422 (br), 2887, 1489, 1442, 1350, 1210, 1150, 1097, 917 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.45−7.28 (m, 5H), 5.87 (dq, 1H, J = 8.8, 16.4 Hz), 5.71 (dq, 1H, J = 1.5, 8.8, 16.4 Hz), 5.03 (d, 1H, J = 6.8 Hz), 4.74 (d, 1H, J = 6.8 Hz), 4.60 (d, 1H, J = 3.8 Hz), 4.33 (q, 1H, J = 5.6, 10.4 Hz), 3.45 (s, 3H), 2.73 (d, 1H, J = 5.6 Hz), 1.78 (d, 3H, J = 5.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 131.9, 129.7, 128.7, 128.6, 128.3, 122.3, 94.5, 87.7, 84.3, 74.2, 70.9, 55.9, 17.9. Elemental anal. calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37; O, 19.49. Found: C, 73.08; H, 7.38. *syn*-**15c** (only the distinguishable ^{1}H NMR peaks are reported): ^{1}H NMR (400 MHz) δ 4.43 (q, 1H, J = 7.1 Hz, 1H).

***N*,*N*-Dibenzyl-3-phenylprop-2-yn-1-amine (17).** A solution of *N*,*N*-dibenzyl-prop-2-yn-1-amine (5 g, 21 mmol), 1-iodobenzene (2.4 mL, 21 mmol), and freshly distilled triethylamine (0.8 mL) in THF (10 mL) was added dropwise to a solution of CuI (238 mg) and $Pd(PPh_3)_2Cl_2$ (322 mg) in THF (10 mL). When the reaction was completed, the mixture was hydrolyzed with an aqueous NH_3/NH_4Cl (1:3) solution and diluted with ether. The combined organic layers were washed with brine and dried over anhydrous magnesium sulfate and filtered off. The solvent was evaporated in vacuo, and the product was isolated by chromatography (pentane/Et_2O 95:5) to yield 5.7 g (88%) of **17** as a yellow solid (mp 62 °C). IR (neat) ν = 2824, 1488, 1454, 1351, 1310, 755, 738 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.78−7.50 (m, 15H), 4.03 (s, 4H), 3.74 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.2, 132.1, 129.4, 128.6, 128.3, 127.4, 86.2, 84.7, 57.9, 42.3. Elemental anal. calcd for $C_{23}H_{21}N$: C, 88.71; H, 6.80; N, 4.50. Found: C, 88.71; H, 6.72; N, 4.49.

***anti*-1-Cyclohexyl-2-(dibenzylamino)-4-phenylbut-3-yn-1-ol (*anti*-18a).** This compound was prepared according to the general procedure C, using cyclohexane carboxaldehyde (0.13 mL, 1.1 mmol). Purification by FC (pentane/Et_2O 90:10) gave pure homopropargylic alcohol *anti*-**18a** (385 mg, 91%) as a yellow oil. The diastereoselectivity of the reaction was determined by ^{1}H NMR to be >97:3. *anti*-**18a**: IR (neat) ν = 3448 (br), 2923, 2360, 1489, 1449, 1070, 745 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.61−7.28 (m, 15H), 3.82 (d, 2H, J = 13.6 Hz), 3.80 (d, 1H, J = 7.8 Hz), 3.79−3.66 (m, 1H), 3.58 (d, 2H, J = 13.6 Hz), 2.01 (d, 1H, J = 4.6 Hz), 1.89−0.94 (m, 11H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.4, 132.1, 129.2, 128.5, 128.4, 127.2, 122.9, 87.9, 85.3, 75.9, 56.1, 56.0, 39.2, 30.7, 26.9, 26.5, 26.3, 24.8. Elemental anal. calcd for $C_{30}H_{33}NO_3$: C, 85.06; H, 7.85; N, 3.31; O, 3.78. Found: C, 84.76; H, 7.75; N, 3.29.

***anti*-(2-Dibenzylamino)-1,4-diphenylbut-3-yn-1-ol (*anti*-18b).** This compound was prepared according to the general procedure C, using benzaldehyde (0.12 mL, 1.1 mmol). Purification by FC (pentane/Et_2O 90:10) gave pure homopropargylic alcohol *anti*-**18b** (356 mg, 86%) as a yellow oil. The diastereoselectivity of the reaction was determined by ^{1}H NMR to be >97:3. *anti*-**18b**: IR (neat) ν = 3398 (br), 3027, 2974, 1490, 1453, 1026, 975 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.71−7.24 (m, 20H), 4.97 (d, 1H, J = 7.8 Hz), 4.09 (d, 1H, J = 8.1 Hz), 4.00 (d, 2H, J = 13.6 Hz), 3.64 (d, 2H, J = 13.6 Hz), 2.96 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 141.2, 138.9, 132.2, 128.9, 128.6, 128.5, 128.4, 128.2, 128.1, 127.5, 127.2, 122.9, 88.3, 84.9, 74.7, 59.9, 55.9. Elemental anal. calcd for $C_{30}H_{27}NO$: C, 86.30; H, 6.52; N, 3.35; O, 3.83. Found: C, 86.28; H, 6.59; N, 3.41.

***anti*-(*E*)-3-(Dibenzylamino)-phenylhept-en-1-yn-4-ol (*anti*-18c).** This compound was prepared according to the general procedure C, using crotonaldehyde (0.09 mL, 1.1 mmol). Purification by FC (pentane/Et_2O 80:20) gave pure homopropargylic alcohol

anti-**18c** (304 mg, 80%) and *syn*-**18c** (10 mg, 2.6%) as yellow oils. The diastereoselectivity of the reaction was determined by ^{1}H NMR to be 95:5. *anti*-**18c**: IR (neat) ν = 3419 (br), 3060, 2913, 1489, 1452, 1070, 961 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.62−7.28 (m, 15H), 5.89−5.83 (m, 1H), 5.64 (dq, 1H, J = 1.5, J = 6.6, 15.2 Hz), 4.34−4.31 (m, 1H), 3.99 (d, 2H, J = 13.6 Hz), 3.77 (d, 1H, J = 7.6 Hz), 3.57 (d, 2H, J = 13.6 Hz), 2.55 (s, 1H), 1.83 (d, 3H, J = 6.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.3, 132.1, 131.3, 129.0, 128.4, 128.3, 127.2, 122.9, 87.8, 84.7, 72.9, 58.2, 56.0, 17.9. Elemental anal. calcd for $C_{27}H_{27}NO$: C, 85.00; H, 7.13; N, 3.67; O, 4.19. Found: C, 85.08; H, 7.14; N, 3.73.

syn-**18c**: IR (neat) ν = 3429 (br), 3027, 2920, 1489, 1452, 1070, 963 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.52−7.28 (m, 15H), 5.86 (dq, 1H, J = 6.6, 3.6 Hz), 5.41 (dq, 1H, J = 1.8, 6.6, 13.6 Hz), 4.16 (dd, 1H, ^1J = 6.8, 9.6 Hz), 4.03 (s, 1H), 3.98 (d, 2H, J = 13.4 Hz), 3.55 (d, 2H, J = 13.4 Hz), 3.47 (d, 1H, J = 9.9 Hz), 1.72 (dd, 3H, J = 1.5, 6.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.2, 131.8, 129.8, 129.2, 128.6, 128.4, 127.5, 122.9, 87.7, 83.6, 71.1, 58.6, 55.1, 17.9.

1-Methoxymethoxy-penta-1,2-diene (20) and (3-Methoxymethoxy-propa-1,2-dienyl)-benzene (21). These compounds were obtained by hydrolysis of the corresponding copper derivatives and were analyzed without further purification. **20**: ^{1}H NMR (400 MHz) δ 6.58 (dt, 1H, J = 2.5, 5.8 Hz), 5.88 (q, 1H, J = 5.8 Hz), 4.80 (s, 2H), 3.42 (s, 3H), 2.17−2.04 (m, 2H), 1.03 (t, 3H, J = 7.3 Hz). **21**: ^{1}H NMR (400 MHz) δ 7.49−7.28 (m, 5H), 7.03 (d, 1H J = 5.8 Hz), 6.79 (d, 1H, J = 5.8 Hz), 4.91 (s, 2H), 3.50 (s, 3H).

1-Cyclohexyl-4-trimethylsilanyl-but-3-yne-1,2-diol (22). *anti*-**12a** was dissolved in $CDCl_3$ and stirred at room temperature overnight to give pure diol **22** without further purification. IR (neat) ν = 3378 (br), 2922, 2852, 2171, 1449, 1405, 1248, 1035, 962, 839, 758 cm^{-1}; ^{1}H NMR (400 MHz) δ 4.42 (d, J = 3.5 Hz, 1H), 3.34 (dd, J = 3.8, 10.8 Hz, 1H), 2.03 (d, 1H, J = 12.9 Hz), 1.76−0.98 (m, 11H), 0.17 (s, 9H); ^{13}C NMR (100 MHz) δ 51.9, 90.2, 40.3, 26.8, 26.2, 25.9, 25.6, 13.5. Elemental anal. calcd for $C_{13}H_{24}O_2Si$: C, 64.95; H, 10.06; O, 13.31; Si, 11.68. Found: C, 64.65; H, 10.46.

Acknowledgment. We thank Clariant for financial support to N.A. We also thank Prof. J. Normant for many interesting discussions. We thank Prof. B. Silvi for fruitful assistance. Calculations have been performed on the IBM SP4 supercomputers at CRIHAN (Saint Etienne du Rouvray, France).

Supporting Information Available: ^{1}H and ^{13}C NMR spectra of **7**−**10**, **11a**,**b**,**g**, **12a**, **13a**−**e**, **14**, **15a**−**c**, **17**, **18a**−**c**, and **22**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO062344Z