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Substitution of Secondary Propargylic Phosphates Using Aryl-Lithium-Based Copper Reagents †

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† This paper is dedicated to late Professor Jiro Tsuji.

Abstract: The substitution of secondary propargylic phosphates ROP(O)$(OEt)_2$ where R = [$Ph(CH_2)_2$] C(H)(C≡CTMS)] $Ph(CH_2)_2CH(OP(O)(OEt)_2)$(C≡CTMS) with copper reagents derived from PhLi and copper salts such as CuCl, CuCN, and $Cu(acac)_2$ was studied to establish an ArLi-based reagent system. Among the reagents prepared, PhLi/CuCl (2:1) showed 98% α regioselectivity (rs), while PhLi/$Cu(acac)_2$ was γ selective (>99% rs). PhLi prepared in situ from PhI and PhBr by Li-halogen exchange with *t*-BuLi was also used for the α selective substitution. A study using the (*S*)-phosphate disclosed 99% enantiospecificity (es) and the inversion of the stereochemistry. The substitution of five phosphates with substituted aryl reagents produced the corresponding propargylic products with high rs and es values. Similar reactivity and selectivity were observed with 2-furyl and 2-thienyl reagents, which were prepared via direct lithiation with *n*-BuLi.

Keywords: aryl lithium; substitution; coupling; secondary carbon; propargylic; regioselectivity; enantiospecificity; copper

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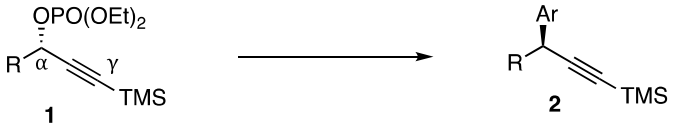
1. Introduction

Coupling reaction of secondary alcohol derivatives with organometallic reagents is a promising method to construct chiral centers on secondary carbons. Thus far, alkyl, allylic, and propargylic alcohol derivatives have been investigated as substrates [1–3]. Among them, alkyl substrates are less reactive than the other substrates that are activated by the double or triple bond. Consequently, only a few reagent/catalyst/leaving group systems have been published [4–7]. Among these, the highly reactive system developed by us consists of the $PySO_3$ leaving group, Grignard reagents, and $Cu(OTf)_2$ as a catalyst [7]. In contrast, various reagents/catalyst systems have been developed for the allylic coupling at secondary carbons [8–10]. For organic synthesis, regiocontrol between α and γ carbons and stereocontrol in it, as well as convenience in reagent/catalyst preparation, are highly important. The copper-catalyzed allylic substitution of allylic picolinates with alkyl and aryl Grignard reagents developed by us meets these requirements and proceeds with high S_N2' selectivity, furnishing tertiary carbons [11,12] and quaternary carbons [13,14].

The α-substitution using enantioenriched secondary propargylic alcohol derivatives has also been studied to develop ammonium salt/ArMgBr/Cu cat. [15], salicylate/ArMgCl/Cu cat. [16], bromide/heteroaryl cuprate [17], and sulfonate/$TMSCF_3$/Cu cat./KF [18]. The α-substitution using racemic substrates was reported as well [19–22]. Furthermore, asymmetric version using chiral ligands was developed by Fu [23–25] and Nishibayashi [26,27]. Propargylic reactions have been studied by Professor Tsuji after his palladium-catalyzed reactions using allylic alcohol derivatives [28]. In consideration of his way of the research development and the experimental convenience mentioned above, we explored

Cu-catalyzed propargylic substitution with aryl Grignard reagents on the basis of our allylic substitution. We found the α selective substitution of phosphate **1** with ArMgBr by using CuCN and $CuBr{\cdot}Me_2S$ to give acetylenes **2** (Scheme 1) and the γ regioselective reaction with $Cu(acac)_2$ [29]. The substitution was successfully applied for the synthesis of biologically active compounds [29–32]. With these results in mind, we focused our attention on aryl lithium compounds (ArLi), with the expectation that several preparations of ArLi would expand the scope of the reagents. Herein, we present the results along this line (Scheme 1).



previous work ArMgBr with CuCN or $CuBr{\cdot}Me_2S$

present work ArLi with CuCl

Scheme 1. Propargylic substitution with aryl copper reagents.

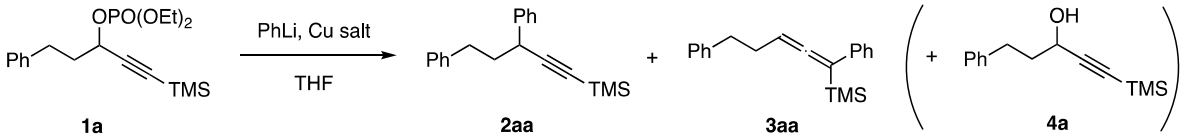
2. Results and Discussion

Racemic phosphates **1a**–**1c** and **7** and enantiomerically enriched phosphates (*S*)-**1**, -**7**, and -**8** were prepared according to the previous methods [29]. The substitution of racemic propargylic phosphate **1a** with copper reagents derived from PhLi and copper salts was studied first (Table 1). Ratios of acetylene **2aa**, the regioisomer **3aa**, and **1a** (if recovered) were determined by ^1H NMR spectroscopy and are summarized in entries. Alcohol **4a** was not formed. The reaction of **1a** with PhLi, without any copper salt, gave a mixture of unidentified products and recovered **1a** (Entry 1). The reaction with a phenylcopper reagent prepared from PhLi and CuCN (formal structure PhCu·LiCN) was slow, and a roughly 1:1 mixture of **2aa** and regioisomer **3aa** was produced after 17 h (Entry 2). In contrast, α selective reaction was realized with phenyl cuprate, and the desired product, **2aa**, was obtained with 94% regioselectivity (rs) (Entry 3), whereas the catalytic use of CuCN retarded the reaction. Moderate γ selectivity was observed using reagents derived with $CuBr{\cdot}Me_2S$ and with $CuBr_2$ (Entries 4 and 5). Phenyl copper derived from CuCl was also γ selective (Entry 6). Fortunately, phenyl cuprate derived from CuCl disclosed high α selectivity, which was higher than that achieved using the CuCN-derived phenyl cuprate (Entry 7 vs. Entry 3). Products **2aa** and **3aa**, in a 98:2 ratio, were isolated in a 76% yield after chromatography on silica gel (Entry 7).

The substitution conditions used in Entry 7 were applied to PhLi, which was prepared from iodo- and bromobenzene by Li-halogen exchange with *t*-BuLi. An X-shape flask [33] with two bottoms was used for our convenience. Briefly, CuCl was placed in one bottom, and lithiation of PhI in Et_2O was carried out in the other bottom at 0 °C for 30 min. The solution was diluted with THF and mixed with CuCl by tilting the flask. Racemic phosphate **1a** was added to the resulting reagent, and the mixture was stirred at 0 °C for 1 h to afford **2aa** in an 80% yield with 98% rs (Entry 8). Bromobenzene was converted to the phenyl reagent in a similar way, and **2aa** was obtained in a 73% yield with 97% rs (Entry 9). These results indicate that LiI and LiBr produced by the lithiation affected neither the reactivity nor the rs.

In addition, a reagent derived from PhLi, $Cu(acac)_2$, and $MgBr_2$ was found to be γ regioselective (Entry 10). Without $MgBr_2$, a mixture of unidentified products and the unreacted phosphate was obtained.

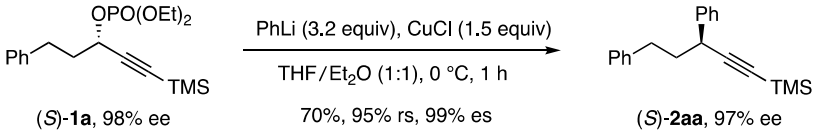
Table 1. Substitution of phosphate **1a** with PhLi-based reagents.



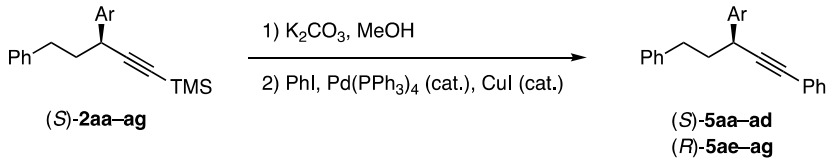
Entry	Ph Reagent	Cu Salt	PhLi [1]/Cu Salt	Temp.	Time	2aa/3aa/1a [2]	Yield (%)
1	PhLi	–	–	rt	6 h	– [3]	–
2	PhLi	CuCN	2.5:3	rt	17 h	44:56:0	nd [4]
3	PhLi	CuCN	3:1.5	rt	2 h	94:6:0	nd [4]
4	PhLi, $MgBr_2$ [5]	$CuBr{\cdot}Me_2S$	3:3	0 °C	2 h	13:87:0	nd [4]
5	PhLi	$CuBr_2$	3:1.5	0 °C	2 h	7:45:48	nd [4]
6	PhLi	CuCl	2.5:3	0 °C	7 h	17:83:0	nd [4]
7	PhLi	CuCl	3:1.5	0 °C	2 h	98:2:0	76%
8	PhI, *t*-BuLi [6]	CuCl	3:1.5	0 °C	1 h	98:2:0	80%
9	PhBr, *t*-BuLi [6]	CuCl	3:1.5	0 °C	2 h	97:3:0	73%
10	PhLi, $MgBr_2$ [5]	$Cu(acac)_2$	3.6:2:5	0 °C	4 h	1:>99:0	85%

[1] PhLi in *c*-hexane and Et_2O from Kanto, Japan, was used in Entries 1–7 and 10. [2] Determined by ^1H NMR. [3] A mixture of **1a** and unidentified products. [4] nd: not determined. [5] Added $MgBr_2$ in Entries 4 (6 equiv.) and 10 (5 equiv.), respectively. [6] Lithiation in Et_2O.

The reaction conditions used in Entry 7 were applied to enantiomerically enriched phosphate (*S*)-**1a** of 98% ee to determine enantiospecificity (es) [34] and a stereochemical course (Scheme 2). A slightly higher equiv. of PhLi (3.2 equiv.) was used to ensure the formation of the cuprate. The reaction gave (*S*)-**2aa** in a 70% yield, and the HPLC analysis of the product on chiral stationary (abbreviated as chiral HPLC) disclosed 97% ee, which was calculated to be 99% es. Furthermore, the (*S*) configuration was assigned to the product by comparing the retention times of the derived phenylacetylene (*S*)-**5aa** with the reported data [29] (Scheme 3). These results indicate the inversion of the stereochemistry with marginal racemization.

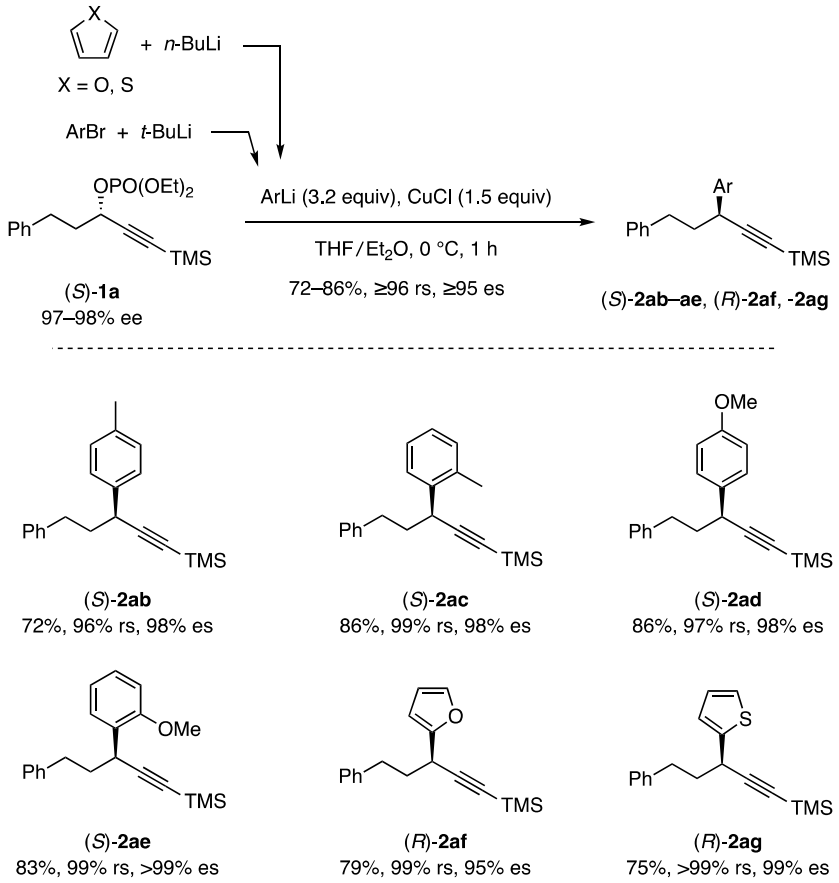


Scheme 2. Stereochemistry of the propargylic substitution.



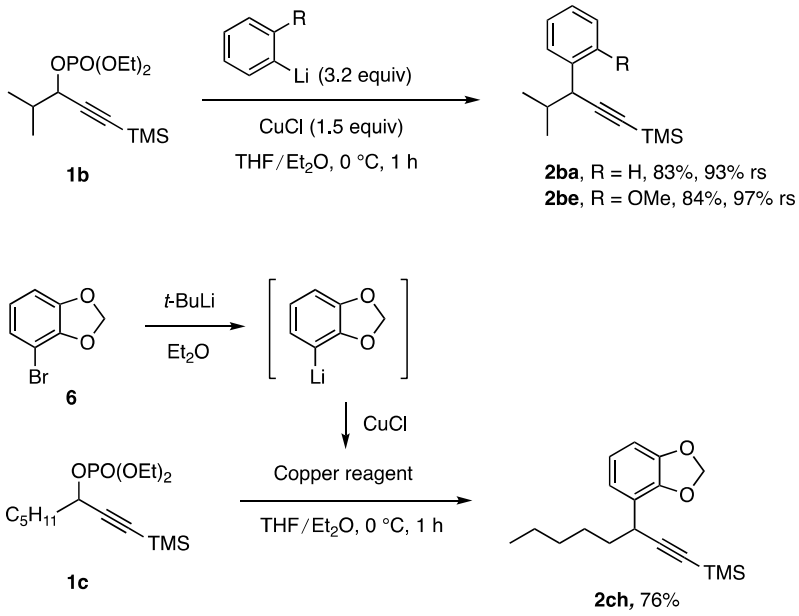
Scheme 3. Conversion to phenylacetylenes for determination of es and the absolute configuration. Ar for substrates and products: **aa**, Ph; **ab**, 4-MeC_6H_4; **ac**, 2-MeC_6H_4; **ad**, 4-$MeOC_6H_4$; **ae**, 2-$MeOC_6H_4$; **af**, 2-furyl; **ag**, 2-thienyl.

Several reagents prepared via the Li-Br exchange with *t*-BuLi or the direct lithiation with *n*-BuLi were subjected to the substitution with (*S*)-**1a** (97–98% ee) at 0 °C for 1 h. The isolated yields, rs, and es are delineated in Scheme 4.



Scheme 4. Propargylic substitution with ArLi-based copper reagents.

The products were converted to phenylacetylenes by the method shown in Scheme 3, and each es of the phenyl derivatives was determined by chiral HPLC analysis. The configurations of (*S*)-**2ab**–(*S*)-**2ae** were established by comparing the retention times with those reported [29]. The same configuration was assigned to the products derived from furan and thiophene by analogy. The (*R*) stereochemistry was assigned by the priority rule. Two tolyl reagents prepared from 4- and 2-bromotoluenes via lithiation afforded (*S*)-**2ab** and -**2ac** in 72% and 86% yields, respectively, with 98% es for both. Similarly, 4- and 2-bromoanisoles produced (*S*)-**2ad** and -**2ae**, respectively, in good yields with high es values. Notably, the 2-substituted reagents afforded a higher rs than the 4-substituted reagents. A similar increase in the rs is presented later (**2be** vs. **2ba** in Scheme 5). The substitution of (*S*)-**1a** with the 2-furyl reagent prepared via the direct lithiation with *n*-BuLi resulted in high selectivity in rs and es, affording (*R*)-**2af** in a 79% yield. In combination with the oxidative conversion of the furan ring to the 2-butene-1,4-dione moiety, the present coupling would be useful in organic synthesis [35–37]. Similarly, the 2-thienyl reagent prepared by the direct lithiation gave (*R*)-**2ag** with high selectivity. Previously, furyl and thienyl copper reagents have been reported to be less nucleophilic for 1,4-addition [38–40], whereas high reactivity is reported for the propargylic substitution [17]. The reactivity of furyl and thienyl reagents in this study was sufficiently high and comparable to that of the aryl reagents shown in Scheme 4.

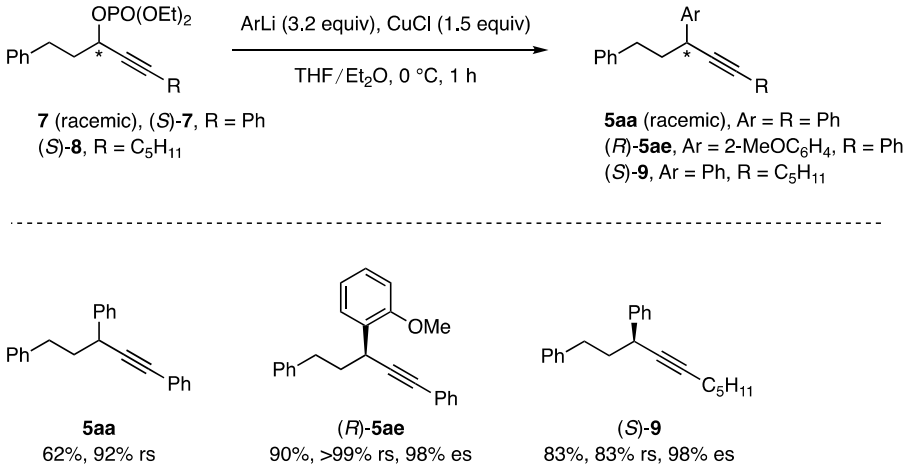


Scheme 5. Further study of propargylic substitution.

Substrates **1b** and **1c** were next subjected to the substitution (Scheme 5). Despite the high steric congestion in **1b**, the reaction proceeded well, although the rs decreased slightly to 93%. In contrast, a high rs (97% rs) was recorded with the 2-$MeOC_6H_4$ reagent to produce **2be** in an 84% yield. A similar ortho effect is mentioned above in the substitution reactions, giving (*S*)-**2ac** and -**2ae** (Scheme 4).

The reaction of **1c** to produce **2ch** was examined next (Scheme 5) to demonstrate the advantage of the present reaction using the ArLi over the previous method, which used the Grignard reagent [29]. 4-Bromo-1,3-benzodioxole (**6**) was converted to the copper reagent via the Li-Br exchange, and the reaction with phosphate **1c** proceeded smoothly to afford **2ch** in a 76% yield. No signal for the allenylic regioisomer was identified in the ^{1}H NMR spectrum probably due to the ortho effect observed above. Bromide **6** is convertible to the corresponding Grignard reagent [41], which would produce **2ch** by using the original method [29]. However, a part of the Grignard solution will be lost by titration, and the remaining solution after the use will be discarded; thus, the usage efficiency of bromide **6** via the Grignard reagent would not be high. In contrast, bromide **6** is converted quantitatively to the lithium reagent by the Li-Br exchange. This reaction would be an example to show that the exchange would especially be convenient for the substitution reaction using bromide and iodide that are prepared by a multistep procedure.

To evaluate the contribution of the TMS group on the regioselectivity, propargylic phosphates possessing phenylacetylenic and pentylacetylenic moieties were subjected to the substitution reaction (Scheme 6). The reaction of phenylacetylenic phosphate **7** with the PhLi-base reagent afforded **5aa** with a 92% rs. The rs was somewhat low compared to that of the reaction using TMS-acetylenic phosphate **1a** (98% rs in Table 1, Entry 7). In contrast, a high rs of >99% was observed for the substitution with the 2-$MeOC_6H_4$ reagent, giving (*R*)-**5ae** from (*S*)-**7**. Pentylacetylenic phosphate (*S*)-**8** produced (*S*)-**9** with an 83% rs. These results suggested that the rs of pentylacetylenic and other alkyl acetylenic phosphates would be low compared to that of TMS-acetylenic phosphates; thus, no further studies were examined.



Scheme 6. Propargylic substitution of phenyl and alkyl acetylenic phosphates.

3. Materials and Methods

3.1. General

The ^{1}H (300 or 400 MHz) and ^{13}C NMR (75 or 100 MHz) spectroscopic data were recorded in $CDCl_3$, using Me_4Si (δ = 0 ppm) and the centerline of the triplet (δ = 77.1 ppm), respectively, as internal standards. Signal patterns are indicated as br s (broad singlet), s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). Coupling constants (J) are given in Hertz (Hz). The ^{13}C–APT data (APT: attached proton test) are added to ^{13}C chemical shifts with minus (for C and CH_2) and plus (for CH and CH_3) signs. The solvents that were distilled prior to use are THF (from Na/benzophenone), Et_2O (from Na/benzophenone), and CH_2Cl_2 (from CaH_2). After the reaction was quenched, the organic extracts were concentrated by using an evaporator. The silica gel used for chromatography was purchased (Merck (Tokyo, Japan), silica gel 60; KANTO, silica gel 60N). PhLi in *c*-hexane/Et_2O, *t*-BuLi in *n*-pentane, and *n*-BuLi in hexane were purchased from Kanto, Japan, while CuCl and $Cu(acac)_2$ were obtained from Tokyo Chemical Industry (TCI) (Tokyo, Japan) and used without purification.

According to the previous method [29], racemic phosphates **1a–c** and **7** and enantiomerically enriched phosphates (*S*)-**1a** (97–98% ee), (*S*)-**7** (96% ee), and (*S*)-**8** (95% ee) were synthesized. The synthesis of (*S*)-**1a**, **-7**, and **-8** is described in the Supplementary Materials. 4-Bromo-1,3-benzodioxole (**6**) was prepared according to the literature method [41,42].

Ratios of acetylenes and allenes produced by the coupling reactions were determined by integration of the diagnostic signals in ^{1}H NMR spectra and converted to the regioselectivity (rs). HPLC analyses of the derived phenylacetylenes were performed using chiral stationary columns (abbreviated as chiral HPLC) to determine the enantiomeric ratios and absolute configurations. The enantiomer ratios were converted to the enantiospecificity (es) according to the following equation: (% ee of the product) × 100/(% ee of the phosphate) [34].

3.2. Representative Procedures of the Coupling Reaction

3.2.1. Method A Using Commercial PhLi (Table 1, Entry 7)

To an ice-cold suspension of CuCl (21.9 mg, 0.221 mmol) in Et_2O (1 mL) and THF (0.5 mL) was added PhLi (1.13 M in *c*-hexane/Et_2O, 0.40 mL, 0.452 mmol) dropwise. The mixture was stirred at 0 °C for 30 min, and then a solution of racemic phosphate **1a** (54.5 mg, 0.148 mmol) in THF (1 mL) was added. The mixture was stirred for 2 h and diluted with saturated NH_4Cl and a small amount of 28% NH_4OH. The resulting mixture was extracted with EtOAc twice. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated to leave an oil, which was purified by chromatography on silica gel to afford acetylene **2aa** (33.1 mg, 76% yield, 98% rs by ^{1}H NMR analysis).

3.2.2. Method B Using PhLi Derived from PhI and *t*-BuLi (Table 1, Entry 8)

To an ice-cold solution of PhI (0.060 mL, 0.538 mmol) in Et_2O (0.7 mL) was added *t*-BuLi (1.59 M in pentane, 0.56 mL, 0.89 mmol). After 30 min, THF (0.7 mL) and CuCl (21.1 mg, 0.213 mmol) were added to the solution. The mixture was stirred for 30 min at 0 °C, and then a solution of racemic phosphate **1a** (54.2 mg, 0.147 mmol) in THF (0.7 mL) was added. The resulting mixture was stirred at 0 °C for 1 h and diluted with saturated NH_4Cl and a small amount of 28% NH_4OH. Extraction of the products and purification were carried out as described in Method A to afford **2aa** (34.6 mg, 80% yield, 98% rs by ^1H NMR analysis).

3.2.3. Method C Using PhLi Derived from PhBr and *t*-BuLi (Table 1, Entry 9)

To a solution of PhBr (0.050 mL, 0.478 mmol) in Et_2O (1.5 mL) at −15 °C was added *t*-BuLi (1.59 M in pentane, 0.61 mL, 0.97 mmol). After 30 min, THF (0.4 mL) and CuCl (21.6 mg, 0.218 mmol) were added to the solution. The mixture was stirred at 0 °C for 1 h, and then a THF solution of racemic phosphate **1a** (59.1 mg, 0.160 mmol) was added. The resulting mixture was stirred at 0 °C for 2 h and diluted with saturated NH_4Cl and a small amount of 28% NH_4OH. Extraction of the products and purification were carried out as described in Method A to afford **2aa** (34.2 mg, 73% yield, 97% rs by ^1H NMR analysis).

3.3. Representative Procedure for the Conversion of TMS-Acetylenes to Phenylacetylenes

To a solution of acetylene (*S*)-**2aa** (184 mg, 0.630 mmol) in MeOH (1.3 mL) was added K_2CO_3 (104 mg, 0.753 mmol). The mixture was stirred at room temperature for 2 h, diluted with Et_2O, and filtered through a pad of Celite. The filtrate was concentrated to afford an oil, which was purified by chromatography on silica gel with hexane/EtOAc for the next reaction.

To a solution of the above acetylene, PhI (0.084 mL, 0.753 mmol), *t*-$BuNH_2$ (0.66 mL, 6.23 mmol), and $Pd(PPh_3)_4$ (73.0 mg, 0.0632 mmol) in benzene (6 mL) was added CuI (36.0 mg, 0.189 mmol). The mixture was stirred at room temperature for 14 h and diluted with saturated NH_4Cl. The resulting mixture was extracted with EtOAc twice. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated to afford an oil, which was purified by chromatography on silica gel with hexane/EtOAc to afford acetylene (*S*)-**5aa** (146 mg, 78% yield).

3.4. Experiments and Characterization of the Products

3.4.1. Synthesis of (*S*)-(3,5-Diphenylpent-1-yn-1-yl)trimethylsilane [(*S*)-**2aa**], Its Conversion to Ph-Acetylene (*S*)-**5aa**, and Chiral HPLC Analysis

According to Method A, PhLi (1.13 M in *c*-hexane/Et_2O, 0.46 mL, 0.52 mmol) was mixed with CuCl (23.9 mg, 0.241 mmol) in Et_2O (0.8 mL) and THF (0.4 mL) at 0 °C for 30 min. A solution of (*S*)-**1a** (98% ee, 60.0 mg, 0.163 mmol) in THF (0.5 mL) was added to the copper reagent, and the mixture was stirred at 0 °C for 1 h to afford (*S*)-**2aa** (33.5 mg, 70% yield): 95% rs; 99% es by chiral HPLC analysis using Chiralcel OJ-H, hexane/*i*-PrOH (99.9:0.1), 0.2 mL/min, 25 °C, and t_R/min = 37.3 (minor) and 44.3 (major); ^1H NMR (300 MHz, $CDCl_3$) δ 0.21 (s, 9 H), 1.99–2.08 (m, 2 H), 2.76 (dt, J = 3.3, 8.5 Hz, 2 H), 3.65 (t, J = 7.2 Hz, 1 H), and 7.16–7.37 (m, 10 H); and ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.3 (+), 33.5 (−), 38.2 (+), 40.3 (−), 87.9 (−), 108.1 (−), 126.0 (+), 126.8 (+), 127.5 (+), 128.4 (+), 128.5 (+), 128.6 (+), 141.6 (−), and 141.8 (−). The ^1H, ^{13}C, and ^{13}C-APT NMR spectra were consistent with those reported [29]. The absolute configuration of (*S*)-**2aa** was determined by the chiral HPLC analysis of the derived phenylacetylene (*S*)-**5aa** (see below).

The procedure was described as a representative example (vide supra): ^1H NMR (300 MHz, $CDCl_3$) δ 2.08–2.22 (m, 2 H), 2.85 (dt, J = 3.0, 7.4, 2 H), 3.84 (t, J = 7.4 Hz, 1 H), and 7.15–7.51 (m, 15 H); and ^{13}C NMR (75 MHz, $CDCl_3$) δ 33.7 (−), 37.9 (+), 40.2 (−), 83.9 (−), 91.2 (−), 123.8 (−), 126.0 (+), 126.9 (+), 127.6 (+), 127.9 (+), 128.3 (+), 128.5 (+), 128.6 (+), 131.7 (+), 141.7 (−), and 141.9 (−). The spectra were consistent with those reported [29].

Chiral HPLC analysis using Chiralcel OD-H, hexane/*i*-PrOH (99.5:0.5), 0.3 mL/min, 25 °C, t_R/min = 23.2 (major), and 25.5 (minor): 98% es; (*S*)-configuration by comparing the relative t_R values with the published values [29]: t_R/min = 35.3 for (*S*)-isomer and 38.7 for (*R*)-isomer.

3.4.2. Synthesis of (*S*)-Trimethyl[5-phenyl-3-(p-tolyl)pent-1-yn-1-yl]silane [(*S*)-**2ab**], Its Conversion to Ph-Acetylene (*S*)-**5ab**, and Chiral HPLC Analysis

According to Method C, lithiation of 4-bromotoluene (0.060 mL, 0.490 mmol) in Et_2O (0.7 mL) with *t*-BuLi (1.59 M, 0.56 mL, 0.890 mmol) (0 °C for 30 min) was followed by the addition of THF (0.35 mL) and a reaction with CuCl (19.9 mg, 0.201 mmol) (0 °C for 15 min). A solution of (*S*)-**1a** (98% ee, 50.2 mg, 0.136 mmol) in THF (0.35 mL) was added to the copper reagent, and the mixture was stirred at 0 °C for 1 h to give (*S*)-**2ab** (30.2 mg, 72% yield): 96% rs; 98% es by chiral HPLC analysis of the corresponding Ph-acetylene (*S*)-**5ab** (vide infra); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.20 (s, 9 H), 1.97–2.07 (m, 2 H), 2.33 (s, 3 H), 2.75 (dt, *J* = 2.7, 7.5 Hz, 2 H), 3.61 (t, *J* = 7.5 Hz, 1 H), and 7.10–7.32 (m, 9 H); and ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.3 (+), 21.1 (+), 33.5 (−), 37.8 (+), 40.2 (−), 87.6 (−), 108.4 (−), 125.9 (+), 127.4 (+), 128.4 (+), 128.6 (+), 129.2 (+), 136.3 (−), 138.6 (−), and 141.8 (−). The ^{1}H, ^{13}C, and ^{13}C-APT NMR spectra were consistent with those reported [29].

According to the representative procedure, the reaction of (*S*)-**2ab** (39.7 mg, 0.130 mmol) with K_2CO_3 (25.0 mg, 0.181 mmol) in MeOH (1.3 mL) at rt for 3 h afforded the desilylated acetylene, and the subsequent coupling reaction with PhI (0.020 mL, 0.179 mmol) in benzene (1.1 mL), using *t*-$BuNH_2$ (0.130 mL, 1.23 mmol), $Pd(PPh_3)_4$ (18.8 mg, 0.0163 mmol), and CuI (22.5 mg, 0.118 mmol), at rt for 14 h gave acetylene (*S*)-**5ab** (31.9 mg, 79% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.04–2.22 (m, 2 H), 2.34 (s, 3 H), 2.80–2.87 (m, 2 H), 3.81 (dd, *J* = 7.8, 6.6 Hz, 1 H), 7.13–7.48 (m, 12 H), and 7.45–7.50 (m, 2 H). The ^{1}H spectrum was consistent with that reported [29].

Chiral HPLC analysis using Chiralcel OD-H, hexane/*i*-PrOH (99.8:0.2), 0.3 mL/min, 25 °C, t_R/min = 28.5 (major), and 35.0 (minor): 98% es; (*S*)-configuration by comparing the relative t_R values with the published data [29]: t_R/min = 32.6 for (*S*)-isomer and 40.9 for (*R*)-isomer.

3.4.3. Synthesis of (*S*)-Trimethyl[5-phenyl-3-(*o*-tolyl)pent-1-yn-1-yl]silane [(*S*)-**2ac**], Its Conversion to Ph-Acetylene (*S*)-**5ac**, and Chiral HPLC Analysis

According to Method C, lithiation of 2-bromotoluene (0.080 mL, 0.664 mmol) in Et_2O (1 mL) with *t*-BuLi (1.59 M, 0.84 mL, 1.34 mmol) (0 °C for 30 min) was followed by the addition of THF (0.5 mL) and a reaction with CuCl (29.3 mg, 0.296 mmol) (0 °C for 15 min). A solution of (*S*)-**1a** (98% ee, 76.3 mg, 0.207 mmol) in THF (1 mL) was added to the copper reagent, and the mixture was stirred at 0 °C for 1 h to afford (*S*)-**2ac** (54.4 mg, 86% yield): 99% rs; 98% es by chiral HPLC analysis of the corresponding Ph-acetylene (*R*)-**5ac** (vide infra); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.21 (s, 9 H), 1.89–2.04 (m, 2 H), 2.18 (s, 3 H), 2.72–2.94 (m, 2 H), 3.79 (dd, *J* = 8.8, 5.8 Hz, 1 H), 7.07–7.34 (m, 8 H), and 7.52 (d, *J* = 7.5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.3 (+), 19.0 (+), 33.8 (−), 34.7 (+), 38.7 (−), 87.3 (−), 108.4 (−), 126.0 (+), 126.3 (+), 126.7 (+), 127.6 (+), 128.4 (+), 128.6 (+), 130.5 (+), 134.9 (−), 139.8 (−), and 141.7 (−). The ^{1}H, ^{13}C, and ^{13}C-APT NMR spectra were consistent with those reported [29].

According to the representative procedure, the reaction of (*S*)-**2ac** (54.4 mg, 0.177 mmol) with K_2CO_3 (34.6 mg, 0.250 mmol) in MeOH (1.8 mL) at rt for 3 h gave the desilylated acetylene, and the subsequent coupling reaction with PhI (0.030 mL, 0.269 mmol) in benzene (1.5 mL), using *t*-$BuNH_2$ (0.260 mL, 2.45 mmol), $Pd(PPh_3)_4$ (23.1 mg, 0.020 mmol), and CuI (41.7 mg, 0.219 mmol), at rt for 14 h afforded acetylene (*R*)-**5ac** (47.0 mg, 85% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.97–2.18 (m, 2 H), 2.24 (s, 3 H), 2.81–3.03 (m, 2 H), 3.99 (dd, *J* = 9.3, 5.1 Hz, 1 H), 7.11–7.35 (m, 11 H), 7.43–7.50 (m, 2 H), and 7.59 (d, *J* = 6.9 Hz, 1 H). The ^{1}H spectrum was consistent with the reported data [29].

Chiral HPLC analysis using Chiralcel OD-H, hexane/*i*-PrOH (99.8:0.2), 0.3 mL/min, 25 °C, and t_R/min = 31.6 (minor) and 35.5 (major): 98% es; (*R*)-configuration by comparing

the relative t_R values with the published data [29]: t_R/min = 33.5 for (*S*)-isomer and 39.6 for (*R*)-isomer.

3.4.4. Synthesis of (*S*)-[3-(4-Methoxyphenyl)-5-phenylpent-1-yn-1-yl]trimethylsilane [(*S*)-**2ad**], Its Conversion to Ph-Acetylene (*S*)-**5ad**, and Chiral HPLC Analysis

According to Method C, the lithiation of 4-bromoanisole (0.060 mL, 0.479 mmol) in Et_2O (0.7 mL) with *t*-BuLi (1.59 M in pentane, 0.58 mL, 0.922 mmol) (0 °C for 30 min) was followed by the addition of THF (0.4 mL) and a reaction with CuCl (21.6 mg, 0.218 mmol) (0 °C for 30 min). A solution of (*S*)-**1a** (98% ee, 53.2 mg, 0.144 mmol) in THF (0.4 mL) was added to the copper reagent, and the mixture was stirred at 0 °C for 1 h to give (*S*)-**2ad** (45.9 mg, 86% yield): 97% rs; 98% es by chiral HPLC analysis of the corresponding Ph-acetylene (vide infra); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.20 (s, 9 H), 1.96–2.06 (m, 2 H), 2.70–2.78 (m, 2 H), 3.60 (t, *J* = 7.1 Hz, 1 H), 3.79 (s, 3 H), 6.85 (d, *J* = 9.0 Hz, 2 H), and 7.16–7.32 (m, 7 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.3 (+), 33.5 (−), 37.4 (+), 40.3 (−), 55.4 (+), 87.6 (−), 108.5 (−), 113.9 (+), 125.9 (+), 128.4 (+), 128.5 (+), 128.6 (+), 133.7 (−), 141.8 (−), and 158.5 (−). The ^{1}H, ^{13}C, and ^{13}C-APT NMR spectra were consistent with those reported [29].

According to the representative procedure, the reaction of (*S*)-**2ad** (40.8 mg, 0.127 mmol) with K_2CO_3 (26.5 mg, 0.192 mmol) in MeOH (1.3 mL) at rt for 3 h gave the desilylated acetylene, and the subsequent coupling reaction with PhI (0.020 mL, 0.179 mmol) in benzene (1.1 mL), using *t*-$BuNH_2$ (0.140 mL, 1.32 mmol), $Pd(PPh_3)_4$ (27.4 mg, 0.0237 mmol), and CuI (16.4 mg, 0.0861 mmol), at rt for 14 h afforded acetylene (*S*)-**5ad** (29.4 mg, 71% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.05–2.21 (m, 2 H), 2.78–2.87 (m, 2 H), 3.80 (s, 3 H), 3.74–3.87 (m, 1 H), 6.88 (d, *J* = 9.0 Hz, 2 H), 7.16–7.36 (m, 10 H), and 7.43–7.50 (m, 2 H). The ^{1}H spectrum was consistent with that reported [29].

Chiral HPLC analysis using Chiralcel OD-H, hexane/*i*-PrOH (99.5:0.5), 0.3 mL/min, 25 °C, and t_R/min = 34.2 (major) and 44.9 (minor): 98% es; (*S*)-configuration by comparing the relative t_R values with the published data [29]: t_R/min = 38.5 for (*S*)-isomer and 51.2 for (*R*)-isomer.

3.4.5. Synthesis of (*S*)-[3-(2-Methoxyphenyl)-5-phenylpent-1-yn-1-yl]trimethylsilane [(*S*)-**2ae**], Its Conversion to Ph-Acetylene (*S*)-**5ae**, and Chiral HPLC Analysis

According to Method C, lithiation of 2-bromoanisole (0.070 mL, 0.569 mmol) in Et_2O (0.9 mL) with *t*-BuLi (1.59 M, 0.69 mL, 1.10 mmol) (0 °C for 30 min) was followed by the addition of THF (0.4 mL) and a reaction with CuCl (24.9 mg, 0.252 mmol) (0 °C for 30 min). A solution of (*S*)-**1a** (98% ee, 62.9 mg, 0.171 mmol) in THF (0.5 mL) was added to the copper reagent, and the mixture was stirred at 0 °C for 1 h to produce (*S*)-**2ae** (45.8 mg, 83% yield): 99% rs; >99% es by chiral HPLC analysis of the corresponding Ph-acetylene (*R*)-**5ae** (vide infra); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.21 (s, 9 H), 1.83–2.11 (m, 2 H), 2.68–2.88 (m, 2 H), 3.76 (s, 3 H), 4.13 (dd, *J* = 8.7, 5.1 Hz, 1 H), 6.82 (d, *J* = 8.1 Hz, 1 H), 6.96 (t, *J* = 7.4 Hz, 1 H), 7.13–7.30 (m, 6 H), and 7.60 (dd, *J* = 7.6, 1.6 Hz, 1 H); and ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.3 (+), 31.9 (+), 33.7 (−), 38.2 (−), 55.4 (+), 87.1 (−), 108.7 (−), 110.4 (+), 120.7 (+), 125.8 (+), 127.9 (+), 128.3 (+), 128.6 (+), 129.9 (−), 142.2 (−), and 156.2 (−). The ^{1}H, ^{13}C, and ^{13}C-APT NMR spectra were consistent with those reported [29].

According to the representative procedure, the reaction of (*S*)-**2ae** (37.1 mg, 0.0983 mmol) with K_2CO_3 (27.3 mg, 0.198 mmol) in MeOH (1.3 mL) at rt for 3 h afforded the desilylated acetylene, and the subsequent coupling reaction with PhI (0.020 mL, 0.179 mmol) in benzene (1.1 mL), using *t*-$BuNH_2$ (0.14 mL, 1.32 mmol), $Pd(PPh_3)_4$ (24.1 mg, 0.021 mmol), and CuI (11.5 mg, 0.060 mmol), at rt for 14 h gave acetylene (*R*)-**5ae** (22.1 mg, 69% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.96–2.21 (m, 2 H), 2.77–2.97 (m, 2 H), 3.80 (s, 3 H), 4.33 (dd, *J* = 8.8, 5.3 Hz, 1 H), 6.85 (dd, *J* = 8.1, 1.2 Hz, 1 H), 6.97 (dt, *J* = 1.1, 7.2 Hz, 1 H), 7.13–7.35 (m, 9 H), 7.45–7.51 (m, 2 H), and 7.64 (dd, *J* = 7.8, 1.5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.4 (+), 33.8 (−), 38.2 (−), 55.4 (+), 83.1 (−), 91.8 (−), 110.5 (+), 120.7 (+), 124.0 (−), 125.8 (+), 127.7 (+), 127.9 (+), 128.29 (+), 128.31 (+), 128.59 (+), 128.62 (+), 130.2 (−), 131.8 (+), 142.1 (−), and 156.2 (−). The ^{1}H, ^{13}C, and ^{13}C-APT NMR spectra were consistent with those reported [29].

Chiral HPLC analysis using Chiralcel OD-H, hexane/*i*-PrOH (99.5:0.5), 0.3 mL/min, 25 °C, and t_R/min = 24.2 (major) and 28.0 (minor): >99% es; (*R*)-configuration by comparing the relative t_R values with the published data [29]: t_R/min = 35.1 for (*R*)-isomer and 40.0 for (*S*)-isomer.

3.4.6. Synthesis of (*R*)-[3-(Furan-2-yl)-5-phenylpent-1-yn-1-yl]trimethylsilane [(*R*)-**2af**], Its Conversion to Ph-Acetylene (*S*)-**5af**, and Chiral HPLC Analysis

To an ice-cold solution of furan (0.040 mL, 0.552 mmol) in THF (0.4 mL) was added *n*-BuLi (1.65 M, 0.29 mL, 0.479 mmol) dropwise. The solution was stirred at 0 °C for 30 min. According to Method C, CuCl (20.5 mg, 0.207 mmol) was added to the solution, and, after 15 min of stirring at 0 °C, a solution of phosphate (*S*)-**1a** (97% ee, 54.7 mg, 0.148 mmol) in THF (0.4 mL) was then added. The mixture was stirred at 0 °C for 1 h to afford (*R*)-**2af** (33.0 mg, 79% yield): 99% rs; 95% es by chiral HPLC analysis of the corresponding Ph-acetylene (*R*)-**5af** (vide infra); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.20 (s, 9 H), 2.02–2.22 (m, 2 H), 2.77 (t, *J* = 8.0 Hz, 2 H), 3.75 (dd, *J* = 8.2, 5.8 Hz, 1 H), 6.21 (d, *J* = 3.2 Hz, 1 H), 6.30 (dd, *J* = 3.0, 2.2 Hz, 1 H), and 7.16–7.35 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.2 (+), 32.0 (+), 33.1 (−), 36.3 (−), 87.4 (−), 105.2 (−), 106.0 (+), 110.3 (+), 126.0 (+), 128.5 (+), 128.6 (+), 141.6 (−), 141.7 (+), and 154.1 (−); and HRMS (FD) calcd for $C_{18}H_{26}OSi$ $[M]^+$ 282.14399, found 282.14264.

According to the representative procedure, the reaction of (*R*)-**2af** (24.8 mg, 0.0878 mmol) with K_2CO_3 (22.7 mg, 0.164 mmol) in MeOH (0.9 mL) at rt for 3 h gave the desilylated acetylene, and the subsequent coupling reaction with PhI (0.020 mL, 0.179 mmol) in benzene (0.8 mL), using *t*-$BuNH_2$ (0.10 mL, 0.94 mmol), $Pd(PPh_3)_4$ (13.5 mg, 0.0117 mmol), and CuI (8.6 mg, 0.045 mmol), at rt for 16 h afforded Ph-acetylene (*R*)-**5af** (18.0 mg, 73% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.12–2.33 (m, 2 H), 2.85 (t, *J* = 7.8 Hz, 2 H), 3.86 (dd, *J* = 8.2, 5.8 Hz, 1 H), 6.28 (dt, *J* = 3.3, 0.8 Hz, 1 H), 6.33 (dd, *J* = 3.3, 2.1 Hz, 1 H), 7.16–7.34 (m, 8 H), 7.36 (dd, *J* = 2.1, 0.9 Hz, 1 H), and 7.43–7.50 (m, 2 H).

Chiral HPLC analysis using Chiralpak AD-H, hexane/*i*-PrOH (99.5:0.5), 0.3 mL/min, 25 °C, and t_R/min = 22.9 (minor) and 26.5 (major): 95% es; (*R*)-configuration was assigned by analogy with that shown in Scheme 4.

3.4.7. Synthesis of (*R*)-Trimethyl[5-phenyl-3-(thiophen-2-yl)pent-1-yn-1-yl]silane [(*R*)-**2ag**], Its Conversion to Ph-Acetylene (*S*)-**5ag**, and Chiral HPLC Analysis

To an ice-cold solution of thiophene (0.050 mL, 0.636 mmol) in THF (0.4 mL) was added *n*-BuLi (1.65 M, 0.31 mL, 0.51 mmol) dropwise. The solution was stirred at 0 °C for 30 min. According to Method C, CuCl (22.9 mg, 0.231 mmol) was added to the solution, and, after 15 min of stirring at 0 °C, a solution of phosphate (*S*)-**1a** (98% ee, 57.4 mg, 0.156 mmol) in THF (0.4 mL) was added. The mixture was stirred at 0 °C for 1 h to afford (*R*)-**2ag** (34.8 mg, 75% yield): >99% rs; 99% es by chiral HPLC analysis of the corresponding Ph-acetylene (vide infra); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.21 (s, 9 H), 2.09–2.17 (m, 2 H), 2.77–2.83 (m, 2 H), 3.93 (t, *J* = 7.2 Hz, 1 H), 6.93 (dd, *J* = 5.0, 3.8 Hz, 1 H), 6.96–6.98 (m, 1 H), and 7.16–7.32 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.2 (+), 33.3 (−), 33.5 (+), 40.2 (−), 87.9 (−), 107.1 (−), 124.0 (+), 124.6 (+), 126.1 (+), 126.7 (+), 128.6 (+), 128.7 (+), 141.6 (−), and 145.2 (−); and HRMS (FD) calcd for $C_{18}H_{22}SSi$ $[M]^+$ 298.12115, found 298.11989.

According to the representative procedure, the reaction of (*R*)-**2ag** (34.8 mg, 0.117 mmol) with K_2CO_3 (26.1 mg, 0.189 mmol) in MeOH (1.3 mL) at rt for 3 h afforded the desilylated acetylene, and the subsequent coupling reaction with PhI (0.020 mL, 0.179 mmol) in benzene (1 mL), using *t*-$BuNH_2$ (0.13 mL, 1.23 mmol), $Pd(PPh_3)_4$ (15.8 mg, 0.0137 mmol), and CuI (7.1 mg, 0.0373 mmol), at rt for 16 h produced Ph-acetylene (*R*)-**5ag** (23.5 mg, 67% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.24 (dt, *J* = 8.4, 7.2, 2 H), 2.88 (dd, *J* = 9.3, 6.6 Hz, 2 H), 4.13 (t, *J* = 7.2 Hz, 1 H), 6.96 (dd, *J* = 5.0, 3.4 Hz, 1 H), 7.02–7.05 (m, 1 H), 7.17–7.36 (m, 9 H), and 7.44–7.52 (m, 2 H).

Chiral HPLC analysis using Chiralpak AD-H, hexane/*i*-PrOH (99.5:0.5), 0.3 mL/min, and 25 °C, t_R/min = 26.1 (minor) and 28.7 (major): 99% es; (*R*)-configuration was assigned by analogy with that shown in Scheme 4.

3.4.8. Synthesis of Trimethyl(4-methyl-3-phenylpent-1-yn-1-yl)silane (**2ba**)

According to Method A, PhLi (1.13 M, 0.57, mL, 0.644 mmol) and, after 15 min at 0 °C, a solution of **1b** (56.4 mg, 0.184 mmol) in THF (0.5 mL) was added to CuCl (25.7 mg, 0.260 mmol) in THF (0.4 mL) and Et_2O (0.9 mL). The mixture was stirred at 0 °C for 1 h to produce **2ba** (35.0 mg, 83% yield): 93% rs; and ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.19 (s, 9 H), 0.90 (d, J = 6.6 Hz, 3 H), 0.98 (d, J = 6.9 Hz, 3 H), 1.88–2.00 (m, 1 H), 3.54 (d, J = 5.7 Hz, 1 H), and 7.18–7.33 (m, 5 H). The ^{1}H NMR spectrum was consistent with that reported [29].

3.4.9. Synthesis of [3-(2-Methoxyphenyl)-4-methylpent-1-yn-1-yl]trimethylsilane (**2be**)

According to Method C, lithiation of 2-bromoanisole (0.080 mL, 0.650 mmol) in Et_2O (1 mL) with *t*-BuLi (1.59 M, 0.77 mL, 1.22 mmol) (0 °C for 30 min) was followed by the addition of THF (0.5 mL) and a reaction with CuCl (27.1 mg, 0.274 mmol) (0 °C for 15 min). A solution of **1b** (58.1 mg, 0.190 mmol) in THF (0.5 mL) was added to the copper reagent, and the mixture was stirred at 0 °C for 1 h to produce **2be** (41.3 mg, 84% yield): 97% rs; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.18 (s, 9 H), 0.86 (d, J = 6.9 Hz, 3 H), 1.01 (d, J = 6.9 Hz, 3 H), 1.89–2.02 (m, 1 H), 3.80 (s, 3 H), 4.06 (d, J = 5.1 Hz, 1 H), 6.83 (d, J = 7.6 Hz, 1 H), 6.94 (t, J = 7.6 Hz, 1 H), 7.20 (dt, J = 1.8, 7.6 Hz, 1 H), and 7.49 (dd, J = 7.6, 1.8 Hz, 1 H); and ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.3 (+), 18.1 (+), 21.5 (+), 32.6 (+), 39.0 (+), 55.4 (+), 87.5 (−), 107.5 (−), 110.3 (+), 120.3 (+), 127.6 (+), 129.4 (−), 129.5 (+), and 156.4 (−). The ^{1}H, ^{13}C, and ^{13}C–APT NMR spectra were consistent with the reported data [29].

3.4.10. Synthesis of [3-(Benzo[d][1,3]dioxol-4-yl)oct-1-yn-1-yl]trimethylsilane (**2ch**)

According to Method C, lithiation of 2-bromocatechol derivative **6** (139.0 mg, 0.691 mmol) in Et_2O (1 mL) with *t*-BuLi (1.59 M, 0.82 mL, 1.30 mmol) (0 °C for 30 min) was followed by the addition of THF (0.5 mL) and a reaction with CuCl (28.5 mg, 0.288 mmol) (0 °C for 15 min). A solution of **1c** (68.1 mg, 0.204 mmol) in THF (0.5 mL) was added to the copper reagent, and the mixture was stirred at 0 °C for 1 h to afford **2ch** (51.3 mg, 76% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.17 (s, 9 H), 0.88 (t, J = 6.8, 3 H), 1.23–1.52 (m, 6 H), 1.65–1.79 (m, 2 H), 3.81 (dd, J = 7.6, 6.4 Hz, 1 H), 5.905 (d, J = 1.4 Hz, 1 H), 5.940 (d, J = 1.4 Hz, 1 H), 6.71 (dd, J = 8.0, 1.4 Hz, 1 H), 6.81 (t, J = 8.0 Hz, 1 H), and 6.98 (dd, J = 8.0, 0.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.2 (+), 14.1 (+), 22.6 (−), 26.9 (−), 31.4 (−), 32.8 (+), 36.4 (−), 86.9 (−), 100.7 (−), 107.1 (+), 107.5 (−), 121.1 (+), 121.6 (+), 123.7 (−), 144.5 (−), and 147.1 (−); and HRMS (FD) calcd for $C_{18}H_{26}O_2Si$ $[M]^+$ 302.17021, found 302.17080.

3.4.11. Synthesis of Pent-1-yne-1,3,5-triyltribenzene (**5aa**)

According to Method A, PhLi (1.13 M, 0.48 mL, 0.542 mmol) and, after 15 min at 0 °C, a solution of **7** (57.6 mg, 0.155 mmol) in THF (0.4 mL) were added to CuCl (20.5 mg, 0.207 mmol) in THF (0.4 mL) and Et_2O (0.8 mL). The mixture was stirred at 0 °C for 1 h to produce **5aa** (27.9 mg, 62% yield, 92% rs). The ^{1}H NMR spectrum was consistent with that derived from TMS-acetylene **2aa**.

3.4.12. Synthesis of (*R*)-[3-(2-Methoxyphenyl)pent-1-yne-1,5-diyl]dibenzene [(*R*)-**5ae**]

According to Method C, lithiation of 2-bromoanisole (0.060 mL, 0.488 mmol) in Et_2O (0.7 mL) with *t*-BuLi (1.59 M, 0.57 mL, 0.906 mmol) (0 °C for 30 min) was followed by the addition of THF (0.35 mL) and a reaction with CuCl (19.8 mg, 0.200 mmol) (0 °C for 15 min). A solution of (*S*)-**7** (96% ee, 52.2 mg, 0.140 mmol) in THF (0.35 mL) was added to the copper reagent, and the mixture was stirred at 0 °C for 1 h to afford (*R*)-**5ae** (41.1 mg, 90% yield, >99% rs, 98% es by chiral HPLC analysis). The ^{1}H NMR spectrum was consistent with that reported [29]. (*R*)-Configuration was determined by comparing the relative t_R values with those of (*R*)-**5ae**, which was derived from (*S*)-**2ae** (vide supra).

3.4.13. Synthesis of (*S*)-Dec-4-yne-1,3-diyldibenzene [(S)-**9**]

According to Method A, PhLi (1.13 M, 0.54 mL, 0.61 mmol) and, after 15 min at 0 °C, a solution of (*S*)-**8** (95% ee, 64.3 mg, 0.175 mmol) in THF (0.45 mL) were added to CuCl

(25.4 mg, 0.257 mmol) in THF (0.45 mL) and Et_2O (0.9 mL). The mixture was stirred at 0 °C for 1 h to give (*S*)-**9** (42.5 mg, 83% yield): 83% rs; 98% es by chiral HPLC analysis, using Chiralcel OJ-H, hexane/*i*-PrOH (99.9:0.1), 0.3 mL/min, 25 °C, t_R/min = 38.1 (minor), and 44.7 (major); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 (t, J = 7.0 Hz, 3 H), 1.24–1.52 (m, 4 H), 1.52–1.63 (m, 2 H), 2.01 (q, J = 8.0 Hz, 2 H), 2.26 (dt, J = 2.3, 6.6 Hz, 2 H), 2.68–2.86 (m, 2 H), 3.60 (tt, J = 6.9, 2.1 Hz, 1 H), and 7.14–7.39 (m, 10 H); and ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1 (+), 18.9 (−), 22.3 (−), 28.9 (−), 31.2 (−), 33.7 (−), 37.4 (+), 40.6 (−), 81.4 (−), 83.9 (−), 125.9 (+), 126.6 (+), 127.5 (+), 128.40 (+), 128.45 (+), 128.6 (+), 142.0 (−), and 142.8 (−). The ^{1}H, ^{13}C, and ^{13}C–APT NMR spectra were consistent with the reported data [29]. (*S*)-Configuration was assigned by analogy with that shown in Scheme 4.

*3.5. Synthesis of (1,5-Diphenylpenta-1,2-dien-1-yl)trimethylsilane (**3aa**) (Table 1, Entry 10)*

To an ice-cold mixture of $Cu(acac)_2$ (87.3 mg, 0.334 mmol) and $MgBr_2$ in THF (0.20 M, 4.2 mL, 0.84 mmol) was added PhLi (1.13 M, 0.54 mL, 0.61 mmol) dropwise. The mixture was stirred at 0 °C for 1 h, and phosphate **1a** (61.5 mg, 0.167 mmol) in THF (1.7 mL) was added. The reaction was carried out at 0 °C for 4 h and diluted with saturated NH_4Cl and 28% NH_4OH. The product was extracted with EtOAc twice. The combined extracts were dried over $MgSO_4$ and concentrated. The residual oil was purified by chromatography on silica gel with hexane/EtOAc to afford allene **3aa** (41.6 mg, 85% yield): >99% rs; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.22 (s, 9 H), 2.33–2.50 (m, 2 H), 2.68–2.86 (m, 2 H), 5.19 (t, J = 6.8 Hz, 1 H), and 7.12–7.32 (m, 10 H); and ^{13}C NMR (75 MHz, $CDCl_3$) δ –0.2 (+), 30.3 (−), 36.0 (−), 86.7 (+), 100.6 (−), 126.0 (+), 126.1 (+), 127.7 (+), 128.43 (+), 128.45 (+), 128.6 (+), 137.9 (−), 141.9 (−), and 208.3 (−). The ^{1}H, ^{13}C, and ^{13}C–APT NMR spectra were consistent with those reported [29].

4. Conclusions

Aryl-lithium-based copper reagents were developed for the propargylic substitution of TMS-acetylenic phosphates. Aryl lithium compounds prepared in situ by the lithium-halogen exchange with *t*-BuLi were converted to highly regioselective and enantiospecific aryl reagents. 2-Furyl and 2-thienyl reagents prepared via the direct lithiation with *n*-BuLi were successful as well. The present propargylic substitution with several preparations of aryl lithiums would be a useful reaction in organic synthesis.

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/catal13071084/s1, general information of experiments, remaining procedures, ^{1}H, ^{13}C, and ^{13}C-APT NMR spectra [29].

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