Stereoselective Synthesis of Chiral 3-Aryl-1-Alkynes from Bromoallenes and Heterocuprates.

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Abstract

The synthesis of chiral 3-aryl-1-alkynes **3** *via* cross-coupling of 3-alkyl- and 3,3-dialkyl-1-bromo-1,2-dienes **1** and arylbromocuprates (RCuBr)MgBr·LiBr **2** was examined. With phenylcopper reagents and its *para*-substituted derivatives, as well as with 2-naphtyl cuprates, the reaction gave compounds **3** with high regioselectivity and good yields on the chemically pure product. On the contrary, employing *ortho*-substituted phenyl reagents and 1-naphtyl cuprates the regioselectivity of the process was very dependent upon the steric requirements of the alkyl substituents on the bromoallenic substrate. Increasing the steric bulk remarkable quantities of isomeric arylallenes **4** were also observed in the reaction mixtures. The high 1,3-*anti* stereoselectivity of the coupling process allowed us to obtain

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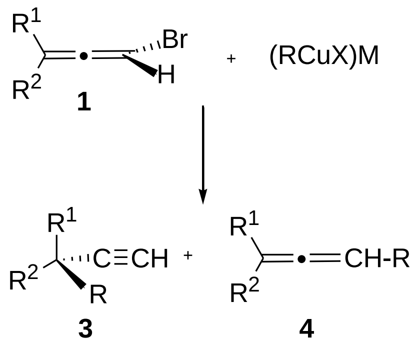
enantiomerically enriched 3-aryl-1-alkynes from optically active allenic substrates indicating thus a simple pathway towards the synthesis of quaternary stereogenic centres characterized by an aryl group. A possible cross-coupling mechanism was also suggested to explain the regio- and stereochemical data. For the preparation of ω-functionalised 3-phenyl-1-alkynes, the reaction of 1-bromo-3-phenylpropadiene with Knochel reagents RCu(CN)ZnCl·2LiCl was also studied; this reaction led to the acetylenic compounds in high yields mainly when the R group (also ω-functionalyzed) on the copper reagent was primary.

Introduction

Simple terminal acetylenic compounds are increasingly used as fundamental substrates in transition metal chemistry for the synthesis of high valued organic compounds (e.g.: sp to sp^2-couplings, oxidative dimerizations, aminoalkylations, silylformylation,... among a few).[1] It is noteworthy the potentiality of optically active 1-alkynes as key intermediates in the preparation of a wide range of chiral molecules.[2]

It was demonstrated that the cross-coupling reaction between optically active allenic bromides **1** and bromocuprates (RCuBr)MgBr·LiBr, **2**, (Scheme 1) was the most simple and convenient way to obtain enantiomerically enriched chiral acetylenes characterized by a tertiary or a quaternary stereogenic centre α to the triple bond.[3]

SCHEME 1.



R^1=H, Alkyl, R^2=Alkyl
(RCuX)M = (RCuBr)MgBr·LiBr, **2**
RCu(CN)ZnCl·2LiCl, **5**
R_2CuLi, **6**; RCu(CN)Li, **7**
R= Alkyl, Phenyl

The reaction proceeded in a highly 1,3-*anti* stereoselective fashion. The regioselectivity of the process appeared to be sensitive to steric interactions, the size of the R substituent in the copper species being the dominant factor.[3d] Indeed employing phenyl or n-alkyl bromocuprates **2**, the acetylenic compounds **3** were obtained in good yields independently of the structure of the allenic bromide. When tertiary, secondary or α-branched primary copper reagents were used, the competitive formation of the allenic derivatives **4** was favoured (Scheme 1).[3a,d] In a second stage of our study we introduced the use of aliphatic zinc-based cuprates RCu(CN)ZnCl·2LiCl, **5** for the same cross-coupling processes.[4] These zinc cyanocuprates (Knochel reagents)[5] reacted with bromoallenes **1** with higher regioselectivity than the corresponding magnesium bromocuprates **2**, affording acetylenes **3** almost quantitatively even when hindered allenic substrates and secondary or α-branched primary copper compounds were used as starting materials. Only when R was a tertiary group the steric requirements of the substrate could have a determining effect on the product distribution. The cross coupling reaction with the Knochel reagents could also be performed, maintaining very high regio- and stereoselectivities, using aliphatic zinc reagents and catalytic amounts of copper salts (10 mol%).[4] Phenyl zinc-based cuprates such as PhCu(CN)ZnCl·2LiCl reacted with compounds **1** affording instead complex mixtures of acetylenic and allenic products (**3** and **4** respectively) both in the stoichiometric and the catalytic reactions.[4] As reported,[3a,b] other types of phenyl copper reagents, such as Ph_2CuLi, **6**, and PhCu(CN)Li, **7**, gave essentially phenylallene derivatives **4**. It appeared therefore evident that chiral 3-phenyl-1-alkynes, **3**, could be obtained with high yields in copper mediated coupling processes only when the phenylbromocuprate (PhCuBr)MgBr·LiBr was used (Scheme 1). Consequently, we extended the scope of our research by elucidating the synthetic utility of the reaction between 1-bromo-1,2-dienes **1** and a series of arylbromocuprates in the preparation of chiral 3-aryl-1-alkynes **3** (R=Ar). The present paper deals with the outcome of the reactions as related to the structural features of the aromatic bromocuprate reagents. An accurate investigation on the stereochemistry of the coupling process was also carried out with enantiomerically enriched bromoallenes.

Taking into account the high selectivity for compounds **3** we obtained when reacting bromoallenes **1** with functionalised zinc-based alkylcyanocuprates **5**,[4] we also explored the reaction of these copper reagents with 3-phenyl-1-bromopropadiene as a potential synthetic approach to functionalised 3-phenyl-1-alkynes. Indeed, it is well known that 3-phenyl-1-bromoallenes react with the alkylbromocuprates **2** to afford mainly substantial amounts of polymeric byproducts.[3a]

Results and Discussion

Coupling of Bromoallenes with Arylbromocuprates.
A. Regiochemical Results.

The complex arylbromocuprates **2a-k** used as nucleophiles were prepared in situ in THF from $LiCuBr_2$ and 1 equiv. of the appropriate aryl Grignard reagent.[3a] The racemic 1-bromo-1,2-dienes **1a-d** were also obtained chemically pure and in high yields (70-90%) from the corresponding propargylic alcohols through well known procedures.[6] According to the experimental conditions previously reported for reactions between compounds **1** and the phenylbromocuprate **2a**,[3a] all the experiments were carried out adding a tetrahydrofuran solution of the bromoallenic substrate **1** to a stirred suspension of two equivalents of the arylcopper reagent **2**, cooled at –70°C. The reaction mixture was then allowed to warm up to room temperature and carefully followed by GC analysis of hydrolyzed samples; in general a reaction time of 30 min at room temperature was adequate for a complete conversion of the substrate into a mixture of 3-aryl-1-alkyne, **3**, and the 1-aryl-1,2-diene, **4**. The two products were separated by fractional distillation or elution on silica-gel column (n-pentane as eluent) and identified by chromatographic and/or spectroscopic methods (Table 1).

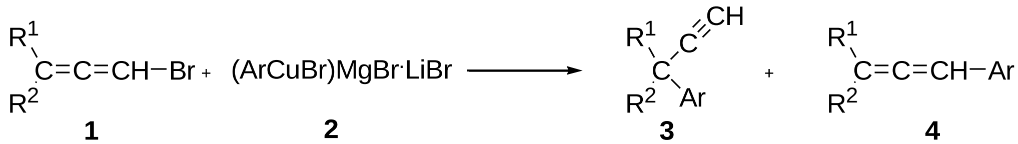
The acetylene/allene ratio, determined by ^{1}H NMR and GC analyses on the crude reaction mixtures, was found to be mainly influenced by the structure of the bromocuprate; the regiochemical results are summarized below:

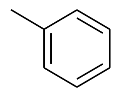
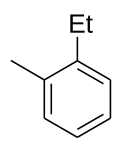
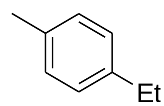
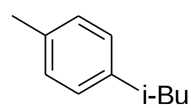
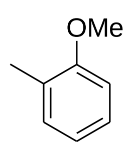
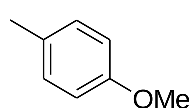
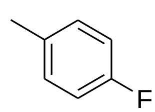
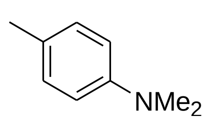
i. phenylbromocuprate **2a** (Table 1, entries 1-3) [3a] and *para*-substituted arylcuprates (Table 1, entries 5,6,11-16) led predominantly to the acetylenic products **3**; independently of the bulkiness of substituents R^1 and R^2 on the bromoallene **1**, product **3** was generally obtained chemically pure (62-86% isolated yields). With *ortho*-substituted arylcuprates we observed greater amounts of the allene derivative **4** which eventually became the main product as the bulkiness of R^1 and R^2 increased enough (Table 1, entries 4, 7-10);

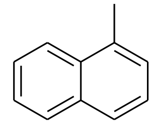
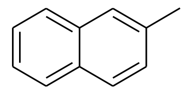
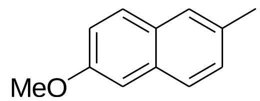
ii. the electronic nature of the substituent on the aromatic ring of the cuprate (electron-donating or electron-withdrawing group) did not significantly affect the regioselectivity of the reaction. Indeed, the acetylenes were always the major products in reactions with *para*-substituited cuprates (Table 1, entries 5, 6, 11-16).

Very similar results were obtained employing naphtylcuprates. Also in these cases we found that the structure of the cuprate played a crucial role in the regioselectivity of the reaction. The 2-naphtylcuprates, **2j** and **2k**, always afforded the corresponding acetylenic products with good yields (Table 1, entries 20-25). When using the 1-naphtylcuprate **2i** instead we observed that an increase in the size of the substituents on the bromoallene **1** disfavoured the alkyne product (Table 1, entries 17-19).

TABLE 1. Coupling Reactions of Arylbromocuprates 2 with Bromoallenes 1 [a]



Entry	Bromoallene, **1**	R^1	R^2	Arylbromocuprate, **2**	Ar	Products **3,4**	Yield (%)[b] **3**	**4**
1	**1b**	H	t-Bu			**ba**	90(81)	10
2	**1c**	Me	Et	**2a**		**ca**	81(65)	19
3	**1d**	Me	t-Bu			**da**	91(84)	9
4	**1d**	Me	t-Bu	**2b**		**db**	62	38
5	**1d**	Me	t-Bu	**2c**		**dc**	92(78)	8
6	**1a**	H	Me	**2d**		**ad**	86(71)	14
7	**1a**	H	Me			**ae**	82(62)	18
8	**1b**	H	t-Bu			**be**	58	42
9	**1c**	Me	Et	**2e**		**ce**	33	67
10	**1d**	Me	t-Bu			**de**	20	80
11	**1b**	H	t-Bu			**bf**	88(75)	12
12	**1c**	Me	Et	**2f**		**cf**	78(62)	22
13	**1d**	Me	t-Bu			**df**	86(75)	14
14	**1d**	Me	t-Bu	**2g**		**dg**	85(68)	15
15	**1b**	H	t-Bu			**bh**	80	20
16	**1d**	Me	t-Bu	**2h**		**dh**	95(86)	5

17	**1a**	H	Me			**ai**	54	46
18	**1b**	H	t-Bu	**2i**		**bi**	40	60
19	**1c**	Me	Et			**ci**	13	87
20	**1a**	H	Me			**aj**	73(52)	27
21	**1b**	H	t-Bu	**2j**		**bj**	83(58)	17
22	**1c**	Me	Et			**cj**	61	39
23	**1d**	Me	t-Bu			**dj**	80(63)	20
24	**1a**	H	Me	**2k**		**ak**	87(74)	13
25	**1d**	Me	t-Bu			**dk**	80	20

[a] All reaction were performed in 10-20 mmol scale by treating **1a-d** with 2 equiv. of the arylcuprate in THF at –70°C and by allowing the reaction mixture to warm to room temperature (30 min.; 100% conversion of **1**). [b] The yields, based on starting **1**, were determined by ^{1}H NMR and GC analysis on the crude reaction mixture after work-up (Isolated yields of >98% pure compounds are shown in parentheses).

B. Stereochemical Results.

In a previous paper,[3a] we reported that (R)-(-)-1-bromo-1,2-butadiene, **(R)-1a**, reacted with the phenylbromocuprate **2a** affording as main product (S)-(+)-3-phenyl-1-butyne, **(S)-3aa**, with 83% 1,3-*anti* stereoselectivity. In the light of this result and taking into account that analogous cross-coupling reactions performed with aliphatic bromocuprates proceeded with almost complete *anti* stereochemistry,[3d] we considered useful to evaluate in general the stereochemical outcome of the coupling reaction between enantiomerically enriched bromoallenes **1** and arylbromocuprates **2**. Chiral 1-alkynes **3**, having a tertiary or a quaternary stereogenic centre characterized by an aryl group in the α-position to the triple bond are generally difficult to prepare enantiomerically enriched *via* conventional procedures[7] and the cross-coupling reaction proposed could then be regarded as a straightforward stereoselective method for their synthesis.

This stereochemical study required the synthesis of the chiral bromoallenes **(S)-1a-d**. These were achieved by reacting the methanesulfonate esters of the corresponding optically active (R)-carbinols with $LiCuBr_2$ or Li_2CuBr_3.[6c,d] The enantiomeric purities of compounds **(S)-1a-d** were determined by GC analyses on a Cydex-B chiral column and/or ^1H NMR in CD_3OD as solvent and heptakis(2,3,6-tri-O-methyl)-β-cyclodextrin as chiral solvating agent (Table 2).[8] The stereochemical outcome of the coupling reaction was studied for those cases in Table 1 where the alkynes **3** were the major products. The optically active acetylenic compounds were isolated in chemically pure form (41-70% yields) and correlated to compounds of known or determinable stereochemistry (Table 2 and Scheme 2).

Thus, a sample of laevorotatory 3-[4-(2-methylpropyl)phenyl]-1-butyne, **(-)-3ad**, obtained from **(S)-1a** (51% ee), was treated with diisobutylaluminium hydride (DIBAH) to yield the corresponding 1-alkene **8ad**. Compound **8ad** was related to dextrorotatory 2-[4-(2-methylpropyl)phenyl]propanoic acid, **(+)-10ad**, of known S stereochemistry [(S)-Ibuprophen, 43% ee][9] by reaction with $KMnO_4$-$NaIO_4$[10] (Scheme 2; Table 2, entry 1). Both the hydroalumination[7] and the oxidative demolition[11] processes were known to proceed in a completely stereospecific manner. Analogously, samples of (-)-3-phenyl-3-methyl-1-pentyne, **(-)-3ca**, obtained from **(S)-1c**, were transformed into the corresponding (+)-2-phenyl-2-methyl-butanoic acid, **(+)-10ca**, of known S stereochemistry[12] (Scheme 2; Table 2, entries 4 and 5). The value of the maximum rotatory power for the acid **(S)-10ca** was evaluated by Cram *via* maximum resolution criteria.[12] However, the relation between the enantiomeric composition and the optical rotation of **(+)10ca** was confirmed by 300 MHz ^1H NMR analysis of the diastereomeric salts obtained by reacting the acid, in $CDCl_3$, with an equimolar amount of optically pure (R)-1-(1-naphtyl)ethylamine. The obtained results perfectly agreed (Table 2, entries 4-5) despite of the experimental error connected with the NMR measurements.

The R configuration and the enantiomeric composition of the alkynes **(-)-3aj** and **(+)-3ba** (obtained from **(S)-1a** and **(S)-1b** respectively) were evaluated by correlation to the corresponding hydroalumination products, the (R)-2-(2-naphtyl)butane, **(R)-9aj**,[13] and (S)-3-phenyl-4,4-dimethyl-1-pentene, **(S)-8ba**,[11a] of known stereochemistry (Scheme 2; Table 2, entries 2 and 3).

All these data (Table 2, entries 1-5) indicated that the coupling reaction occurred with high stereoselectivity (90-100%) and confirmed the 1,3-*anti* mechanism. It is noteworthy that the alkyne **(R)-3ca**, characterized by a quaternary centre at the α-position to the triple bond, was formed with complete stereoselectivity. The stereochemical results were found to be highly reproducible (Table 2, entries 4 and 5).

The significant racemization phenomema (ca. 16-17%) we observed in the coupling reactions yielding alkynes **3** with tertiary propargylic centres (Table 2, entries 1-3), can be thus related to the mobility of the hydrogen atoms to the stereogenic carbon atoms (propargylic and also benzylic) in the reaction conditions. To confirm this hypothesis, compounds **3da**, **3df** and **3dg**, with quaternary stereogenic centres, were synthesized by reacting **(S)-1d** with phenyl-, *p*-methoxyphenyl- and *p*-fluorophenyl-bromocuprates, **2a**, **2f** and **2g** respectively. The R absolute configuration to the obtained chemically pure laevorotatory compounds was assigned on the basis of the 1,3-*anti* stereochemistry now widely proved for the coupling process. The enantiomeric composition of the alkynes was determined by transforming them into the α,β-acetylenic acids **11** and by 300 MHz ^{1}H NMR analysis of the corresponding diastereomeric salts with optically pure (R)-1-(1-naphthyl)ethylamine.

The obtained results (Scheme 2; Table 2, entries 6-8) indicated for these cases a complete absence of racemization phenomena (100% stereoselectivity).

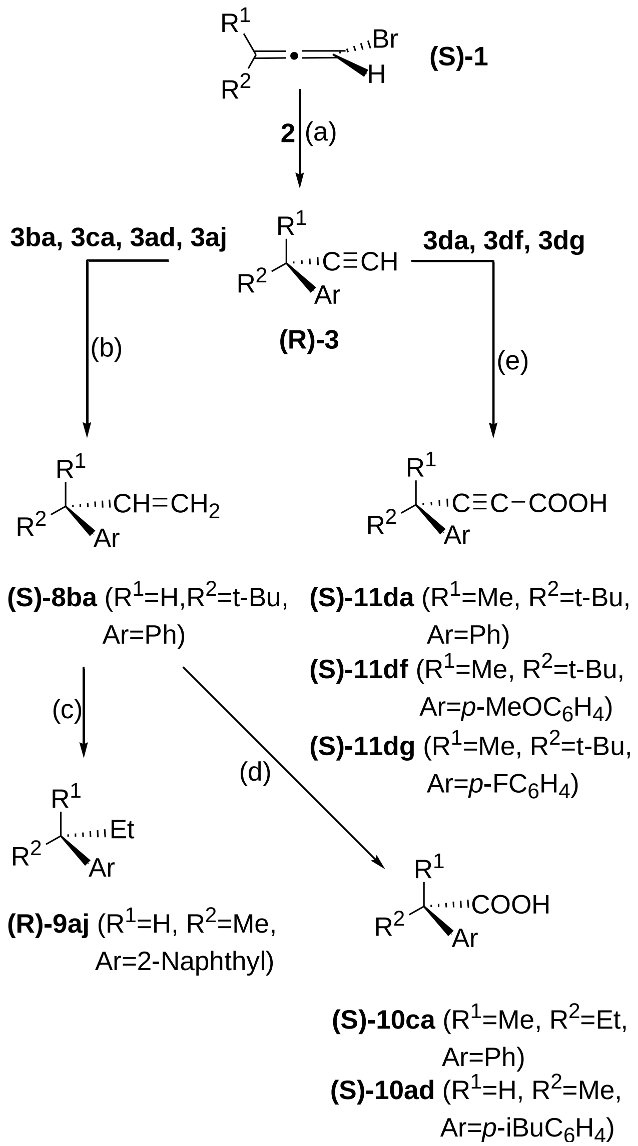
TABLE 2. Stereoselectivity in the Synthesis of 3-Aryl-1-alkynes 3 *via* Coupling Reactions of Arylbromocuprates 2 with Chiral Bromoallenes (S)-1

(S)-1	**(R)-3**	**Correlation Product**	Stereo

Entry		ee (%)[a]		Yield (%)[b]	$[\alpha]_D^{25}$ (heptane)		$[\alpha]_D^{25}$	ee (%)	Selectivity (%)
1	**(S)-1a**	51	**(R)-3ad**	70	-3.95	**(S)-10ad** [c]	+25.6 [d]	43	92
2	**(S)-1a**	51	**(R)-3aj** [e]	52	-6.36	**(R)-9aj** [f]	-12.7 [g]	42	91
3	**(S)-1b**	70	**(R)-3ba**	65	+0.68	**(S)-8ba** [h]	-58.4 [i]	58	91
4	**(S)-1c**	35	**(R)-3ca** [j]	51	-1.32	**(S)-10ca** [k]	+10.6 [l]	35	100
5	**(S)-1c**	35	**(R)-3ca**	68	-1.22	**(S)-10ca** [k]	+10.3 [l]	34 [m]	99
6 [n]	**(S)-1d**	32	**(R)-3da**	64	-1.42	**(S)-11da**	+10.8 [o]	32 [m]	100
7 [n]	**(S)-1d**	32	**(R)-3df**	41	-4.17	**(S)-11df**	-	32 [m]	100
8 [n]	**(S)-1d**	32	**(R)-3dg**	48	-2.51	**(S)-11dg**	-	32 [m]	100

[a] Determined by GC analyses on a Cydex-B chiral column or ^{1}H NMR with heptakis(2,3,6-tri-O-methyl)-β-cyclodextrin as chiral solvating agent (see ref. 8). [b] Isolated yields of pure compounds, obtained by silica gel column chromatography or preparative GC. [c] See ref. 9. [d] EtOH (*c* 3.0). [e] A pure sample of 14% ee (S)-(+)-1-(2-naphthyl)-1,2-butadiene, **(S)-4aj**, was also obtained. [f] See ref. 13. [g] Heptane (*c* 2.4). [h] See ref. 11a. [i] Neat. [j] A pure sample of 22% ee (R)-(-)-1-phenyl-3-methyl-1,2-pentadiene, **(R)-4ca**, was also obtained. [k] See ref. 12. [l] Benzene (*c* 4.4). [m] Determined by ^{1}H NMR of the corresponding diastereomeric salts with optically pure (R)-1-(1-naphthyl)ethylamine. [n] In this case, the absolute configuration of the stereogenic center of compounds **3** and **11** was assigned on the basis of the 1,3-*anti* stereochemistry of the coupling process between heterocuprates and 1-bromo-1,2-dienes to afford alkynes, now widely proved (see also ref. 3,4). [o] $CHCl_3$ (c 8.0).

SCHEME 2. Correlation of 3-Aryl-1-alkynes to Stereochemically Defined Compounds.[a]



[a] (a) See Table 1. (b) i-Bu_2AlH, n-pentane, rt, 40-80 h. (c) i-Bu_2AlH, n-pentane, 40°C, 48 h. (d) $KMnO_4$-$NaIO_4$/K_2CO_3, t-BuOH/H_2O, 0°C, 70-90 h, then diluted H_2SO_4 (5%). (e) n-BuLi (1 equiv), hexane, rt, 10-20 h, reflux, 3-5 h, then solid CO_2, 60 h.

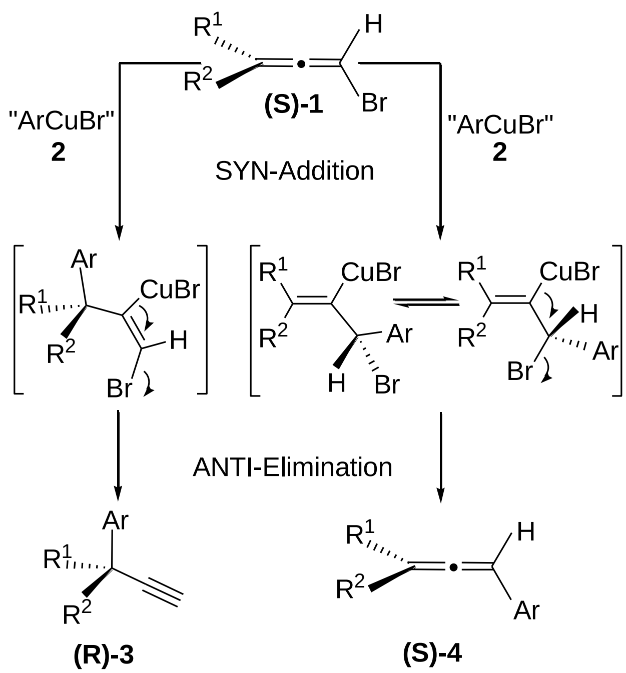
In this context it was also verified that racemic α,β-acetylenic acids **11** could be easily resolved into optically pure enantiomeric forms with (+)-dehydroabietylamine as resolving agent, as reported for (R)(S)-4-phenyl-2-pentynoic acid.[7] Thus, a sample of chemically pure (R)(S)-3-phenyl-3,4,4-trimethyl-1-pentyne, **(R)(S)-3da**, obtained in 84% yield from the coupling reaction between **(R)(S)-1d** and the phenylbromocuprate **2a** (Table 1, entry 3), was treated with equimolar amounts of n-buthyllithium and then with carbon dioxide to yield the racemic 4-phenyl-4,4,5-trimethyl-2-hexynoic acid, **(R)(S)-11da**

(75%). The acid was reacted in diethylether with (+)-dehydroabietylamine and the resulting diastereomeric salts recrystallized three times from 95% ethanol to yield a salt fraction having $[\alpha]_D^{25}$ +15.45 ($CHCl_3$). Alkaline hydrolysis followed by acidification gave the acid **(R)-11da**, $[\alpha]_D^{25}$ –32.70 ($CHCl_3$), which was found optically pure by ^{1}H NMR analysis of its diastereomeric salt with (R)-1-(1-naphthyl)ethylamine. As chiral α,β-acetylenic acids could be easily decarboxylated to the corresponding 1-alkynes without significant racemization phenomena [copper(I) chloride in acetonitrile at room temperature],[7] the resolution/decarboxylation procedure was confirmed to be, at least in some cases, an attractive route to obtain optically active 3-aryl-1-alkynes.

C. Mechanistic Aspects.

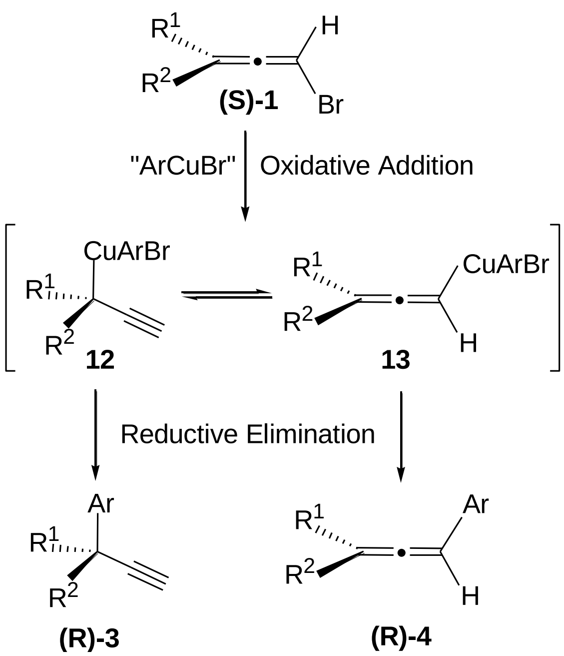
Given the undefined structure of the involved organocopper species, every mechanistic interpretation of the data at this stage have to be speculative. However, both the dynamic and stereochemical results (Tables 1 and 2) are consistent with *syn* addition – *anti* elimination steps, involving alternatively the C_1-C_2 or the C_2-C_3 double bond of the allenic substrate (Scheme 3; for simplicity the complex bromocuprate **2** is presented as the monomeric discrete species "ArCuBr") as previously proposed also for reactions of bromoallenes **1** with aliphatic bromo- and cyanocuprates.[3d] The *syn*-attack of the copper reagent on the C_2-C_3 double bond back-side of the bromine atom followed by an *anti*-elimination would account for the 1,3-*anti* stereoselectivity observed in 1-alkynes **3** formation (Table 2). By increasing the steric bulkiness of Ar, R^1 and R^2 groups on the reagents, the preference for addition of the copper species to the C_1-C_2 bond increased affording the arylallenes **4** (Table 1) with retention of configuration (Scheme 3), by a successive *anti*-elimination step.

SCHEME 3.



From the reaction between **(S)-1a** and 2-naphthylbromocuprate, **2j**, we obtained the 1-alkyne **(R)-3aj** as main product as well as little amounts of chemically pure (S)-1-(2-naphthyl)-1,2-butadiene, **(S)-4aj**, with retention of configuration and extensive racemization, $[\alpha]_D^{25}$ +32.4 (*c* 3.3, n-heptane), (Table 2, entry 2).[14-16] Almost completely racemized (R)-1-phenyl-1,2-butadiene, **(R)-4aa**, $[\alpha]_D^{25}$ –1.20 (*c* 3.0, ethanol) (<1% ee)[17], was generated by reaction of **(R)-1a** (27% ee) with phenylbromocuprate, **2a**, along with (S)-3-phenyl-1-butyne, **(S)-3aa**, (18% ee) as the major product.[3a] The racemization phenomena can be attributed to the contact, during the reaction, of the allenic products with the cuprate or the Cu(0) which might arise from decomposition of the cuprate itself.[18] However, this process shouldn't be very fast in our experimental conditions. A different explanation could be related to the possible presence of multiple mechanisms acting simultaneously. On the other hand, from the reaction between **(S)-1c** and the phenylcuprate **2a**, which afforded (R)-3-phenyl-3-methyl-1-pentyne, **(R)-3ca**, as main product, we obtained the phenylallene **(R)-4ca**, $[\alpha]_D^{25}$ -25.1 (*c* 9.0, n.heptane), racemized and with inversion of configuration (Table 2, entry 4).[3b] As proposed by Corey and Boaz,[19] the *anti*-selectivity for both the acetylenic and the allenic products, as well as the regiochemical results (Table 1), could be rationalized through the mechanism reported in Scheme 4. Initially, the nucleophilic copper attacks *anti* to the bromine yielding the σ-propargylic Cu^{III} intermediate **12** (oxidative addition) which equilibrates to the σ-allenyl derivative **13** *via* a suprafacial 1,3-shift (Scheme 4). The Cu^{III} transient species readily collapse by reductive eliminations to give the alkyne **3** and/or the allene **4** with the observed *anti* stereoselectivity Formation of **4** should be favoured increasing the steric bulkiness of both the substrate and the copper reagent.

SCHEME 4.

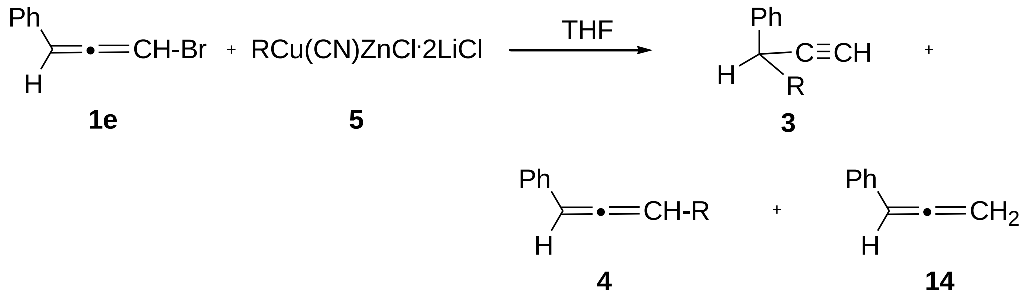


It is nevertheless more likely that 1-alkynes **3** originated essentially from addition-elimination steps as shown in Scheme 3,[3d] while competitive routes with different stereochemistry (such those depicted in Schemes 3 and 4) should account for the arylallenes **4** formation. In all cases in which starting from allenyl or propargyl substrates, an equilibrium between σ-allenyl and σ-propargyl metalcomplexes was postulated (Scheme 4), the formation, with anti stereselectivity, of allenes as the only products was attributed to the higher stability of the σ-allenyl complex. As an example, chiral allenic bromides and 2-propynyl esters in palladium-catalyzed reactions with organozinc reagents gave only allenic products[18] as well as 2-propynyl esters with organocopper(I) derivatives of different nature;[8b,17,21] in all cases a high anti stereochemistry was observed.

D. Coupling of 1-Bromo-3-Phenylpropadiene with Zinc Alkylcyanocuprates.

Zinc alkylcynocuprates RCu(CN)ZnCl · 2LiCl **5a-f** (Knochel reagents)[5] were generated in THF at –10°C from alkylzinc chlorides and the soluble copper salt CuCN · 2LiCl; the necessary organozinc derivatives were obtained from the corresponding Grignard reagents by transmetallation with $ZnCl_2$. In particular, the starting Grignard reagent of **5d** and **5f** were prepared in THF from 3-chloro-1-propanol and 4-bromo-1-trimethylsilyl-1-butyne according to procedures previously reported by Normant[22] and Rossi[23]. When the cyanocuprates **5a-f** were reacted with 1-bromo-3-phenylpropadiene **1e** (molar ratio 2 : 1) the desired 3-phenyl-1-alkynes **3** were selectively obtained (Table 3), contrary to what we previously observed with alkylbromocuprates **2** which afforded essentially polymeric byproducts.[3a] However, once again, the structure of the alkyl in the organocopper species significantly affected the selectivity of the reaction. In general with primary cuprates the reaction proceeded to completion within 1-2 h at –70°C yielding exclusively the acetylenic products **3** (Table 3, entries 1, 4 and 6). With secondary and tertiary copper reagents a decrease in the reaction rate as well as in the chemo and regioselectivity was observed instead. Therefore, the isopropylzinc cuprate **5b** afforded the alkyne **3eb** together with minor amounts of the allenic regioisomer **4eb** (Table 3, entry 2). The tert-butyl derivative **5c** provided substantial amounts of phenylallene **14**, probably *via* metal-halogen exchange processes, along with the expected coupling products **3ec** and **4ec**, (Table 3, entry 3).

TABLE 3. Coupling Reactions of Zinc Alkylcyanocuprates 5 with 1-Bromo-3-phenylpropadiene, 1e.



	Cyanocuprate, 5				Products	Yield (%)[b]		
Entry		R	T (°C)	t (h)	**3,4**	**3**	**4**	**14**
1	**5a**	Et	-70	1	**ea**	100(73)	-	-
2	**5b**	i-Pr	-70→rt	2	**eb**	94	6	-
3	**5c**	t-Bu	-70→rt	3	**ec**[c]	50	12	38
4	**5d**	$ClMgO(CH_2)_3$	-70	2	**ed**	100(77)[d]	-	-
5[e]	**5d**	$ClMgO(CH_2)_3$	-70→rt	1	**ed**	100(80)[d]	-	-
6	**5e**	$CH_2=CH(CH_2)_2$	-70	1	**ee**	100(69)	-	-
7[e]	**5e**	$CH_2=CH(CH_2)_2$	-70→rt	1	**ee**	100(82)	-	-
8	**5f**	$Me_3SiC\equiv C(CH_2)_2$	-70→rt	2	**ef**	100(68)	-	-

[a] Except as noted all reactions were run in 10-20 mmol scale by treating **1e** with 2 equiv. of zinc cyanocuprate **5** in THF at –70°C and by allowing the reaction mixture to warm to room temperature. [b] The yields, based on starting **1e**, were determined by ^{1}H NMR and GC analysis on the crude reaction mixture after work-up (Isolated yields of >98% pure compounds are shown in parentheses). [c] Compounds **3ec** and **4ec** are identical to **3ba** and **4ba** respectively. [d] As acetylenic carbinol. [e] The reaction was performed by treating **1e** with 2 equiv. of the desired organozinc reagent (RZnCl) in the presence of 10 mol % of CuCN·2LiCl.

These data completely agreed with the results previously obtained by reacting alkylcyanocuprates **5** with aliphatic 1-bromoallenes **1a-d**.[4] They also suggested that an appropriate selection of the structure of the Knochel reagent (primary or secondary) in the cross-coupling with **1e** could yield a large variety of functionalized 3-phenyl-1-alkynes, such as α,ω-acetylenic carbinols, α,ω-enynes, and α,ω-diynes, useful synthetic intermediates and not easily available *via* simple alternative methods.[24] In this context it is worthwhile noting that the coupling reaction could be performed with primary alkylzinc chlorides in the presence of catalytic amounts (10%) of CuCN · 2LiCl affording quantitatively the 1-alkynes **3** isolated in high yields (Table 3, entries 5 and 7).[4] The reaction rate of the catalytic process was generally slower than that of the stoichiometric one, but an increase in the reaction temperature (-70°C to r.t.) overcame this inconvenience (Table 3, entries 5 and 7 v/s entries 4 and 6).

Conclusions

The 1,3-substitution on the allenic bromides **1** with arylbromocuprates **2** was found to be a very useful method of obtaining a large variety of 3-aryl-1-alkynes **3** with good yields. The chemoselectivity of the process depended on several factors, the structure of the aryl group of the copper reagent playing a key role. Indeed considerable amounts of allenic by-products **4** , deriving from a direct substitution, were detected as the size of this group increased.

The stereochemical results indicated that the acetylenic compounds were formed in an unambiguous ANTI fashion with very high optical yields. In particular, starting from optically active 3,3-dialkyl-1-bromoallenes the 1,3-substitution process appeared as a stereospecific synthetic pathway for the construction of enantiomerically enriched quaternary stereogenic centres, characterized by an aryl and an ethynyl group. Since a triple bond represents a very useful synthetic moiety, the reported method can be applied to the preparation of a large variety of optically active organic molecules.

From the stereochemical results we proposed also that the coupling reaction which afforded the 1-alkynes **3** proceeded *via* an addition-elimination mechanism rather than through a Cu^{III} intermediate.

From a synthetic point of view it is noteworthy that the cross-coupling reaction of primary functionalised Knochel reagents with 1-bromo-3-phenylpropadiene **1e** afforded selectively ω-functionalised 3-phenyl-1-alkynes in high yields.

Experimental Section

General Procedure for Coupling Reactions of Arylbromocuprates 2a-k with Bromoallenes 1a-d: Synthesis of 3-Aryl-1-alkynes (3) (Tables 1 and 2). All reactions were carried out at least in duplicate. The required arylbromocuprate **2** (40 mmol) in THF (120 mL) was cooled at –70°C, and a solution of the 1-bromo-1,2-diene **1** (20 mmol) in THF (20 ml) was added over a period of 5 min. After stirring was continued at –70°C for 10 min, the cooling bath was removed and the mixture was allowed to warm to room temperature (30 min). Generally the reaction mixture was quenched with saturated ammonium chloride solution (100 ml), while dilute sodium hydroxide was used in the reactions carried out with the *p*-N,N-dimethylaminophenyl-cuprate **2h** (entries 15 and 16 in Table 1). The organic materials were extracted with diethyl ether (3x100 ml), and the combined extracts were washed with water, then dried (Na_2SO_4) and analyzed by GC and GC-MS. The solvents were removed at reduced pressure (10-20 mmHg) and a ^{1}H NMR spectrum of the crude product was determined. Successive fractional distillation (Fischer-Spaltrohr column) and/or column silica gel chromatography (pentane as eluent) afforded pure samples of alkynes **3** and, in most cases, arylallenes **4,** which were identified and characterized by spectroscopic and analytical data; when necessary, larger scale reactions or preparative GC were used for these separations. Most of the products were also identified by spectroscopic or chromatographic comparison with authentic samples.[3a,8,25]

~~**3-[4-(2-Methylpropyl)phenyl]-1-butyne (3ad):**~~

~~**3-(2-Methoxyphenyl)-1-butyne (3ae):**~~

~~**3-(1-Naphthyl)-1-butyne (3ai):**~~

~~**3-(2-Naphthyl)-1-butyne (3aj):**~~

~~**3-[(6-Methoxy)-2-naphthyl)]-1-butyne (3ak):**~~

~~**3-(2-Methoxyphenyl)-4,4-dimethyl-1-pentyne (3be):**~~

~~**3-(4-Methoxyphenyl)-4,4-dimethyl-1-pentyne (3bf):**~~

~~**3-(4-Dimethylaminophenyl)-4,4-dimethyl-1-pentyne (3bh):**~~

3-(1-Naphthyl)-4,4-dimethyl-1-pentyne (3bi):

3-(2-Naphthyl)-4,4-dimethyl-1-pentyne (3bj):

3-(2-Methoxyphenyl)-3-methyl-1-pentyne (3ce)

3-(4-Methoxyphenyl)-3-methyl-1-pentyne (3cf):

3-(1-Naphthyl)-3-methyl-1-pentyne (3ci):

3-(2-Naphthyl)-3-methyl-1-pentyne (3cj):

3-(2-Ethylphenyl)-3,4,4-trimethyl-1-pentyne (3db):

3-(4-Ethylphenyl)-3,4,4-trimethyl-1-pentyne (3dc):

3-(2-Methoxyphenyl)-3,4,4-trimethyl-1-pentyne (3de):

3-(4-Methoxyphenyl)-3,4,4-trimethyl-1-pentyne (3df):

3-(4-Fluorophenyl)-3,4,4-trimethyl-1-pentyne (3dg):

3-(4-Dimethylaminophenyl)-3,4,4-trimethyl-1-pentyne (3dh):

3-(2-Naphthyl)-3,4,4-trimethyl-1-pentyne (3dj):

3-[(6-Methoxy)-2-naphthyl)]-3,4,4-trimethyl-1-pentyne (3dk):

General Procedure for the Hydroalumination of (R)-3-Aryl-1-alkynes (R)-3: Optically active 3-Aryl-1-alkenes (8) (Scheme 2, Table 2). In a typical experiment, 10-20 mmol of the alkyne **(R)-3** were added, at 0°C, to a solution of diisobutylaluminium hydride (DIBAH) (15-40 mmol) in anhydrous n-pentane (30-60 mL). The reaction mixture was stirred at room temperature for the desired time (40-80 h; the progress of the reaction was monitored by GC) and was then cautiously hydrolysed with water and dilute sulphuric acid. The organic materials were extracted with n-pentane; the combined extracts were washed with water, dried (Na_2SO_4) and evaporated to dryness. Optically active products **8** were obtained chemically pure by fractional distillation.

(R)-3-[4-(2-Methylpropyl)phenyl]-1-butene [(R)-8ad]: 99% yield; ^{1}H NMR δ 0.90 (d, *J* = 6.6 Hz, 6H), 1.35 (d, *J* = 7.1 Hz, 3H), 1.85 (m, 1H), 2.44 (d, *J* = 7.2 Hz, 2H), 3.45 (m, 1H), 5.01 (m, 1H), 5.06 (m, 1H), 6.02 (ddd, *J* = 16.9, 10.4, 6.5 Hz, 1H), 7.10 (m, 4H); ^{13}C NMR δ 20.6, 22.2, 30.1, 42.7, 44.9, 112.9, 127.0, 129.3, 139.6, 142.9, 143.7. Anal. Calcd. for $C_{14}H_{20}$: C, 89.29; H, 10.71. Found: C, 89.31; H, 10.69.

(S)-4,4-Dimethyl-3-phenyl-1-pentene [(S)-8ba] (Entry 3 in Table 2): 90% yield; bp 84°C (7 mmHg); $[\alpha]_D^{25}$-58.4 (neat, d_4^{25} 0.8808); ^{1}H NMR δ 0.89 (s, 9H), 3.01 (d, *J* = 9.6 Hz, 1H), 5.03 (dd, *J* = 2.0, 16.6 Hz, 1H), 5.07 (dd, *J* = 2.0, 10.0 Hz, 1H), 6.26 (dt, *J* = 9.6, 16.6 Hz, 1H), 7.22 (m, 5H). [Optically pure **(S)-8ba** is reported to have $[\alpha]_D^{25}$ –101 (neat)].[11a]

(R)-3-Methyl-3-phenyl-1-pentene [(R)-8ca] : 95% yield; bp 89°C (17 mmHg); ^{1}H NMR δ 0.76 (t, J = 7.4 Hz, 3H), 1.34 (s, 3H), 1.79 (m, 2H), 5.03 (dd, *J* = 1.4, 17.5 Hz, 1H), 5.10 (dd, *J* = 21.4, 10.8 Hz, 1H), 6.00 (dd, *J* = 10.8, 17.5 Hz, 1H), 7.10-7.40 (m, 5H);); ^{13}C NMR δ 8.7, 24.2, 33.3, 44.4, 111.9, 125.8, 126.9, 128.1, 147.1, 147.6; GC-MS(EI) *m/z* (rel int) 160 (M^+, 10), 145 (6), 131 (100), 115 (18), 103 (8), 91 (54), 77 (11), 65 (6), 51 (9). Anal. Calcd. for $C_{12}H_{16}$: C, 89.94; H, 10.06. Found: C, 90.03; H, 9.97.

Hydroalumination of (R)-3-(2-Naphthyl)-1-butyne (R)-3aj to (R)-2-(2-Naphthyl)butane (R)-9aj (Entry 2 in Table 2). A solution of **(R)-3aj** [1.0 g, 5.56 mmol, $[\alpha]_D^{25}$-6.36 (heptane)] in n-pentane (5 mL) was added, at 0°C, to 30 mmol of DIBAH. The reaction mixture was stirred for 72 h at room temperature, then a further amount of DIBAH (10 mmol) was added. After stirring was continued at 40°C for 48h, the mixture was hydrolysed as above. Usual work-up and successive fractional distillation gave chemically pure **(R)-9aj** (0.52 g, 51% yield): bp 93°C (0.9 mmHg); $[\alpha]_D^{25}$-12.7 (*c* 4.7, heptane). ^{1}H NMR δ 0.84 (t, *J* = 7.3 Hz, 3H), 1.31 (d, *J* = 6.9 Hz, 3H), 1.68 (dq, *J* = 6.9, 7.3 Hz, 2H), 2.75 (m, 1H), 7.37-7.81 (m, 7H). [Optically pure **(R)-9aj** is reported to have $[\alpha]_D^{25}$ -30.2 (heptane)].[13]

$KMnO_4/NaIO_4$ oxidative demolition of (R)-2-[4-(2-Methylpropyl)phenyl]-1-butene (R)-8ad : (S)-2-[4-(2-Methylpropyl)phenyl]propanoic acid [(S)-10ad] (Entry 1 in Table 2). An aqueous solution (1250 mL) containing 26.3 g (123 mmol) of $NaIO_4$, 0.33 g (2.1 mmol) of $KMnO_4$ and 2.26 g (16.4

mmol) of K_2CO_3 was added to a well-stirred ice-cooled solution of 2.65 g (14 mmol) of **(R)-8ad** in 60% aqueous tert-butanol (1420 mL). The reaction mixture was stirred at 0°C for 65 h, then treated with $NaHSO_3$ and alkalinized with solid NaOH. The MnO_2 precipitate was eliminated by filtration and the clarified mixture was concentrated in vacuum (17 mmHg), extracted with diethyl ether and acidified with diluted H_2SO_4 (5%). The acid aqueous phase was extracted with ether and the combined extracts were dried (Na_2SO_4) and concentrated in vacuum. Fractional distillation gave chemically pure **(S)-10ad** (2.10g, 73% yield): b.p. 110°C (0.1 mmHg); $[\alpha]_D^{25}$ +25.6 (*c* 3.0, EtOH); ^{1}H NMR: δ 0.89 (d, *J* = 6.6 Hz, 6H) 1.50(d, *J* = 7.1 Hz, 3H), 1.84 (m, 1H), 2.45 (d, *J* = 7.0 Hz, 2H), 3.71 (q, *J* = 7.1 Hz, 1H), 7.17 (m, 4H).; ^{13}C NMR: δ 17.9, 22.2, 30.0, 44.8, 127.4, 129.6, 137.2, 141.1, 181.0. [Optically pure **(S)-10ad** is reported to have $[\alpha]_D^{25}$ +60.0 (EtOH)].[9]

(S)-2-Phenyl-2-methylbutanoic acid [(S)-10ca] (Entry 4 in Table 2). According to the above procedure, 2.7 g (17 mmol) of (R)-3-phenyl-3-methyl-1-pentene **(R)-8ca** were treated, at 0°C for 94 h, with the $KMnO_4$/$NaIO_4$ oxidation system. Usual workup and successive fractional distillation gave chemically pure **(S)-10ca** (2.7 g, 87% yield): bp 124°C (1.5 mmHg); mp 64-69°C; $[\alpha]_D^{25}$ +10.6 (*c* 4.4, benzene). ^{1}H NMR δ 0.85 (t, *J* = 7.4 Hz, 3H), 1.55 (s, 3H), 2.05 (m, 2H), 7.20-7.50 (m, 5H). [Optically pure **(S)-10ca** is reported to have $[\alpha]_D^{25}$ +30.2 (benzene)].[12]

The enantiomeric excess (ee) of a sample of **(S)-10ca** having $[\alpha]_D^{25}$ +10.3 (*c* 4.4, benzene) **(see Entry 5 in Table 2)** was determined to be 34% by ^{1}H NMR analysis of the diastereomeric salts obtained by reacting the product, in $CDCl_3$, with an equimolar amount of optically pure (R)-1-(1-naphthyl)ethylamine: ^{1}H NMR: δ 1.17 [s, 0.99H, (RR)-<u>*Me*</u>C(Ph)COO^-], 1.19 [s, 2.01H, (SR)-<u>*Me*</u>C(Ph)COO^-]).

General Procedure for the Synthesis of 4-Aryl-4,5,5-trimethyl-2-hexynoic Acids 11 starting from 3-Aryl-1-alkynes 3 (Scheme 2, Table 2). A solution of the appropriate, racemic or optically active, akyne **3** (10-15 mmol) in hexane (10-15 mL) was added dropwise, at 0°C, to an equimolar amount of nbutyllithium 1.6 N in hexane. The resulting mixture was stirred at room temperature for 10-15 h, heated under reflux for 3-5 h, and treated with solid carbon dioxide for 60 h. After quenching with ice and diluted H_2SO_4 (5%), the organic materials were extracted with ether and the α,β-acetylenic acid **11** was purified through his sodium salt. Distillation gave the pure acid.

(R)(S)-4-Phenyl-4,5,5-trimethyl-2-hexynoic Acid [(R)(S)-11da]: 75% yield; bp 145°C (0.01 mmHg); ^{1}H NMR δ 0.99 (s, 9H), 1.71 (s, 3H), 7.30 (m, 3H), 7.47 (m, 2H), 10.62 (s, 1H); ^{13}C NMR δ 22.5, 26.4, 37.8, 48.1, 75.9, 97.7, 127.2, 127.8, 128.8, 141.0, 158.5. Anal. Calcd. for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.38; H, 7.86.

(S)-4-Phenyl-4,5,5-trimethyl-2-hexynoic Acid [(S)-11da] (Entry 6 in Table 2): 80% yield; bp 145°C (0.01 mmHg); $[\alpha]_D^{25}$ +10.80 (*c* 8.0, $CHCl_3$); the ^{1}H and ^{13}C NMR spectra were identical with those of the racemic compound **(R)(S)-11da** (see above). The enantiomeric excess (ee) of the sample was determined to be 32% by ^{1}H NMR analysis of the diastereomeric salts obtained by reacting the product, in $CDCl_3$, with an equimolar amount of optically pure (R)-1-(1-naphthyl)ethylamine: ^{1}H NMR: δ 0.76 [s, 5.94H, (SR)-*t-Bu*C(Ph)] 0.77 [s, 3.06H, (RR)-*t-Bu*C(Ph)].

(S)-4-(4-Methoxyphenyl)-4,5,5-trimethyl-2-hexynoic Acid [(S)-11df] (Entry 7 in Table 2): 74% yield; ^{1}H NMR δ 0.98 (s, 9H), 1.68 (s, 3H), 3.81 (s, 3H), 6.85 (m, 2H), 7.37 (m, 2H); ^{13}C NMR δ 22.6, 26.3, 37.7, 47.3, 55.2, 75.3, 97.7, 112.7, 129.4, 132.8, 157.9, 158.4. Anal. Calcd. for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.90; H, 7.69. The enantiomeric excess (ee) of the sample was determined to be 32% by ^{1}H NMR analysis of the diastereomeric salts obtained by reacting the product, in $CDCl_3$, with an equimolar amount of optically pure (R)-1-(1-naphthyl)ethylamine: ^{1}H NMR: δ 3.624 [s, 1.02H, (RR)-O*Me*], 3.651 [s, 1.98H, (SR)-O*Me*].

(S)-4-(4-Fluorophenyl)-4,5,5-trimethyl-2-hexynoic Acid [(S)-11dg] (Entry 8 in Table 2): 88% yield; ^{1}H NMR δ 0.91 (s, 9H), 1.62 (s, 3H), 6.93 (m, 2H), 7.36 (m, 2H), 8.29 (s, 1H); ^{13}C NMR δ 22.5, 26.0, 37.6, 47.4, 75.7, 96.8, 114.3 (d, J_{CF} = 21.2 Hz), 130.1 (d, J_{CF} = 7.9 Hz), 136.6 (d, J_{CF} = 3.4 Hz), 158.1, 162.0 (d, J_{CF} = 247 Hz). Anal. Calcd. for $C_{15}H_{17}FO_2$: C, 72.56; H, 6.90. Found: C, 72.64; H, 6.93.

The enantiomeric excess (ee) of the sample was determined to be 32% by ^{1}H NMR analysis of the diastereomeric salts obtained by reacting the product, in $CDCl_3$, with an equimolar amount of optically pure (R)-1-(1-naphthyl)ethylamine: ^{1}H NMR: δ 1.321 [s, 1.02H, (RR)-*Me*C(Ar)], 1.327 [s, 1.98H, (SR)-*Me*C(Ar)].

Resolution of (R)(S)-4-Phenyl-4,5,5-trimethyl-2-hexynoic Acid (R)(S)-11da. A solution of the racemic α,β-acetylenic acid **11da** (13.7 g, 60 mmol) in diethyl ether (50 mL) was added to a stirred solution of (+)-dehydroabietylamine (17.2 g, 60 mmol) in ether (200 mL) at 0°C. The mixture was stirred at room temperature and the insoluble salt was filtered off, washed with diethyl ether, dried in vacuum [29.0 g, 94% yield; mp 80°C; $[\alpha]_D^{25}$ +24.32 (*c* 5.0, $CHCl_3$)], and then recrystallized three times from 95% ethanol to yield a fraction (6.5 g, 22%) having mp 196°C, and $[\alpha]_D^{25}$ +15.45 (*c* 5.0, $CHCl_3$). This salt fraction was treated, at 0°C, with aqueous NaOH (20%) and the dehydroabietylamine extracted with ether. The aqueous solution was acidified with 5% HCl and extracted with ether (200 mL). The combined extracts were washed with water, dried (Na_2SO_4) and distilled to give the pure acid **(R)-11da** (2.58 g, 89%); bp 145°C (0.01 mmHg); $[\alpha]_D^{25}$ –32.70 (*c* 8.3, $CHCl_3$). The spectral and analytical data were identical with those of the racemic mixture. The enantiomeric excess (ee) of the sample was determined to be 100% as the ^{1}H NMR analysis of the diastereomeric salt obtained with optically pure (R)-1-(1-naphthyl)ethylamine showed only a signal for the t-Bu moiety of the product: ^{1}H NMR: δ 0.77 [s, 9H, (RR)-*t-Bu*C(Ph)] (see above).

General Procedure for Coupling Reactions of Zinc Cyanocuprates 5a-f with 1-Bromo-3-phenylpropadiene 1e: Synthesis of 3-Phenyl-1-alkynes (3ea-ef) (Table 3). All reactions were carried out at least in duplicate. A solution of the required alkylmagnesium halide (20 mmol) in THF (20mL) was added, at 0°C, to a stirred THF solution of $ZnCl_2$ (20mmol, 10 mL). The mixture was stirred for 30 min at room temperature, then treated, at –10°C, with a solution of 18 mmol of CuCN·2LiCl prepared in

THF (50 mL) [Some reactions were performed in the presence of a catalytic amount of the cuprous salt (1.8 mmol, 10 mol% relative to the organozinc reagent; entries 5 and 7 in Table 3)]. Stirring was continued at 0°C during 30 min, then the reaction mixture was cooled at –70°C and the 1-bromo-3-phenylpropadiene **1e** (1.80 g, 9 mmol) in THF (10 ml) was added over a period of 5 min. Stirring was continued at –70°C and the mixture was monitored for completion by GC. When necessary, the cooling bath was removed and the mixture was allowed to warm to room temperature. Standard work-up and successive fractional distillation (Fischer-Spaltrohr column) and/or column silica gel chromatography (pentane as eluent) afforded pure samples of alkynes **3** characterized by spectral and analytical data. Some products were identified by spectroscopic or chromatographic comparison with authentic samples.[3a]

New products **3ed-ef** were as follows:

3-Phenyl-1-hexyn-6-ol (3ed): ^{1}H NMR δ 1.60-1.90 (m, 4H), 2.03 (s, 1H), 2.28 (d, *J* = 2.5 Hz, 1H), 3.62 (t, J = 6.2 Hz, 2H), 3.66 (m, 1H), 7.30 (m, 5H); ^{13}C NMR δ 30.2, 34.4, 37.3, 62.4, 71.2 (≡CH), 85.7 (-C≡), 126.8, 127.3, 128.5, 141.2; GC-MS(EI) *m/z* (rel int) 174 (M^+), 156 (4), 130 (26), 129 (30), 128 (18), 115 (100), 91 (4), 89 (25), 77 (7), 65 (10), 63 (12), 51 (11). Anal. Calcd. for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.68; H, 8.06.

3-Phenyl-6-hepten-1-yne (3ee): ^{1}H NMR δ 1.78-1.91 (m, 2H), 2.14-2.27 (m, 2H), 2.27 (d, *J* = 2.5 Hz, 1H), 3.65 (m, 1H), 4.99 (m, 1H), 5.05 (m, 1H), 5.81 (ddt, *J* = 6.6, 10.3, 17.0 Hz, 1H), 7.18-7.40 (m, 5H); ^{13}C NMR δ 31.3, 36.9, 37.4, 71.1 (≡CH), 85.7 (-C≡), 115.3, 126.8, 127.4, 128.5, 137.7, 141.4; GC-MS(EI) *m/z* (rel int) 170 (M^+, 3), 169 (2), 155 (28), 142 (20), 141 (15), 129 (16), 128 (36), 127 (11), 115 (100), 91 (15), 89 (17), 79 (8). Anal. Calcd. for $C_{13}H_{14}$: C, 91.71; H, 8.29. Found: C, 91.68; H, 8.32.

1-Trimethylsilyl-5-phenyl-1,6-heptadiyne (3ef): ^{1}H NMR δ 0.16 (s, 9H), 1.90-2.02 (m, 2H), 2.20-2.45 (m, 2H), 2.28 (d, *J* = 2.4 Hz, 1H), 3.79 (m, 1H), 7.20-7.40 (m, 5H); ^{13}C NMR δ 0.1, 17.8, 36.4, 37.1, 71.4 (≡CH), 85.1 (-C≡), 85.4 (-C≡), 106.1 (≡C-Si), 127.0, 127.4, 128.6, 140.5; GC-MS(EI) *m/z* (rel int) 240 (M^+, 2), 239 (3), 225 (61), 209 (21), 197 (17), 195 (25), 181 (26), 167 (20), 166 (19), 165 (20), 128 (23), 115 (49), 73 (100). Anal. Calcd. for $C_{16}H_{20}Si$: C, 79.93; H, 8.38. Found: C, 79.85; H, 8.40.

Supporting information available: General Remarks and Spectral and Analytical data for all new acetylenic **3** and allenic **4** cross-coupling products. This materials is available free of charge via Internet at http://pubs.acs.org

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