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Studies on Cu(I)-catalyzed synthesis of simple 3-substituted 1,2-allenes and optically active 2-substituted secondary 2,3-allenols

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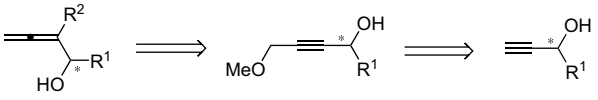
ABSTRACT

The sequential treatment of terminal alkynes or propargylic alcohols with *n*-BuLi and MOMCl afforded the corresponding propargylic methyl ethers, which would react with primary alkyl Grignard reagents under the catalysis of CuBr to afford 3-substituted 1,2-allenes or 2-substituted secondary 2,3-allenols, respectively. The reaction may be applied to the synthesis of optically active 2-substituted secondary 2,3-allenols with up to >99% ee without any protection to the free hydroxyl group in the starting 4-hydroxy-2-alkynyl methyl ethers.

1. Introduction

The synthesis of allenes is of current interest due to their high and unique reactivities demonstrated in organic synthesis.[1,2] Of particular interest is the chemistry of 2,3-allenols,[3] which have been used for the synthesis of 2,5-dihydrofurans,[4] epoxides,[5] 3-halo-3-alkenals,[6] etc. Thus, there is a need to develop a general, convenient, and practical synthesis of optically active 2,3-allenols with the chiral centers connected with the hydroxyl group. The racemic form of this class of compounds is usually prepared by metal-mediated reaction of propargylic bromide with aldehydes[7] or ketones[8] and the Crabbé reaction of propargylic alcohols.[9] Furthermore, optically active 2,3-allenols are usually prepared by the enantioselective reduction of 1,2-allenyl ketones,[10] the reaction of optically active propargylic/allenic metallic reagents with aldehydes,[11] Crabbé reaction of optically active terminal propargylic alcohols,[12] chiral ligand-mediated reaction of propargylic/allenic metallic reagents with aldehydes,[13] the reduction of optically active 4-hydroxy-2-alkynyl methyl ether with $LiAlH_4$,[10] the diastereoselective 1,2-addition of optically active 1,2-allenyl aldehydes or ketones with Grignard reagents,[14] and the kinetic resolution of racemic 2,3-allenols.[15] However, the synthesis of optically active 2,3-allenols is still not so easy since some of the reagents or catalyst for these known methods are not easily available or expensive[10–14] and the kinetic resolution of racemic 2,3-allenols is restricted to the substrates with one or two carbon units such as methyl, ethyl, ethenyl, or acetylenyl directly connected to the hydroxylated carbon atom.[15] In this paper we wish to report a relatively general synthesis of optically active 2,3-allenols from the easily available propargylic alcohols (Scheme 1).



Scheme 1.

2. Results and discussion

To examine this method, firstly, the reaction of methyl 3-phenylpropargyl ether **1a** with *n*-C_4H_9MgBr was studied with different amounts of CuBr and the Grignard reagent.[16] No product was formed without catalyst (entry 1, Table 1). Further studies indicated that 10 mol % of CuBr and 2 equiv of *n*-C_4H_9MgBr were enough to ensure a good yield of 3-phenylhepta-1,2-diene **2a** (Table 1).

Then we designed a one-pot procedure for the synthesis of 3-substituted 1,2-allenes **2** from simple terminal alkynes **3** (Table 2). *n*-BuLi was added dropwise to a solution of terminal alkynes **3** in Et_2O at -40 °C. After half an hour, MOMCl was added dropwise at the same temperature, the resulting mixture was then treated with 10–20 mol % CuBr at room temperature, which was followed by dropwise addition of the Grignard reagent. In this way,

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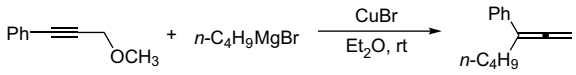
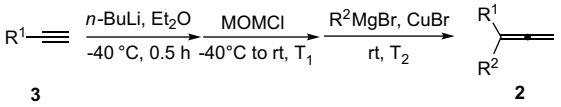
Table 1
CuBr-catalyzed reaction of **1a** with *n*-C_4H_9MgBr



1a **2a**

Entry	CuBr (mol %)	*n*-C_4H_9MgBr (equiv)	Yield (%)
1	0	2	0
2	1.5	2	60
3	5	2	72
4	10	2	81
5	20	2	82
6	10	1.5	77
7	10	1.2	48

Table 2
One-pot synthesis of 3-substituted 1,2-allenes **2** from terminal alkynes **3**



3 **2**

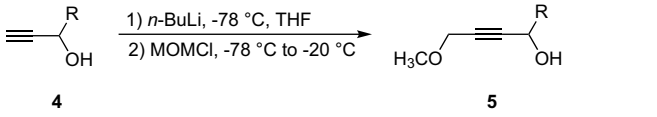
Entry	R^1	R^2	R^2MgBr (equiv)	CuBr (equiv)	T_1 (h)	T_2 (h)	Isolated yield (%)
1	Ph (**3a**)	*n*-C_4H_9	2.0	0.2	1.5	1.5	86 (**2a**)
2	*n*-C_4H_9 (**3b**)	Ph	2.0	0.1	0.5	15.5	57[a] (**2a**)
3	Ph (**3a**)	C_2H_5	2.0	0.2	2	1	75 (**2b**)
4	*n*-C_6H_{13} (**3c**)	Ph	2.0	0.1	0.5	15.5	60[a] (**2c**)

[a] Biphenyl was formed in about 5–6% yield.

3-substituted 1,2-allenes **2** were formed in moderate to good yields from terminal alkynes in a one-pot manner.

Then, we proposed to synthesize optically active 2-substituted secondary 2,3-allenols by following the same protocol. Firstly, we tried to synthesize racemic 2-substituted secondary 2,3-allenols from terminal propargylic alcohols via a one-pot procedure described above, unfortunately, a complicated mixture was formed. Then, we started to pursue the step-wise procedure.

By treating the racemic propargylic alcohols **4** with *n*-BuLi and the subsequent reaction with MOMCl, the racemic 4-hydroxy-4-aryl-2-butynyl methyl ethers **5** were prepared in moderate yields (Scheme 2).



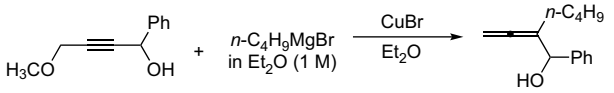
4 **5**

5a R = Ph (60%)
5b R = *p*-$CH_3C_6H_4$ (69%)
5c R = *m,p*-$OCH_2OC_6H_3$ (60%)
5d R = *p*-$CH_3OC_6H_4$ (68%)

Scheme 2.

Then racemic 4-hydroxy-4-phenyl-2-butynyl methyl ether **5a** was used as the model substrate to optimize the condition for its reaction with *n*-C_4H_9MgBr. When racemic **5a** was treated with 3 equiv of *n*-C_4H_9MgBr in THF under the catalysis of 20 mol % CuBr at −20 °C, no 2-butyl-1-phenyl-2,3-butadienol **6a** was formed (entry 1, Table 3). The reaction with 4 equiv of *n*-C_4H_9MgBr in Et_2O under the catalysis of 10 mol % CuBr at −30 °C gave the product **6a** in moderate yield (43%) (entry 2, Table 3). The effect of the amounts of CuBr on the yield of **6a** is not obvious (compare entries 2–5, Table 3). Then we tried to optimize the reaction temperature (compare entries 6–9, Table 3), the best reaction temperature was found to be

Table 3
CuBr-catalyzed reaction of racemic **5a** with *n*-C_4H_9MgBr



5a **6a**

Entry	*n*-C_4H_9MgBr (equiv)	Catalyst (mol %)	Temp (°C)	NMR yield of **6a**[a] (%)
1[b]	3	20	−20	0
2	4	10	−30	43
3	4	20	−30	52
4	4	30	−30	52
5	4	50	−30	53
6	4	20	rt	Complicated
7	4	20	0	Complicated
8	4	20	−20	48
9	4	20	−40	30
10	4.5	20	−30	53
11	4.67	20	−30	55 (53)
12	4.83	20	−30	45
13	5	20	−30	46
14	4.67[c]	20	−30	27 (26)

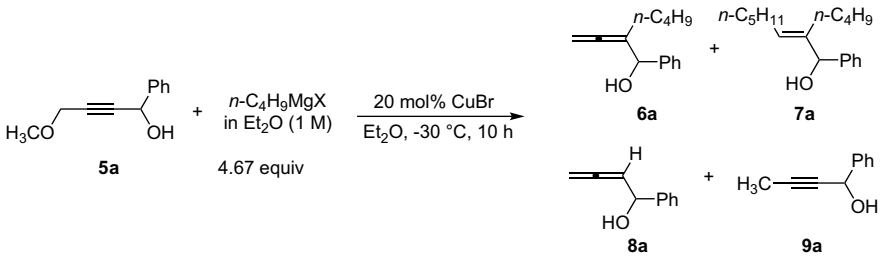
[a] Yields were determined by ^1H NMR analysis with 1,3,5-trimethylbenzene as the internal standard. The isolated yield is given in the parentheses.
[b] THF was used as solvent.
[c] A solution of *n*-C_4H_9MgCl (1.0 M) in Et_2O was used.

−30 °C, at which the reaction afforded the product **6a** in 52% NMR yield (entry 3, Table 3). When the reaction was conducted with 4.5 or 4.67 equiv of the Grignard reagent, the yield was slightly higher (entries 10 and 11, Table 3). The best result was obtained when the reaction was conducted by asymmetric synthesis at −30 °C with 4.67 equiv of *n*-C_4H_9MgBr, affording the target product **6a** in 55% NMR yield (53% isolated yield) (entry 11, Table 3).

It should be noted that when a solution of *n*-C_4H_9MgCl (1.0 M) in Et_2O was used, the yield of racemic **6a** was only 26% (entry 14, Table 3). After careful analysis of the reaction mixture, the byproducts are allylic alcohol **7a**, which was formed by the reaction of **6a** with *n*-C_4H_9MgX,[17] the hydrometallation–elimination product **8a**, and the direct reduction product **9a**. However, the reaction with *n*-C_4H_9MgBr gave a much better selectivity (Scheme 3).

With the optimized reaction conditions in hand (entry 11, Table 3), the scope of the CuBr-catalyzed reaction of racemic 4-hydroxy-4-aryl-2-butynyl methyl ethers **5** with R^2MgBr was studied (Table 4). It can be concluded that 4-hydroxy-4-aryl-2-butynyl methyl ethers **5** with different Grignard reagents can be used to prepare differently substituted 2-alkyl-2,3-allenols **6** in moderate yields. It should be noted that with the increased steric hindrance of R^1, the yield dropped probably due to the possible steric interaction between R^1 and R^2 (compare entry 3 with entry 4, Table 4). It should be also noted that when R^1 is methyl, its reaction with *n*-C_4H_9MgBr is low yielding (entry 9, Table 4). The reaction of **5a** with 4 equiv of phenyl magnesium bromide afforded 1,2-diphenyl-2,3-butadienol **6i** in low yield (22%) with 39% of the reactant being recovered (entry 10, Table 4); when the reaction temperature was raised from −30 °C to room temperature, both 1,2-diphenyl-2,3-butadienol **6i** and 1,2,4-triphenyl-2-butenol **7i** were formed in 33% NMR yield in the crude reaction mixture (entry 11, Table 4), which was formed by the carbometalation of the resulting 2,3-allenols with PhMgBr;[17] When 6 equiv of Grignard reagent were used, 1,2,4-tripheny-2-butenol **7i** was formed in 48% isolated yield as the only product (entry 12, Table 4). In addition, when vinyl magnesium chloride or allyl magnesium chloride in THF solution was added, only trace amount of the product was afforded.

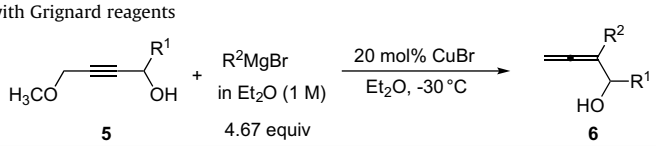
It is known that optically active terminal propargylic alcohols **4** can be easily prepared from racemic propargylic alcohols **4** through



X	Isolated yields[a]				Recovery of
	6a(%)	**7a**(%)	**8a** (%)	**9a** (%)	**5a**[a](%)
Cl	26 (27)	6 (9)	17 (21)	12 (17)	(6)
Br	51 (53)	7 (9)	9 (12)	8 (11)	(4)

Scheme 3. [a]The NMR yields are given in the parentheses with 1,3,5-trimethylbenzene as the internal standard.

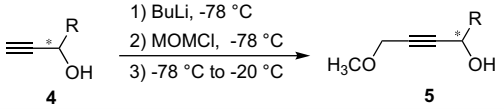
Table 4
CuBr-catalyzed reaction of racemic 4-hydroxy-4-aryl-2-butynyl methyl ethers **5** with Grignard reagents



Entry	R^1	R^2	Yield of **6**[a] (%)	Recovery of **5**[a] (%)
1	Ph (**5a**)	n-C_4H_9	51 (53) (**6a**)	(4)
2	p-$CH_3C_6H_4$ (**5b**)	n-C_4H_9	50 (52) (**6b**)	(2)
3	m,p-$OCH_2OC_6H_3$ (**5c**)	n-C_4H_9	33 (33) (**6c**)	(6)
4	p-$CH_3OC_6H_4$ (**5d**)	n-C_4H_9	45 (50) (**6d**)	(1)
5	Ph (**5a**)	C_2H_5	35 (36) (**6e**)	(1)
6	Ph (**5a**)	n-C_3H_7	43 (46) (**6f**)	(6)
7	Ph (**5a**)	n-C_5H_{11}	48 (50) (**6g**)	(2)
8	Ph (**5a**)	n-C_6H_{13}	44 (56) (**6h**)	(5)
9	CH_3 (**5e**)	n-C_4H_9[b]	(7)	(20)
10	Ph (**5a**)	Ph[b]	22 (25) (**6i**)	(39)
11[c]	Ph (**5a**)	Ph[b]	33 (33)[d] (**6i**)	(0)
12[c]	Ph (**5a**)	Ph[e]	[f]	(0)

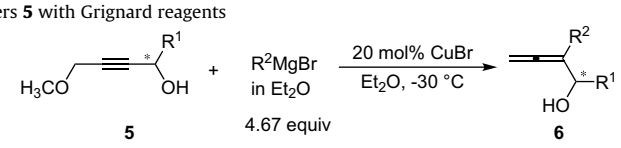
[a] The NMR yields are given in the parentheses with 1,3,5-trimethylbenzene as the internal standard.
[b] Grignard reagent (4 equiv) was used.
[c] The reaction temperature was raised from −30 °C to room temperature.
[d] 1,2,4-Triphenyl-2-butenol **7i** was formed in 33% NMR yield in the crude reaction mixture.
[e] Grignard reagent (6 equiv) was used.
[f] 1,2,4-Triphenyl-2-butenol **7i** was formed in 48% isolated yield.

Table 5
Synthesis of optically active 4-hydroxy-4-aryl-2-butynyl methyl ethers **5**



Entry	R	Time (h)	ee of **4** (%)	**5**	
				Isolated yield (%)	ee (%)
1	Ph (*S*-**4a**)	19	99.6	63 (*R*-**5a**)	98.2
2	Ph (*R*-**4a**)	16	99.9	66 (*S*-**5a**)	96.1
3	p-$CH_3C_6H_4$ (*S*-**4b**)	14	99.9	67 (*R*-**5b**)	99.2
4	p-$CH_3C_6H_4$ (*R*-**4b**)	20	99.5	61 (*S*-**5b**)	98.6
5	m,p-$OCH_2OC_6H_3$ (*S*-**4c**)	22	99.3	62 (*R*-**5c**)	98.6
6	m,p-$OCH_2OC_6H_3$ (*R*-**4c**)	23	96.0	57 (*S*-**5c**)	97.1
7	p-$CH_3OC_6H_4$ (*S*-**4d**)	16	97.2	61 (*R*-**5d**)	96.7
8	p-$CH_3OC_6H_4$ (*R*-**4d**)	16	96.7	61 (*S*-**5d**)	96.4

Table 6
CuBr-catalyzed reaction of optically active 4-hydroxy-4-aryl-2-butynyl methyl ethers **5** with Grignard reagents



Entry	R^1	R^2	ee of **5** (%)	**6**		Recovery of **5**[a] (%)
				Isolated yield[a] (%)	ee (%)	
1	Ph (*R*-**5a**)	n-C_4H_9	98.2	50 (53) (*R*-**6a**)	99.5	(4)
2	Ph (*S*-**5a**)	n-C_4H_9	96.1	48 (52) (*S*-**6a**)	99.2	(6)
3	p-$CH_3C_6H_4$ (*R*-**5b**)	n-C_4H_9	99.2	47 (45) (*R*-**6b**)	97.5	(0)
4	p-$CH_3C_6H_4$ (*S*-**5b**)	n-C_4H_9	98.6	45 (46) (*S*-**6b**)	98.9	(0)
5	m,p-$OCH_2OC_6H_3$ (*R*-**5c**)	n-C_4H_9	98.6	26 (30) (*R*-**6c**)	98.5	(6)
6	m,p-$OCH_2OC_6H_3$ (*S*-**5c**)	n-C_4H_9	97.1	28 (33) (*S*-**6c**)	96.9	(6)
7	p-$CH_3OC_6H_4$ (*R*-**5d**)	n-C_4H_9	96.7	48 (51) (*R*-**6d**)	95.3	(7)
8	p-$CH_3OC_6H_4$ (*S*-**5d**)	n-C_4H_9	96.4	49 (56) (*S*-**6d**)	95.8	(0)
9	Ph (*R*-**5e**)	C_2H_5	98.2	40 (38) (*R*-**6e**)	99.5	(8)
10	Ph (*S*-**5e**)	C_2H_5	96.1	35 (40) (*S*-**6e**)	99.5	(5)
11	Ph (*R*-**5f**)	n-C_3H_7	98.2	37 (41) (*R*-**6f**)	99.7	(7)
12	Ph (*S*-**5f**)	n-C_3H_7	96.1	39 (42) (*S*-**6f**)	97.9	(5)
13	Ph (*R*-**5g**)	n-C_5H_{11}	98.2	49 (57) (*R*-**6g**)	99.6	(11)
14	Ph (*R*-**5h**)	n-C_6H_{13}	98.2	51 (58) (*R*-**6h**)	99.6	(10)

[a] The NMR yields are given in the parentheses with 1,3,5-trimethylbenzene as the internal standard.

Novozym 435-catalyzed kinetic resolution.[18] By treating the optically active propargylic alcohols **4** with n-BuLi and the subsequent reaction with MOMCl, the optically active 4-hydroxy-4-aryl-2-butynyl methyl ethers **5** were prepared in moderate yields (Table 5).

The reaction of these optically active 4-hydroxy-4-aryl-2-butynyl methyl ethers **5** with R^2MgBr afforded the optically active α-allenols **6** without obvious racemization (Table 6).

3. Conclusion

We have developed a one-pot procedure for the synthesis of 3-substituted 1,2-allenes from terminal alkynes and a new route for

the synthesis of optically active 2-substituted secondary 2,3-allenols from optically active 4-hydroxy-4-aryl-2-butynyl methyl ethers. Due to the easy availability of the starting materials and the synthetic potential of the products,[3–6] this method may be useful in organic synthesis. Further studies in this area are being pursued in our laboratory.

4. Experimental section

4.1. Synthesis of 3-substituted 1,2-allenes

4.1.1. 3-Phenyl-1,2-heptadiene (**2a**)

Typical procedure. To a solution of phenylacetylene **3a** (1.020 g, 10.0 mmol) in anhydrous ether (20.0 mL) was added dropwise a solution of *n*-BuLi in hexanes (4.0 mL, 2.5 M in hexanes, 10.0 mmol) at −40 °C under nitrogen within 10 min. After being stirred for 0.5 h, MOMCl (0.810 g, 10.1 mmol) was added dropwise at −40 °C, which was followed by warming up to room temperature naturally for about 1.5 h. Then CuBr (0.280 g, 1.95 mmol) and a solution of *n*-C_4H_9MgBr in Et_2O (20.0 mL, 1 M in Et_2O, 20.0 mmol) were added dropwise sequentially to the reaction mixture for 0.5 h at room temperature. After being stirred for 1.5 h as monitored by TLC, the reaction mixture was quenched with an aqueous solution of saturated ammonium chloride (5 mL), extracted with ether (3×20 mL), washed with saturated brine (20 mL), and dried over anhydrous sodium sulfate. Evaporation and column chromatography on silica gel (eluent: petroleum ether/ethyl acetate=40/1) afforded **2a**[19] (1.473 g, 86%): liquid; 7.46–7.40 (m, 2H), 7.37–7.30 (m, 2H), 7.24–7.17 (m, 1H), 5.08 (t, *J*=3.3 Hz, 2H), 2.48–2.38 (m, 2H), 1.62–1.50 (m, 2H), 1.50–1.36 (m, 2H), 0.95 (t, *J*=7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.6, 136.5, 128.3, 126.5, 125.9, 105.0, 78.0, 30.0, 29.2, 22.5, 14.0; IR (neat) ν (cm^{-1}) 2956, 2929, 2860, 1940, 1597, 1494, 1452, 1378, 1075; MS (70 eV, EI) *m*/*z* (%): 172 (M^+, 8.76), 130 (100).

The following compounds were prepared similarly.

4.1.2. 3-Phenyl-1,2-heptadiene (**2a**)

The reaction of 1-hexyne **3b** (0.823 g, 10.0 mmol), *n*-BuLi (4.2 mL, 2.5 M in hexanes, 10.5 mmol), MOMCl (0.76 mL, *d*=1.06 g/mL, 0.806 g, 10.5 mmol), CuBr (0.144 g, 1.0 mmol), and PhMgBr (20.0 mL, 1 M in Et_2O, 20.0 mmol) in anhydrous ether (20.0 mL) afforded **2a**[19] (0.978 g, 57%): liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 7.48–7.43 (m, 2H), 7.39–7.32 (m, 2H), 7.26–7.19 (m, 1H), 5.10 (t, *J*=3.3 Hz, 2H), 2.50–2.41 (m, 2H), 1.64–1.53 (m, 2H), 1.53–1.39 (m, 2H), 0.98 (t, *J*=7.4 Hz, 3H).

4.1.3. 3-Phenyl-1,2-pentadiene (**2b**)

The reaction of phenylacetylene **3a** (1.024 g, 10.0 mmol), *n*-BuLi (4 mL, 2.5 M in hexanes, 10.0 mmol), MOMCl (0.815 g, 10.1 mmol), CuBr (0.280 g, 1.95 mmol), and C_2H_5MgBr (20.0 mL, 1 M in Et_2O, 20.0 mmol) in anhydrous ether (20.0 mL) afforded **2b**[19] (1.086 g, 75%): liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 7.46–7.40 (m, 2H), 7.37–7.30 (m, 2H), 7.25–7.18 (m, 1H), 5.12 (t, *J*=3.6 Hz, 2H), 2.50–2.39 (m, 2H), 1.17 (t, *J*=7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.3, 136.5, 128.3, 126.5, 125.9, 106.7, 78.8, 22.3, 12.4; IR (neat) ν (cm^{-1}) 2967, 2931, 2872, 1941, 1597, 1494, 1453, 1379, 1075, 1031; MS (70 eV, EI) *m*/*z* (%): 144 (M^+, 69.8), 129 (100).

4.1.4. 3-Phenyl-1,2-nonadiene (**2c**)

The reaction of 1-octyne **3c** (1.102 g, 10.0 mmol), *n*-BuLi (4.2 mL, 2.5 M in hexanes, 10.5 mmol), MOMCl (0.76 mL, *d*=1.06 g/mL, 0.806 g, 10.5 mmol), CuBr (0.144 g, 1.0 mmol), and PhMgBr (20.0 mL, 1 M in Et_2O, 20.0 mmol) in anhydrous ether (20.0 mL) afforded **2c**[19] (1.201 g, 60%): liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 7.46–7.41 (m, 2H), 7.38–7.30 (m, 2H), 7.25–7.18 (m, 1H), 5.08 (t, *J*=3.2 Hz, 2H), 2.47–2.38 (m, 2H), 1.62–1.51 (m, 2H), 1.49–1.29 (m, 6H), 0.92 (t, *J*=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.6, 136.5, 128.3, 126.5, 125.9, 105.0, 78.0, 31.7, 29.5, 29.1, 27.8, 22.7, 14.1; IR (neat) ν (cm^{-1}) 2955, 2928, 2857, 1941, 1597, 1494, 1452, 1378, 1075; MS (70 eV, EI) *m*/*z* (%): 200 (M^+, 8.56), 130 (100).

4.2. Synthesis of racemic 4-hydroxy-4-aryl-2-alkynyl methyl ethers

The (*R*)- and (*S*)-**5a**–**5d** have been fully characterized (see Sections 4.4.1–4.4.8), thus, only the ^1H NMR spectra were recorded for the racemic **5a**–**5d**.

4.2.1. 4-Hydroxy-4-phenyl-2-butynyl methyl ether (**5a**)

To a solution of 1-phenyl-2-propynol **4a** (1.3310 g, 10.1 mmol) in anhydrous Et_2O (20 mL) was added dropwise *n*-BuLi (8.0 mL, 2.5 M in hexanes, 20.0 mmol) at −78 °C under nitrogen within 8 min. After addition, the resulting solution was stirred at −78 °C for 0.5 h, which was followed by dropwise addition of MOMCl (0.68 mL, *d*=1.06 g/mL, 0.72 g, 9.0 mmol). The resulting mixture was warmed up to −30 °C naturally. After being stirred for 16 h as monitored by TLC, the mixture was quenched with 1 N HCl (10 mL) and extracted with ether (3×10 mL). The combined organic layer was washed with saturated brine (20 mL) and dried over anhydrous sodium sulfate. After evaporation, the residue was purified by flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate=5/1) to afford **5a**[10] (0.9508 g, 60%): oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.56–7.50 (m, 2H), 7.42–7.30 (m, 3H), 5.51 (s, 1H), 4.18 (d, *J*=2.0 Hz, 2H), 3.39 (s, 3H), 2.54 (br s, 1H).

4.2.2. 4-Hydroxy-4-(4′-methylphenyl)-2-butynyl methyl ether (**5b**)

Typical procedure. To a solution of 1-(4′-methylphenyl)-2-propynol **4b** (1.4652 g, 10.0 mmol) in anhydrous THF (30 mL) was added dropwise *n*-BuLi (8.8 mL, 2.5 M in hexanes, 22.0 mmol) at −78 °C under nitrogen within 10 min. After addition, the resulting solution was stirred at −78 °C for 0.5 h, which was followed by dropwise addition of MOMCl (1.14 mL, *d*=1.06 g/mL, 1.21 g, 15.0 mmol). The resulting mixture was warmed up to −20 °C naturally. After being stirred for 12 h as monitored by TLC, the mixture was quenched with an aqueous solution of saturated ammonium chloride (5 mL) and extracted with ether (3×10 mL). The combined organic layer was washed with saturated brine (10 mL) and dried over anhydrous sodium sulfate. After evaporation, the residue was purified by flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate=5/1 to 3/1) to afford **5b** (1.3118 g, 69%): oil; ^1H NMR (300 MHz, $CDCl_3$) δ 7.43 (d, *J*=7.9 Hz, 2H), 7.19 (d, *J*=7.9 Hz, 2H), 5.48 (dt, J_1=6.0 Hz, J_2=1.5 Hz, 1H), 4.19 (d, *J*=1.5 Hz, 2H), 3.40 (s, 3H), 2.36 (s, 3H), 2.27 (br s, 1H).

The following compounds were prepared according to this procedure.

4.2.3. 4-Hydroxy-4-(3′,4′-methylenedioxyphenyl)-2-butynyl methyl ether (**5c**)

The reaction of 1-(3′,4′-methylenedioxyphenyl)-2-propynol **4c** (1.7588 g, 10.0 mmol), *n*-BuLi (8.8 mL, 2.5 M in hexanes, 22.0 mmol), and MOMCl (1.16 mL, *d*=1.06 g/mL, 1.208 g, 15.0 mmol) in anhydrous THF (30 mL) afforded **5c** (1.3208 g, 60%): oil; ^1H NMR (300 MHz, $CDCl_3$) δ 7.04 (d, *J*=1.8 Hz, 1H), 6.99 (ddd, J_1=7.9 Hz, J_2=1.8 Hz, J_3=0.6 Hz, 1H), 6.78 (d, *J*=7.9 Hz, 1H), 5.96 (s, 2H), 5.41 (dt, J_1=5.7 Hz, J_2=1.5 Hz, 1H), 4.18 (d, *J*=1.5 Hz, 2H), 3.39 (s, 3H), 2.46 (d, *J*=5.7 Hz, 1H).

4.2.4. 4-Hydroxy-4-(4′-methoxyphenyl)-2-butynyl methyl ether (**5d**)

The reaction of 1-(4′-methoxyphenyl)-2-propynol **4d** (1.330 g, 8.2 mmol), *n*-BuLi (7.25 mL, 2.5 M in hexanes, 18.1 mmol), and MOMCl (0.75 mL, *d*=1.06 g/mL, 0.795 g, 9.9 mmol) in anhydrous THF

(30 mL) afforded **5d** (1.1562 g, 68%): oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49–7.43 (m, 2H), 6.93–6.87 (m, 2H), 5.47 (d, J=5.4 Hz, 1H), 4.19 (d, J=1.5 Hz, 2H), 3.81 (s, 3H), 3.40 (s, 3H), 2.24 (d, J=5.4 Hz, 1H).

4.3. CuBr-catalyzed reaction of racemic 4-aryl-4-hydroxy-2-butynyl methyl ethers 5a–5d with Grignard reagents

The (*R*)- and (*S*)-**6a–6i** have been fully characterized (see Section 4.5), thus, only the ^{1}H NMR spectra were recorded for the racemic **6a–6i**.

*4.3.1. Synthesis of 2-butyl-1-phenyl-2,3-butadien-1-ol (**6a**), 2-butyl-1-phenyl-2-octen-1-ol (**7a**), 1-phenyl-2,3-butadien-1-ol (**8a**), and 1-phenyl-2-butyn-1-ol (**9a**)*

Typical procedure. To a dried Schlenk tube were added CuBr (8.9 mg. 0.06 mmol), anhydrous Et_2O (1.6 mL), and 4-hydroxy-4-phenyl-2-butynyl methyl ether **5a** (52.6 mg, 0.30 mmol) at room temperature. A solution of *n*-C_4H_9MgCl in Et_2O (1.4 mL, 1 M in Et_2O, 1.4 mmol) was then added dropwise to this resulting mixture at −30 °C under nitrogen. After the addition was over, the reaction mixture was stirred for 10 h at −30 °C as monitored by TLC, quenched with saturated ammonium chloride solution (2 mL) at −30 °C, extracted with ether at room temperature (3×10 mL), washed with saturated brine (10 mL), and dried over anhydrous sodium sulfate. According to the ^{1}H NMR analysis of the crude reaction mixture there was 6% of **5a** remaining. Evaporation and column chromatography on silica gel (eluent: petroleum ether/ethyl acetate=20/1 to 10/1) afforded **6a**[20] (16.0 mg, 26%), **7a** (4.5 mg, 6%), **8a**[17] (7.5 mg, 17%), and **9a**[21] (5.1 mg, 12%).

Compound **6a**: liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.26 (m, 5H), 5.13–5.07 (m, 1H), 5.05–4.96 (m, 2H), 2.27 (d, J=4.5 Hz, 1H), 1.88–1.73 (m, 2H), 1.43–1.19 (m, 4H), 0.84 (t, J=7.1 Hz, 3H).

Compound **7a**: liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.24 (m, 5H), 5.61 (t, J=7.2 Hz, 1H), 5.16 (d, J=2.7 Hz, 1H), 2.10–1.92 (m, 3H), 1.89–1.76 (m, 2H), 1.44–1.10 (m, 10H), 0.90 (t, J=6.8 Hz, 3H), 0.82 (t, J=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.8, 141.2, 128.2, 127.3, 126.5, 78.2, 31.7, 31.6, 29.5, 27.6, 27.5, 23.0, 22.6, 14.1, 13.9; IR (neat) ν (cm^{-1}) 3386, 2958, 2869, 1603, 1454, 1377, 1009; MS (70 eV, EI) *m*/*z* (%): 260 (M^+, 67.0), 189 (100); HRMS calcd for $C_{18}H_{28}O$ (M^+): 260.2140, found: 260.2137.

Compound **8a**: liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44–7.26 (m, 5H), 5.45 (q, J=6.6 Hz, 1H), 5.32–5.25 (m, 1H), 5.00–4.88 (m, 2H), 2.16 (d, J=3.9 Hz, 1H).

Compound **9a**: liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57–7.51 (m, 2H), 7.42–7.29 (m, 3H), 5.47–5.40 (m, 1H), 2.15 (d, J=6.0 Hz, 1H), 1.91 (d, J=2.4 Hz, 3H).

*4.3.2. Synthesis of 2-butyl-1-phenyl-2,3-butadien-1-ol (**6a**), 2-butyl-1-phenyl-2-octen-1-ol (**7a**), 1-phenyl-2,3-butadien-1-ol (**8a**), and 1-phenyl-2-butyn-1-ol (**9a**)*

To a mixture of 4-hydroxy-4-phenyl-2-butynyl methyl ether **5a** (52.9 mg, 0.30 mmol) and CuBr (8.7 mg, 0.06 mmol) in anhydrous Et_2O (1.6 mL) was added dropwise a solution of *n*-C_4H_9MgBr in Et_2O (1.4 mL, 1 M in Et_2O, 1.4 mmol) to afford **6a**[20] (31.1 mg, 51%), **7a** (5.4 mg, 7%), **8a**[17] (4.0 mg, 9%), and **9a**[21] (3.7 mg, 8%). According to the ^{1}H NMR analysis of the crude reaction mixture there was 4% of **5a** remaining.

*4.3.3. 2-Butyl-1-(4′-methylphenyl)-2,3-butadien-1-ol (**6b**)*

To a mixture of 4-hydroxy-4-(4′-methylphenyl)-2-butynyl methyl ether **5b** (56.8 mg, 0.30 mmol) and CuBr (8.6 mg, 0.10 mmol) in anhydrous Et_2O (1.6 mL) was added dropwise a solution of *n*-C_4H_9MgBr in Et_2O (1.4 mL, 1 M in Et_2O, 1.4 mmol) to afford **6b**[6b] (32.2 mg, 50%): liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, J=8.1 Hz, 2H), 7.15 (d, J=7.8 Hz, 2H), 5.08–4.95 (m, 3H), 2.35 (s, 3H), 2.20 (d, J=4.2 Hz, 1H), 1.87–1.73 (m, 2H), 1.44–1.17 (m, 4H), 0.84 (t, J=7.2 Hz, 3H). According to the ^{1}H NMR analysis of the crude reaction mixture there was 2% of **5b** remaining.

*4.3.4. 2-Butyl-1-(3′,4′-methylenedioxyphenyl)-2,3-butadien-1-ol (**6c**)*

To a mixture of 4-hydroxy-4-(3′,4′-methylenedioxyphenyl)-2-butynyl methyl ether **5c** (65.7 mg, 0.30 mmol) and CuBr (8.7 mg, 0.06 mmol) in anhydrous Et_2O (1.6 mL) was added dropwise a solution of *n*-C_4H_9MgBr in Et_2O (1.4 mL, 1 M in Et_2O, 1.4 mmol) to afford **6c**[6b] (24.1 mg, 33%): liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.88–6.85 (m, 1H), 6.83 (dd, J_1=7.8 Hz, J_2=1.5 Hz, 1H), 6.76 (d, J=7.8 Hz, 1H), 5.95 (s, 2H), 5.06–4.95 (m, 3H), 2.24 (d, J=3.6 Hz, 1H), 1.89–1.69 (m, 2H), 1.44–1.20 (m, 4H), 0.85 (t, J=7.2 Hz, 3H). According to the ^{1}H NMR analysis of the crude reaction mixture there was 6% of **5c** remaining.

*4.3.5. 2-Butyl-1-(4′-methoxyphenyl)-2,3-butadien-1-ol (**6d**)*

To a mixture of 4-hydroxy-4-(4′-methoxyphenyl)-2-butynyl methyl ether **5d** (61.3 mg, 0.30 mmol) and CuBr (8.6 mg, 0.06 mmol) in anhydrous Et_2O (1.6 mL) was added dropwise a solution of *n*-C_4H_9MgBr in Et_2O (1.4 mL, 1 M in Et_2O, 1.4 mmol) to afford **6d**[6b] (30.9 mg, 45%): liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32–7.26 (m, 2H), 6.91–6.84 (m, 2H), 5.06–4.95 (m, 3H), 3.81 (s, 3H), 2.21 (d, J=3.9 Hz, 1H), 1.87–1.71 (m, 2H), 1.43–1.18 (m, 4H), 0.84 (t, J=7.2 Hz, 3H). According to the ^{1}H NMR analysis of the crude reaction mixture there was 1% of **5d** remaining.

*4.3.6. 2-Ethyl-1-phenyl-2,3-butadien-1-ol (**6e**)*

To a mixture of 4-hydroxy-4-phenyl-2-butynyl methyl ether **5a** (53.5 mg, 0.30 mmol) and CuBr (8.6 mg, 0.06 mmol) in anhydrous Et_2O (1.6 mL) was added dropwise a solution of C_2H_5MgBr in Et_2O (1.4 mL, 1 M in Et_2O, 1.4 mmol) to afford **6e**[13a] (19.0 mg, 35%): liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41–7.27 (m, 5H), 5.14–5.09 (m, 1H), 5.09–4.98 (m, 2H), 2.24 (d, J=3.9 Hz, 1H), 1.90–1.75 (m, 2H), 0.97 (t, J=7.4 Hz, 3H). According to the ^{1}H NMR analysis of the crude reaction mixture there was 1% of **5a** remaining.

*4.3.7. 1-Phenyl-2-propyl-2,3-butadien-1-ol (**6f**)*

To a mixture of 4-hydroxy-4-phenyl-2-butynyl methyl ether **5a** (51.8 mg, 0.29 mmol) and CuBr (8.6 mg, 0.06 mmol) in anhydrous Et_2O (1.6 mL) was added dropwise a solution of *n*-C_3H_7MgBr in Et_2O (1.4 mL, 1 M in Et_2O, 1.4 mmol) to afford **6f**[22] (24.0 mg, 43%): liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42–7.27 (m, 5H), 5.13–5.07 (m, 1H), 5.06–4.95 (m, 2H), 2.27 (d, J=4.5 Hz, 1H); 1.87–1.72 (m, 2H), 1.48–1.34 (m, 2H), 0.86 (t, J=7.2 Hz, 3H). According to the ^{1}H NMR analysis of the crude reaction mixture there was 6% of **5a** remaining.

*4.3.8. 2-Pentyl-1-phenyl-2,3-butadien-1-ol (**6g**)*

To a mixture of 4-hydroxy-4-phenyl-2-butynyl methyl ether **5a** (52.1 mg, 0.30 mmol) and CuBr (8.8 mg, 0.06 mmol) in anhydrous Et_2O (1.6 mL) was added dropwise a solution of *n*-$C_5H_{11}MgBr$ in Et_2O (1.4 mL, 1 M in Et_2O, 1.4 mmol) to afford **6g**[23] (30.8 mg, 48%): liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.27 (m, 5H), 5.13–5.06 (m, 1H), 5.06–4.95 (m, 2H), 2.24 (d, J=4.2 Hz, 1H), 1.90–1.72 (m, 2H), 1.46–1.35 (m, 2H), 1.32–1.18 (m, 4H), 0.84 (t, J=6.9 Hz, 3H). According to the ^{1}H NMR analysis of the crude reaction mixture there was 2% of **5a** remaining.

*4.3.9. 2-Hexyl-1-phenyl-2,3-butadien-1-ol (**6h**)*

To a mixture of 4-hydroxy-4-phenyl-2-butynyl methyl ether **5a** (53.1 mg, 0.30 mmol) and CuBr (8.7 mg, 0.06 mmol) in anhydrous Et_2O (1.6 mL) was added dropwise a solution of *n*-$C_6H_{13}MgBr$ in Et_2O (1.4 mL, 1 M in Et_2O, 1.4 mmol) to afford **6h**[24] (30.8 mg, 44%):

liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42–7.26 (m, 5H), 5.12–5.06 (m, 1H), 5.06–4.95 (m, 2H), 2.27 (d, J=4.2 Hz, 1H); 1.90–1.72 (m, 2H), 1.46–1.33 (m, 2H), 1.33–1.16 (m, 6H), 0.86 (t, J=6.6 Hz, 3H). According to the ^{1}H NMR analysis of the crude reaction mixture there was 5% of **5a** remaining.

4.3.10. 1,2-Diphenyl-2,3-butadien-1-ol (*6i*)

To a mixture of 4-hydroxy-4-phenyl-2-butynyl methyl ether **5a** (52.0 mg, 0.30 mmol) and CuBr (8.9 mg, 0.06 mmol) in anhydrous Et_2O (1.8 mL) was added dropwise a solution of PhMgBr in Et_2O (1.2 mL, 1 M in Et_2O, 1.2 mmol) to afford **6i**[20] (14.1 mg, 22%): liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49–7.43 (m, 2H), 7.40–7.32 (m, 3H), 7.32–7.23 (m, 4H), 7.22–7.14 (m, 1H), 5.76–5.68 (m, 1H), 5.31 (dd, J_1=6.0 Hz, J_2=2.4 Hz, 1H), 5.25 (dd, J_1=6.0 Hz, J_2=2.4 Hz, 1H), 2.32 (d, J=5.7 Hz, 1H). According to the ^{1}H NMR analysis of the crude reaction mixture there was 39% of **5a** remaining.

4.3.11. 1,2,4-Triphenyl-2-butenol (*7i*)

To a mixture of 4-hydroxy-4-phenyl-2-butynyl methyl ether **5a** (51.8 mg, 0.29 mmol) and CuBr (8.8 mg, 0.06 mmol) in anhydrous Et_2O (1.2 mL) was added dropwise a solution of PhMgBr in Et_2O (1.8 mL, 1 M in Et_2O, 1.8 mmol) to afford **7i** (42.3 mg, 48%): liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30–7.16 (m, 11H), 7.12 (d, J=7.2 Hz, 2H), 7.00–6.94 (m, 2H), 6.05 (t, J=7.4 Hz, 1H), 5.44 (s, 1H), 3.27 (d, J=7.2 Hz, 2H), 2.15 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.9, 141.9, 140.7, 137.4, 129.4, 128.4, 128.3, 128.1, 128.0, 127.4, 127.1, 127.0, 126.6, 125.9, 78.4, 34.8; IR (neat) ν (cm^{-1}) 3408, 1601, 1493, 1452, 1064, 1029, 1007; MS (70 eV, EI) m/z (%): 300 (M^+, 5.16), 282 (M^+-H_2O, 47.8), 194 (100); HRMS calcd for $C_{22}H_{20}O$ (M^+): 300.1514, found: 300.1512.

4.4. Synthesis of optically active 4-hydroxy-4-aryl-2-alkynyl methyl ethers (5a–5d)

4.4.1. (4R)-(+)-4-Hydroxy-4-phenyl-2-butynyl methyl ether (R-(+)-*5a*)

Typical procedure. To a solution of (1*S*)-(+)-1-phenyl-2-propynol *S*-(+)-**4a**[18] (1.3166 g, 99.6% ee, 10.0 mmol) in anhydrous THF (50 mL) was added dropwise *n*-BuLi (8.8 mL, 2.5 M in hexanes, 22.0 mmol) at −78 °C under nitrogen within 10 min. After addition, the resulting solution was stirred at −78 °C for 0.5 h, which was followed by dropwise addition of MOMCl (1.14 mL, d=1.06 g/mL, 1.21 g, 15.0 mmol). The resulting mixture was warmed up to −20 °C naturally. After being stirred for 19 h as monitored by TLC, the mixture was quenched with an aqueous solution of saturated ammonium chloride (10 mL) and extracted with ether (3×20 mL). The combined organic layer was washed with saturated brine (20 mL) and dried over anhydrous sodium sulfate. After evaporation, the residue was purified by flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate=5/1 to 3/1) to afford *R*-(+)-**5a** (1.1139 g, 63%, 98.2% ee; HPLC condition: Chiralcel AD-H, *n*-hexane/*i*-PrOH=90/10, 0.8 mL/min, λ=230 nm, t_R 13.8 (major), 12.0 (minor); $[\alpha]_D^{20}$ +18.1 (*c* 1.34, $CHCl_3$)): oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58–7.50 (m, 2H), 7.43–7.30 (m, 3H), 5.52 (d, J=6.0 Hz, 1H), 4.19 (d, J=1.8 Hz, 2H), 3.40 (s, 3H), 2.32–2.24 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.4, 128.3, 128.1, 126.4, 86.5, 81.8, 64.1, 59.7, 57.4; IR (neat) ν (cm^{-1}) 3396, 2992, 2264, 1960, 1889, 1812, 1603, 1494, 1453, 1376, 1358, 1279, 1189, 1095, 1003; MS (70 eV, EI) m/z (%): 176 (M^+, 18.4), 115 (100); HRMS calcd for $C_{11}H_{12}O_2$ (M^+): 176.0837, found: 176.0833.

4.4.2. (4S)-(−)-4-Hydroxy-4-phenyl-2-butynyl methyl ether (S-(−)-*5a*)

The reaction of (1*R*)-(−)-1-phenyl-2-propynol *R*-(−)-**4a**[18] (0.6604 g, 99.9% ee, 5.0 mmol), *n*-BuLi (4.4 mL, 2.5 M in hexanes, 11.0 mmol), and MOMCl (0.58 mL, d=1.06 g/mL, 0.615 g, 7.5 mmol) in THF (25 mL) afforded *S*-(−)-**5a**[10] (0.5778 g, 66%, 96.1% ee; HPLC condition: Chiralcel AD-H, *n*-hexane/*i*-PrOH=90/10, 0.8 mL/min, λ=230 nm, t_R 11.7 (major), 13.6 (minor); $[\alpha]_D^{20}$ −16.0 (*c* 0.70, $CHCl_3$)): oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58–7.50 (m, 2H), 7.43–7.30 (m, 3H), 5.52 (d, J=6.0 Hz, 1H), 4.19 (d, J=1.5 Hz, 2H), 3.40 (s, 3H), 2.36 (br s, 1H). This compound has been prepared in the literature[10] in 77% ee. However, according to our careful study, the $[\alpha]_D^{20}$ value reported ($[\alpha]_D^{20}$ −41.5 (*c* 0.28, $CHCl_3$)) therein should be wrong.

4.4.3. (4R)-(+)-4-Hydroxy-4-(4′-methylphenyl)-2-butynyl methyl ether (R-(+)-*5b*)

The reaction of (1*S*)-(+)-1-(4′-methylphenyl)-2-propynol *S*-(+)-**4b**[18] (0.4642 g, 99.9% ee, 3.2 mmol), *n*-BuLi (2.8 mL, 2.5 M in hexanes, 7.0 mmol), and MOMCl (0.36 mL, d=1.06 g/mL, 0.382 g, 4.8 mmol) in anhydrous THF (20 mL) afforded *R*-(+)-**5b** (0.4034 g, 67%, 99.2% ee; HPLC condition: Chiralcel AD-H, *n*-hexane/*i*-PrOH=90/10, 0.8 mL/min, λ=230 nm, t_R 15.3 (major), 12.7 (minor); $[\alpha]_D^{20}$ +16.4 (*c* 0.80, $CHCl_3$)): oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (d, J=8.1 Hz, 2H), 7.19 (d, J=8.1 Hz, 2H), 5.49 (d, J=6.3 Hz, 1H), 4.19 (d, J=1.5 Hz, 2H), 3.40 (s, 3H), 2.36 (s, 3H), 2.21 (d, J=6.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.9, 137.6, 129.0, 126.4, 86.6, 81.6, 64.0, 59.7, 57.4, 21.0; IR (neat) ν (cm^{-1}) 3404, 2928, 2264, 1994, 1908, 1795, 1614, 1513, 1449, 1358, 1279, 1188, 1095, 1002; MS (70 eV, EI) m/z (%): 190 (M^+, 32.2), 115 (100); HRMS calcd for $C_{12}H_{14}O_2$ (M^+): 190.0994, found: 190.0993.

4.4.4. (4S)-(−)-4-Hydroxy-4-(4′-methylphenyl)-2-butynyl methyl ether (S-(−)-*5b*)

The reaction of (1*R*)-(−)-1-(4′-methylphenyl)-2-propynol *R*-(−)-**4b**[18] (0.9112 g, 99.5% ee, 6.2 mmol), *n*-BuLi (5.5 mL, 2.5 M in hexanes, 13.7 mmol), and MOMCl (0.71 mL, d=1.06 g/mL, 0.753 g, 9.4 mmol) in anhydrous THF (30 mL) afforded *S*-(−)-**5b** (0.7201 g, 61%, 98.6% ee; HPLC condition: Chiralcel AD-H, *n*-hexane/*i*-PrOH=90/10, 0.8 mL/min, λ=230 nm, t_R 12.5 (major), 15.1 (minor); $[\alpha]_D^{20}$ −14.1 (*c* 0.75, $CHCl_3$)): oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (d, J=8.1 Hz, 2H), 7.19 (d, J=8.1 Hz, 2H), 5.49 (d, J=6.0 Hz, 1H), 4.19 (d, J=1.5 Hz, 2H), 3.40 (s, 3H), 2.36 (s, 3H), 2.21 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.2, 137.5, 129.2, 126.5, 86.5, 82.0, 64.3, 59.9, 57.6, 21.1; IR (neat) ν (cm^{-1}) 3403, 2928, 2270, 1994, 1909, 1798, 1613, 1512, 1450, 1358, 1188, 1095; MS (70 eV, EI) m/z (%): 190 (M^+, 35.3), 115 (100). Elemental analysis calcd for $C_{12}H_{14}O_2$ (%): C, 75.76; H, 7.42. Found: C, 75.83; H, 7.47.

4.4.5. (4R)-(+)-4-Hydroxy-4-(3′,4′-methylenedioxyphenyl)-2-butynyl methyl ether (R-(+)-*5c*)

The reaction of (1*S*)-(+)-1-(3′,4′-methylenedioxyphenyl)-2-propynol *S*-(+)-**4c**[18] (1.5592 g, 99.3% ee, 8.9 mmol), *n*-BuLi (7.8 mL, 2.5 M in hexanes, 19.5 mmol), and MOMCl (1.00 mL, d=1.06 g/mL, 1.060 g, 13.2 mmol) in anhydrous THF (30 mL) afforded *R*-(+)-**5c** (1.2152 g, 62%, 98.6% ee; HPLC condition: Chiralcel AD-H, *n*-hexane/*i*-PrOH=90/10, 0.8 mL/min, λ=230 nm, t_R 12.7 (major), 11.3 (minor); $[\alpha]_D^{20}$ +30.5 (*c* 0.78, $CHCl_3$)): oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.06–7.03 (m, 1H), 7.00 (ddd, J_1=8.1 Hz, J_2=1.7 Hz, J_3=0.6 Hz, 1H), 6.79 (d, J=8.1 Hz, 1H), 5.97 (s, 2H), 5.43 (dt, J_1=6.0 Hz, J_2=1.7 Hz, 1H), 4.19 (d, J=1.8 Hz, 2H), 3.40 (s, 3H), 2.21 (d, J=6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.5, 147.2, 134.5, 120.0, 107.8, 107.1, 100.9, 86.4, 81.5, 63.7, 59.6, 57.3; IR (neat) ν (cm^{-1}) 3396, 2896, 2270, 2216, 2029, 1854, 1610, 1488, 1444, 1359, 1248, 1188, 1094, 1039; MS (70 eV, EI) m/z (%): 220 (M^+, 100). Elemental analysis calcd for $C_{12}H_{12}O_4$ (%): C, 65.45; H, 5.49. Found: C, 65.42; H, 5.45.

4.4.6. (4S)-(−)-4-Hydroxy-4-(3′,4′-methylenedioxyphenyl)-2-butynyl methyl ether (S-(−)-*5c*)

The reaction of (1*R*)-(−)-1-(3′,4′-methylenedioxyphenyl)-2-propynol *R*-(−)-**4c**[18] (1.5666 g, 96.0% ee, 8.9 mmol), *n*-BuLi (7.8 mL,

2.5 M in hexanes, 19.6 mmol), and MOMCl (1.00 mL, d=1.06 g/mL, 1.060 g, 13.2 mmol) in anhydrous THF (30 mL) afforded *S*-(−)-**5c** (1.1070 g, 57%, 97.1% ee; HPLC condition: Chiralcel AD-H, *n*-hexane/*i*-PrOH=90/10, 0.8 mL/min, λ=230 nm, t_R 11.3 (major), 12.6 (minor); $[\alpha]_D^{20}$ −31.2 (*c* 0.76, $CHCl_3$)): oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.06–7.03 (m, 1H), 7.00 (ddd, J_1=8.1 Hz, J_2=1.8 Hz, J_3=0.6 Hz, 1H), 6.79 (d, J=8.1 Hz, 1H), 5.97 (s, 2H), 5.43 (dt, J_1=6.0 Hz, J_2=1.8 Hz, 1H), 4.19 (d, J=1.5 Hz, 2H), 3.40 (s, 3H), 2.17 (d, J=6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.8, 147.6, 134.5, 120.2, 108.1, 107.3, 101.2, 86.2, 82.2, 64.2, 59.8, 57.7; IR (neat) ν (cm^{-1}) 3396, 2896, 2270, 2029, 1854, 1732, 1610, 1504, 1488, 1359, 1248, 1094, 1039; MS (70 eV, EI) m/z (%): 220 (M^+, 100); HRMS calcd for $C_{12}H_{12}O_4$ (M^+): 220.0736, found: 220.0740.

4.4.7. (4*R*)-(+)-4-Hydroxy-4-(4′-methoxyphenyl)-2-butynyl methyl ether (*R*-(+)-**5d**)

The reaction of (1*S*)-(+)-1-(4′-methoxyphenyl)-2-propynol *S*-(+)-**4d**[18] (1.9950 g, 97.2% ee, 12.3 mmol), *n*-BuLi (10.8 mL, 2.5 M in hexanes, 27.1 mmol), and MOMCl (1.40 mL, d=1.06 g/mL, 1.484 g, 18.5 mmol) in anhydrous THF (30 mL) afforded *R*-(+)-**5d** (1.5444 g, 61%, 96.7% ee; HPLC condition: Chiralcel AD-H, *n*-hexane/*i*-PrOH=90/10, 0.8 mL/min, λ=230 nm, t_R 22.0 (major), 18.0 (minor); $[\alpha]_D^{20}$ +24.6 (*c* 1.06, $CHCl_3$)): oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49–7.42 (m, 2H), 6.93–6.87 (m, 2H), 5.47 (dt, J_1=6.0 Hz, J_2=1.5 Hz, 1H), 4.19 (d, J=1.5 Hz, 2H), 3.81 (s, 3H), 3.40 (s, 3H), 2.24 (d, J=6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 132.8, 127.9, 113.8, 86.6, 81.8, 63.8, 59.8, 57.4, 55.2; IR (neat) ν (cm^{-1}) 3412, 2935, 2276, 2014, 1893, 1611, 1587, 1512, 1359, 1249, 1176, 1093, 1033; MS (70 eV, EI) m/z (%): 206 (M^+, 74.7), 145 (100). Elemental analysis calcd for $C_{12}H_{14}O_3$ (%): C, 69.88; H, 6.84. Found: C, 69.82; H, 6.82.

4.4.8. (4*S*)-(−)-4-Hydroxy-4-(4′-methoxyphenyl)-2-butynyl methyl ether (*S*-(−)-**5d**)

The reaction of (1*R*)-(−)-1-(4-methoxyphenyl)-2-propynol *R*-(−)-**4d**[18] (1.1255 g, 96.7% ee, 7.0 mmol), *n*-BuLi (6.1 mL, 2.5 M in hexanes, 15.3 mmol), and MOMCl (0.80 mL, d=1.06 g/mL, 0.848 g, 10.4 mmol) in THF (30 mL) afforded *S*-(−)-**5d** (0.8744 g, 61%, 96.4% ee; HPLC condition: Chiralcel AD-H, *n*-hexane/*i*-PrOH=90/10, 0.8 mL/min, λ=230 nm, t_R 18.0 (major), 21.9 (minor); $[\alpha]_D^{20}$ −19.5 (*c* 1.33, $CHCl_3$)): oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50–7.43 (m, 2H), 6.93–6.87 (m, 2H), 5.47 (d, J=6.0 Hz, 1H), 4.19 (d, J=1.5 Hz, 2H), 3.81 (s, 3H), 3.39 (s, 3H), 2.28 (d, J=6.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.5, 132.8, 127.9, 113.8, 86.5, 81.9, 63.9, 59.8, 57.6, 55.2; IR (neat) ν (cm^{-1}) 3417, 2936, 2278, 2014, 1893, 1611, 1587, 1514, 1359, 1249, 1174, 1094, 1032; MS (70 eV, EI) m/z (%): 206 (M^+, 62.5), 145 (100); HRMS calcd for $C_{12}H_{14}O_3$ (M^+): 206.0943, found: 206.0943.

4.5. CuBr-catalyzed reaction of optically active 4-aryl-4-hydroxy-2-butynyl methyl ethers 5a–5d with Grignard reagents

4.5.1. (1*R*)-(−)-2-Butyl-1-phenyl-2,3-butadien-1-ol (*R*-(−)-6a)

Typical procedure. To a dried Schlenk tube were added CuBr (8.7 mg. 0.06 mmol), anhydrous Et_2O (1.6 mL), and (4*R*)-(+)-4-hydroxy-4-phenyl-2-butynyl methyl ether *R*-(+)-**5a** (53.0 mg, 98.2% ee, 0.30 mmol) at room temperature. A solution of *n*-C_4H_9MgBr in Et_2O (1.4 mL, 1 M in Et_2O, 1.4 mmol) was then added dropwise to this resulting mixture at −30 °C under nitrogen. After the addition was over, the reaction mixture was stirred for 10.5 h as monitored by TLC, quenched with saturated ammonium chloride solution (2 mL), extracted with ether (3×10 mL), washed with saturated brine (10 mL), and dried over anhydrous sodium sulfate. Evaporation and column chromatography on silica gel (eluent: petroleum ether/ethyl acetate=20/1) afforded *R*-(−)-**6a**[20] (30.2 mg, 50%, 99.5% ee; HPLC condition: Chiralcel OD-H, *n*-hexane/*i*-PrOH=90/10, 0.8 mL/min, λ=230 nm, t_R 12.5 (major), 11.7 (minor); $[\alpha]_D^{20}$ −131.8 (*c* 1.00, $CHCl_3$)): liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.27 (m, 5H), 5.10 (br s, 1H), 5.06–4.95 (m, 2H), 2.27 (br s, 1H), 1.88–1.73 (m, 2H), 1.46–1.19 (m, 4H), 0.84 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.0, 142.1, 128.3, 127.7, 126.7, 108.2, 79.8, 74.1, 29.6, 27.6, 22.3, 13.9; IR (neat) ν (cm^{-1}) 3396, 2929, 1956, 1603, 1494, 1454, 1378, 1190, 1086, 1020; MS (70 eV, EI) m/z (%): 202 (M^+, 2.65), 107 (100). According to the ^{1}H NMR analysis of the crude reaction mixture there was 4% of *R*-(+)-**5a** remaining.

4.5.2. (1*S*)-(+)-2-Butyl-1-phenyl-2,3-butadien-1-ol (*S*-(+)-**6a**)

To a solution of (4*S*)-(−)-4-hydroxy-4-phenyl-2-butynyl methyl ether *S*-(−)-**5a** (52.3 mg, 96.1% ee, 0.30 mmol) and CuBr (8.8 mg, 0.06 mmol) in anhydrous Et_2O (1.6 mL) was added dropwise a solution of *n*-C_4H_9MgBr in Et_2O (1.4 mL, 1 M in Et_2O, 1.4 mmol) to afford *S*-(+)-**6a**[20] (28.6 mg, 48%, 99.2% ee; HPLC condition: Chiralcel OD-H, *n*-hexane/*i*-PrOH=90/10, 0.8 mL/min, λ=230 nm, t_R 11.7 (major), 12.2 (minor); $[\alpha]_D^{20}$ +141.4 (*c* 0.96, $CHCl_3$)): liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.27 (m, 5H), 5.09 (s, 1H), 5.06–4.95 (m, 2H), 2.27 (d, J=3.9 Hz, 1H), 1.88–1.73 (m, 2H), 1.42–1.19 (m, 4H), 0.84 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.0, 142.1, 128.3, 127.7, 126.7, 108.2, 79.8, 74.0, 29.6, 27.5, 22.3, 13.9; IR (neat) ν (cm^{-1}) 3396, 2929, 1956, 1603, 1454, 1020; MS (70 eV, EI) m/z (%): 202 (M^+, 3.19), 107 (100). According to the ^{1}H NMR analysis of the crude reaction mixture there was 6% of *S*-(−)-**5a** remaining.

4.5.3. (1*R*)-(−)-2-Butyl-1-(4′-methylphenyl)-2,3-butadien-1-ol (*R*-(−)-**6b**)

To a solution of (4*R*)-(+)-4-hydroxy-(4′-methylphenyl)-2-butynyl methyl ether *R*-(+)-**5b** (57.2 mg, 99.2% ee, 0.30 mmol) and CuBr (8.8 mg, 0.06 mmol) in anhydrous Et_2O (1.6 mL) was added dropwise a solution of *n*-C_4H_9MgBr in Et_2O (1.4 mL, 1 M in Et_2O, 1.4 mmol) to afford *R*-(−)-**6b** (30.5 mg, 47%, 97.5% ee; HPLC condition: Chiralcel OD-H, *n*-hexane/*i*-PrOH=90/10, 0.8 mL/min, λ=230 nm, t_R 6.3 (major), 5.9 (minor); $[\alpha]_D^{20}$ −107.5 (*c* 0.83, $CHCl_3$)): liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, J=7.8 Hz, 2H), 7.16 (d, J=7.8 Hz, 2H), 5.07–4.96 (m, 3H), 2.35 (s, 3H), 2.23 (d, J=4.2 Hz, 1H), 1.87–1.72 (m, 2H), 1.42–1.19 (m, 4H), 0.85 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.9, 139.1, 137.5, 129.0, 126.7, 108.3, 79.8, 73.8, 29.6, 27.7, 22.3, 21.2, 13.9; IR (neat) ν (cm^{-1}) 3406, 2928, 1955, 1614, 1513, 1030; MS (70 eV, EI) m/z (%): 216 (M^+, 0.58), 201 (M^+-CH_3, 8.16), 121 (100); HRMS calcd for $C_{15}H_{20}O$ (M^+): 216.1514, found: 216.1515.

4.5.4. (1*S*)-(+)-2-Butyl-1-(4′-methylphenyl)-2,3-butadien-1-ol (*S*-(+)-**6b**)

To a solution of (4*S*)-(−)-4-hydroxy-(4′-methylphenyl)-2-butynyl methyl ether *S*-(−)-**5b** (57.3 mg, 98.6% ee, 0.30 mmol) and CuBr (8.6 mg, 0.06 mmol) in Et_2O (1.6 mL) was added dropwise a solution of *n*-C_4H_9MgBr in Et_2O (1.4 mL, 1 M in Et_2O, 1.4 mmol) to afford *S*-(+)-**6b** (29.1 mg, 45%, 98.9% ee; HPLC condition: Chiralcel OD-H, *n*-hexane/*i*-PrOH=90/10, 0.8 mL/min, λ=230 nm, t_R 5.8 (major), 6.3 (minor); $[\alpha]_D^{20}$ +106.2 (*c* 0.76, $CHCl_3$)): liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, J=8.1 Hz, 2H), 7.15 (d, J=8.1 Hz, 2H), 5.08–4.95 (m, 3H), 2.35 (s, 3H), 2.22 (d, J=4.2 Hz, 1H), 1.87–1.72 (m, 2H), 1.42–1.19 (m, 4H), 0.84 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.9, 139.1, 137.5, 129.0, 126.7, 108.3, 79.8, 73.8, 29.6, 27.7, 22.3, 21.2, 13.9; IR (neat) ν (cm^{-1}) 3397, 2927, 1955, 1614, 1513, 1030; MS (70 eV, EI) m/z (%): 216 (M^+, 0.62), 201 (M^+-CH_3, 8.63), 121 (100); HRMS calcd for $C_{15}H_{20}O$ (M^+): 216.1514, found: 216.1512.

4.5.5. (1*R*)-(−)-2-Butyl-1-(3′,4′-methylenedioxyphenyl)-2,3-butadien-1-ol (*R*-(−)-**6c**)

To a mixture of (4*R*)-(+)-4-hydroxy-4-(3′,4′-methylenedioxyphenyl)-2-butynyl methyl ether *R*-(+)-**5c** (68.0 mg, 98.6% ee, 0.31 mmol) and CuBr (8.5 mg, 0.06 mmol) in anhydrous Et_2O (1.6 mL) was added dropwise a solution of *n*-C_4H_9MgBr in Et_2O (1.4 mL, 1 M in Et_2O, 1.4 mmol) to afford *R*-(−)-**6c**[6b] (19.7 mg, 26%,

98.5% ee; HPLC condition: Chiralcel OD-H, *n*-hexane/*i*-PrOH=90/10, 0.8 mL/min, λ=230 nm, t_R 9.8 (major), 7.9 (minor); $[\alpha]_D^{20}$ −97.6 (*c* 1.23, $CHCl_3$)): liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 6.86 (d, *J*=1.5 Hz, 1H), 6.83 (dd, J_1=8.1 Hz, J_2=1.5 Hz, 1H), 6.76 (d, *J*=7.8 Hz, 1H), 5.95 (s, 2H), 5.06–4.95 (m, 3H), 2.26–2.18 (m, 1H), 1.89–1.69 (m, 2H), 1.43–1.19 (m, 4H), 0.84 (t, *J*=7.2 Hz, 3H). According to the ^1H NMR analysis of the crude reaction mixture there was 6% of *R*-(+)-**5c** remaining.

4.5.6. (1*S*)-(+)-2-Butyl-1-(3′,4′-methylenedioxyphenyl)-2,3-butadien-1-ol (*S*-(+)-**6c**)

To a mixture of (4*S*)-(−)-4-hydroxy-4-(3′,4′-methylenedioxyphenyl)-2-butynyl methyl ether *S*-(−)-**5c** (64.5 mg, 97.1% ee, 0.29 mmol) and CuBr (8.6 mg, 0.06 mmol) in anhydrous Et_2O (1.6 mL) was added dropwise a solution of *n*-C_4H_9MgBr in Et_2O (1.4 mL, 1 M in Et_2O, 1.4 mmol) to afford *S*-(+)-**6c**[6b] (20.3 mg, 28%, 96.9% ee; HPLC condition: Chiralcel OD-H, *n*-hexane/*i*-PrOH=90/10, 0.8 mL/min, λ=230 nm, t_R 7.9 (major), 9.9 (minor); $[\alpha]_D^{20}$ +96.2 (*c* 1.11, $CHCl_3$)): liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 6.86 (d, *J*=1.5 Hz, 1H), 6.83 (dd, J_1=7.8 Hz, J_2=1.5 Hz, 1H), 6.76 (d, *J*=7.8 Hz, 1H), 5.95 (s, 2H), 5.06–4.95 (m, 3H), 2.24 (d, *J*=3.9 Hz, 1H), 1.89–1.69 (m, 2H), 1.43–1.19 (m, 4H), 0.84 (t, *J*=7.2 Hz, 3H). According to the ^1H NMR analysis of the crude reaction mixture there was 6% of *S*-(−)-**5c** remaining.

4.5.7. (1*R*)-(−)-2-Butyl-1-(4′-methoxyphenyl)-2,3-butadien-1-ol (*R*-(−)-**6d**)

To a solution of (4*R*)-(+)-4-hydroxy-(4′-methoxyphenyl)-2-butynyl methyl ether *R*-(+)-**5d** (61.0 mg, 96.7% ee, 0.30 mmol) and CuBr (8.8 mg, 0.06 mmol) in anhydrous Et_2O (1.6 mL) was added dropwise a solution of *n*-C_4H_9MgBr in Et_2O (1.4 mL, 1 M in Et_2O, 1.4 mmol) to afford *R*-(−)-**6d**[6b] (33.2 mg, 48%, 95.3% ee; HPLC condition: Chiralcel OD-H, *n*-hexane/*i*-PrOH=90/10, 0.8 mL/min, λ=230 nm, t_R 8.6 (major), 7.4 (minor); $[\alpha]_D^{20}$ −144.6 (*c* 0.57, $CHCl_3$)): liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 7.31–7.27 (m, 2H), 6.90–6.86 (m, 2H), 5.05–4.96 (m, 3H), 3.81 (s, 3H), 2.21 (d, *J*=4.2 Hz, 1H), 1.87–1.71 (m, 2H), 1.43–1.19 (m, 4H), 0.84 (t, *J*=7.2 Hz, 3H). According to the ^1H NMR analysis of the crude reaction mixture there was 7% of *R*-(+)-**5d** remaining.

4.5.8. (1*S*)-(+)-2-Butyl-1-(4′-methoxyphenyl)-2,3-butadien-1-ol (*S*-(+)-**6d**)

To a solution of (4*S*)-(−)-4-hydroxy-(4′-methoxyphenyl)-2-butynyl methyl ether *S*-(−)-**5d** (62.0 mg, 96.4% ee, 0.30 mmol) and CuBr (8.7 mg, 0.06 mmol) in anhydrous Et_2O (1.6 mL) was added dropwise a solution of *n*-C_4H_9MgBr in Et_2O (1.4 mL, 1 M in Et_2O, 1.4 mmol) to afford *S*-(+)-**6d**[6b] (34.3 mg, 49%, 95.8% ee; HPLC condition: Chiralcel OD-H, *n*-hexane/*i*-PrOH=90/10, 0.8 mL/min, λ=230 nm, t_R 7.5 (major), 8.6 (minor); $[\alpha]_D^{20}$ +138.3 (*c* 0.59, $CHCl_3$)): liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32–7.27 (m, 2H), 6.91–6.84 (m, 2H), 5.05–4.96 (m, 3H), 3.80 (s, 3H), 2.25 (d, *J*=4.2 Hz, 1H), 1.87–1.71 (m, 2H), 1.43–1.31 (m, 2H), 1.31–1.19 (m, 2H), 0.84 (t, *J*=7.2 Hz, 3H).

4.5.9. (1*R*)-(−)-2-Ethyl-1-phenyl-2,3-butadien-1-ol (*R*-(−)-**6e**)

To a solution of (4*R*)-(+)-4-hydroxy-4-phenyl-2-butynyl methyl ether *R*-(+)-**5a** (53.2 mg, 98.2% ee, 0.30 mmol) and CuBr (8.8 mg, 0.06 mmol) in anhydrous Et_2O (1.6 mL) was added dropwise a solution of C_2H_5MgBr in Et_2O (1.4 mL, 1 M in Et_2O, 1.4 mmol) to afford *R*-(−)-**6e**[13a] (20.8 mg, 40%, 99.5% ee; HPLC condition: Chiralcel OD-H, *n*-hexane/*i*-PrOH=90/10, 0.8 mL/min, λ=230 nm, t_R 7.8 (major), 7.2 (minor); $[\alpha]_D^{20}$ −129.8 (*c* 0.54, $CHCl_3$)): liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 7.41–7.27 (m, 5H), 5.14–5.09 (m, 1H), 5.09–4.98 (m, 2H), 2.26 (d, *J*=3.3 Hz, 1H), 1.90–1.76 (m, 2H), 0.97 (t, *J*=7.5 Hz, 3H). According to the ^1H NMR analysis of the crude reaction mixture there was 8% of *R*-(+)-**5a** remaining.

4.5.10. (1*S*)-(+)-2-Ethyl-1-phenyl-2,3-butadien-1-ol (*S*-(+)-**6e**)

To a solution of (4*S*)-(−)-4-hydroxy-4-phenyl-2-butynyl methyl ether *S*-(−)-**5a** (49.9 mg, 96.1% ee, 0.28 mmol) and CuBr (8.6 mg, 0.06 mmol) in anhydrous Et_2O (1.6 mL) was added dropwise a solution of C_2H_5MgBr in Et_2O (1.4 mL, 1 M in Et_2O, 1.4 mmol) to afford *S*-(+)-**6e** (17.5 mg, 35%, 99.5% ee; HPLC condition: Chiralcel OD-H, *n*-hexane/*i*-PrOH=90/10, 0.8 mL/min, λ=230 nm, t_R 7.2 (major), 7.8 (minor); $[\alpha]_D^{20}$ +128.7 (*c* 0.35, $CHCl_3$)): liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 7.41–7.27 (m, 5H), 5.14–5.09 (m, 1H), 5.09–4.98 (m, 2H), 2.25 (d, *J*=4.2 Hz, 1H), 1.90–1.76 (m, 2H), 0.97 (t, *J*=7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.9, 142.1, 128.2, 127.6, 126.6, 109.8, 80.0, 74.0, 20.8, 11.9; IR (neat) ν (cm^{-1}) 3384, 2966, 1957, 1603, 1454, 1018; MS (70 eV, EI) *m*/*z* (%): 174 (M^+, 4.33), 173 (M^+−H, 16.6), 107 (100). According to the ^1H NMR analysis of the crude reaction mixture there was 5% of *S*-(−)-**5a** remaining.

4.5.11. (1*R*)-(−)-1-Phenyl-2-propyl-2,3-butadien-1-ol (*R*-(−)-**6f**)

To a solution of (4*R*)-(+)-4-hydroxy-4-phenyl-2-butynyl methyl ether *R*-(+)-**5a** (51.6 mg, 98.2% ee, 0.29 mmol) and CuBr (8.7 mg, 0.06 mmol) in anhydrous Et_2O (1.6 mL) was added dropwise a solution of *n*-C_3H_7MgBr in Et_2O (1.4 mL, 1 M in Et_2O, 1.4 mmol) to afford *R*-(−)-**6f**[13a] (20.2 mg, 37%, 99.7% ee; HPLC condition: Chiralcel OD-H, *n*-hexane/*i*-PrOH=90/10, 0.8 mL/min, λ=230 nm, t_R 7.4 (major), 6.8 (minor); $[\alpha]_D^{20}$ −123.2 (*c* 0.60, $CHCl_3$) (lit.[13a] $[\alpha]_D^{20}$ −120 (*c* 1.75, $CHCl_3$))): liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 7.42–7.27 (m, 5H), 5.13–5.07 (m, 1H), 5.06–4.95 (m, 2H), 2.24 (d, *J*=4.2 Hz, 1H), 1.87–1.72 (m, 2H), 1.48–1.34 (m, 2H), 0.86 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.0, 142.1, 128.3, 127.8, 126.7, 108.1, 79.8, 74.1, 30.0, 20.7, 13.8; IR (neat) ν (cm^{-1}) 3396, 2959, 1956, 1602, 1453, 1016; MS (70 eV, EI) *m*/*z* (%) 188 (M^+, 4.28), 107 (100); HRMS calcd for $C_{13}H_{16}O$ (M^+): 188.1201, found: 188.1203. According to the ^1H NMR analysis of the crude reaction mixture there was 7% of *R*-(+)-**5a** remaining.

4.5.12. (1*S*)-(+)-1-Phenyl-2-propyl-2,3-butadien-1-ol (*S*-(+)-**6f**)

To a solution of (4*S*)-(−)-4-hydroxy-4-phenyl-2-butynyl methyl ether *S*-(−)-**5a** (52.2 mg, 96.1% ee, 0.30 mmol) and CuBr (8.6 mg, 0.06 mmol) in anhydrous Et_2O (1.6 mL) was added dropwise a solution of *n*-C_3H_7MgBr in Et_2O (1.4 mL, 1 M in Et_2O, 1.4 mmol) to afford *S*-(+)-**6f** (21.9 mg, 39%, 97.9% ee; HPLC condition: Chiralcel OD-H, *n*-hexane/*i*-PrOH=90/10, 0.8 mL/min, λ=230 nm, t_R 6.9 (major), 7.4 (minor); $[\alpha]_D^{20}$ +122.2 (*c* 0.72, $CHCl_3$)): liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 7.42–7.27 (m, 5H), 5.13–5.07 (m, 1H), 5.06–4.95 (m, 2H), 2.27 (d, *J*=4.5 Hz, 1H), 1.88–1.70 (m, 2H), 1.48–1.34 (m, 2H), 0.87 (t, *J*=7.2 Hz, 3H). According to the ^1H NMR analysis of the crude reaction mixture there was 5% of *S*-(−)-**5a** remaining.

4.5.13. (1*R*)-(−)-2-Pentyl-1-phenyl-2,3-butadien-1-ol (*R*-(−)-**6g**)

To a solution of (4*R*)-(+)-4-hydroxy-4-phenyl-2-butynyl methyl ether *R*-(+)-**5a** (53.2 mg, 98.2% ee, 0.30 mmol) and CuBr (8.6 mg, 0.06 mmol) in anhydrous Et_2O (1.6 mL) was added dropwise a solution of *n*-$C_5H_{11}MgBr$ in Et_2O (1.4 mL, 1 M in Et_2O, 1.4 mmol) for 8 h to afford *R*-(−)-**6g** (31.8 mg, 49%, 99.6% ee; HPLC condition: Chiralcel OD-H, *n*-hexane/*i*-PrOH=90/10, 0.8 mL/min, λ=230 nm, t_R 6.8 (major), 6.2 (minor); $[\alpha]_D^{20}$ −118.5 (*c* 1.05, $CHCl_3$)): liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40–7.27 (m, 5H), 5.12–5.07 (m, 1H), 5.06–4.95 (m, 2H), 2.31 (d, *J*=3.9 Hz, 1H), 1.92–1.71 (m, 2H), 1.47–1.33 (m, 2H), 1.32–1.18 (m, 4H), 0.85 (t, *J*=6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.0, 142.1, 128.3, 127.7, 126.7, 108.3, 79.8, 74.1, 31.4, 27.8, 27.1, 22.4, 14.0; IR (neat) ν (cm^{-1}) 3387, 2928, 1956, 1603, 1453, 1018; MS (70 eV, EI) *m*/*z* (%) 216 (M^+, 2.89), 201 (M^+−CH_3, 2.69), 107 (100); HRMS calcd for $C_{15}H_{20}O$ (M^+): 216.1514, found: 216.1512. According to the ^1H NMR analysis of the crude reaction mixture there was 11% of *R*-(+)-**5a** remaining.

4.5.14. (1*R*)-(−)-2-Hexyl-1-phenyl-2,3-butadien-1-ol (*R*-(−)-**6h**)

To a solution of (4*R*)-(+)-4-hydroxy-4-phenyl-2-butynyl methyl ether *R*-(+)-**5a** (51.6 mg, 98.2% ee, 0.29 mmol) and CuBr (8.8 mg, 0.06 mmol) in anhydrous Et_2O (1.6 mL) was added dropwise a solution of *n*-$C_6H_{13}MgBr$ in Et_2O (1.4 mL, 1 M in Et_2O, 1.4 mmol) to

afford *R*-(−)-**6h** (34.6 mg, 51%, 99.6% ee; HPLC condition: Chiralcel OD-H, *n*-hexane/*i*-PrOH=90/10, 0.8 mL/min, λ=230 nm, t_R 6.6 (major), 6.1 (minor); $[\alpha]_D^{20}$ −114.8 (*c* 1.12, $CHCl_3$)): liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40–7.27 (m, 5H), 5.12–5.07 (m, 1H), 5.06–4.95 (m, 2H), 2.29 (br s, 1H), 1.87–1.72 (m, 2H), 1.44–1.33 (m, 2H), 1.33–1.15 (m, 6H), 0.85 (t, *J*=6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.0, 142.1, 128.3, 127.7, 126.7, 108.3, 79.8, 74.1, 31.6, 28.9, 27.9, 27.4, 22.6, 14.0; IR (neat) ν (cm^{-1}) 3390, 2927, 1956, 1603, 1454, 1021; MS (70 eV, EI) *m*/*z* (%) 230 (M^+, 5.29), 107 (100); HRMS calcd for $C_{16}H_{22}O$ (M^+): 230.1671, found: 230.1675. According to the ^1H NMR analysis of the crude reaction mixture there was 10% of *R*-(+)-**5a** remaining.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.02.061.

References and notes

1. (a) Moreau, J. L. In *The Chemistry of Ketenes, Allenes, and Related Compounds*; Patai, S., Ed.; John Wiley & Sons: New York, NY, 1980; Part 1; (b) *The Chemistry of Allenes*; Landor, S. R., Ed.; Academic: London, 1982; (c) Schuster, H. F.; Coppola, G. M. *Allenes in Organic Synthesis*; John Wiley & Sons: New York, NY, 1988; (d) Yamamoto, H. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; (e) *Modern Allene Chemistry*; Krause, N., Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, 2004.
2. For reviews on the chemistry of allenes, see: (a) Zimmer, R.; Dinesh, C. U.; Nandanan, E.; Khan, F. A. *Chem. Rev.* **2000**, *100*, 3067; (b) Marshall, J. A. *Chem. Rev.* **2000**, *100*, 3163; (c) Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2000**, *39*, 3590; (d) Bates, R.; Satcharoen, V. *Chem. Soc. Rev.* **2002**, *31*, 12; (e) Sydnes, L. K. *Chem. Rev.* **2003**, *103*, 1133; (f) Ma, S. *Acc. Chem. Res.* **2003**, *36*, 701; (g) Brandsma, L.; Nedolya, N. A. *Synthesis* **2004**, 735; (h) Tius, M. A. *Acc. Chem. Res.* **2003**, *36*, 284; (i) Wei, L.-L.; Xiong, H.; Hsung, R. P. *Acc. Chem. Res.* **2003**, *36*, 773; (j) Lu, X.; Zhang, C.; Xu, Z. *Acc. Chem. Res.* **2001**, *34*, 535; (k) Wang, K. K. *Chem. Rev.* **1996**, *96*, 207; (l) Ma, S. *Chem. Rev.* **2005**, *105*, 2829; (m) Ma, S. *Aldrichimica Acta* **2007**, *40*, 91.
3. Deng, Y.; Gu, Z.; Ma, S. *Chin. J. Org. Chem.* **2006**, *26*, 1468.
4. (a) Olsson, L.-I.; Claesson, A. *Synthesis* **1979**, 743; (b) Nikam, S. S.; Chu, K. H.; Wang, K. K. *J. Org. Chem.* **1986**, *51*, 745; (c) Marshall, J. A.; Wang, X. *J. Org. Chem.* **1990**, *55*, 2995; (d) Marshall, J. A.; Pinney, K. G. *J. Org. Chem.* **1993**, *58*, 7180; (e) Marshall, J. A.; Sehon, C. A. *J. Org. Chem.* **1995**, *60*, 5966; (f) Ma, S.; Gao, W. *Tetrahedron Lett.* **2000**, *41*, 8933; (g) Hoffmann-Röder, A.; Krause, N. *Org. Lett.* **2001**, *3*, 2537.
5. (a) Friesen, R. W.; Blouin, M. *J. Org. Chem.* **1993**, *58*, 1653; (b) Ma, S.; Zhao, S. *J. Am. Chem. Soc.* **1999**, *121*, 7943.
6. (a) Fu, C.; Li, J.; Ma, S. *Chem. Commun.* **2005**, 4119; (b) Li, J.; Fu, C.; Chen, G.; Chai, G.; Ma, S. *Adv. Synth. Catal.* **2008**, *350*, 1376.
7. (a) Wotiz, J. H.; Mancuso, D. E. *J. Org. Chem.* **1957**, *22*, 207; (b) Mukaiyama, T.; Harada, T. *Chem. Lett.* **1981**, 621; (c) Isaac, M. B.; Chan, T.-H. *J. Chem. Soc., Chem. Commun.* **1995**, 1003.
8. (a) Place, P.; Delbecq, F.; Gore, J. *Tetrahedron Lett.* **1978**, *19*, 3801; (b) Flahaut, J.; Miginiac, P. *Helv. Chim. Acta* **1978**, *61*, 2275; (c) Girard, P.; Namy, J. L.; Kagan, H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693.
9. Crabbé, P.; Fillion, H.; André, D.; Luche, J.-L. *J. Chem. Soc., Chem. Commun.* **1979**, 859.
10. Yu, C.-M.; Kim, C.; Kweon, J.-H. *Chem. Commun.* **2004**, 2494.
11. (a) Corey, E. J.; Yu, C.-M.; Lee, D.-H. *J. Am. Chem. Soc.* **1990**, *112*, 878; (b) Marshall, J. A.; Perkins, J. *J. Org. Chem.* **1994**, *59*, 3509; (c) Marshall, J. A.; Adams, N. D. *J. Org. Chem.* **1997**, *62*, 8976; (d) Hernandez, E.; Soderquist, J. A. *Org. Lett.* **2005**, *7*, 5397; (e) Hernandez, E.; Burgos, C. H.; Alicea, E.; Soderquist, J. A. *Org. Lett.* **2006**, *8*, 4089.
12. Ma, S.; Hou, H.; Zhao, S.; Wang, G. *Synthesis* **2002**, 1643.
13. (a) Yu, C.-M.; Yoon, S.-K.; Baek, K.; Lee, J.-Y. *Angew. Chem., Int. Ed.* **1998**, *37*, 2392; (b) Schultz-Fademrecht, C.; Wibbeling, B.; Fröhlich, R.; Hoppe, D. *Org. Lett.* **2001**, *3*, 1221; (c) Inoue, M.; Nakada, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 252; (d) Xia, G.; Yamamoto, H. *J. Am. Chem. Soc.* **2007**, *129*, 496.
14. Marshall, J. A.; Tang, Y. *J. Org. Chem.* **1993**, *58*, 3233.
15. (a) Xu, D.; Li, Z.; Ma, S. *Chem.—Eur. J.* **2002**, *8*, 5012; (b) Xu, D.; Li, Z.; Ma, S. *Tetrahedron: Asymmetry* **2003**, *14*, 3657.
16. Moreau, J.-L.; Gaudemar, M. *J. Organomet. Chem.* **1976**, *108*, 159.
17. Lu, Z.; Ma, S. *Adv. Synth. Catal.* **2007**, *349*, 1225.
18. Xu, D.; Li, Z.; Ma, S. *Tetrahedron Lett.* **2003**, *44*, 6343.
19. Zhou, C.; Li, J.; Lü, B.; Fu, C.; Ma, S. *Org. Lett.* **2008**, *10*, 581.
20. Ma, S.; Gao, W. *J. Org. Chem.* **2002**, *67*, 6104.
21. Ma, S.; Xie, H. *Tetrahedron* **2005**, *61*, 251.
22. Yi, X.; Meng, Y.; Hua, X.; Li, C. *J. Org. Chem.* **1998**, *63*, 7472.
23. Suzuki, M.; Morita, Y.; Noyori, R. *J. Org. Chem.* **1990**, *55*, 441.
24. Ma, S.; Jiao, N.; Yang, Q.; Zheng, Z. *J. Org. Chem.* **2004**, *69*, 6463.