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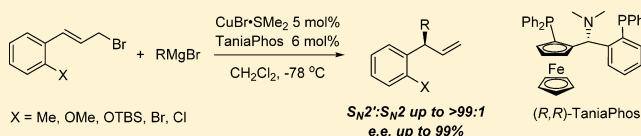
# Regio- and Enantioselective Copper-Catalyzed Allylic Alkylation of Ortho-Substituted Cinnamyl Bromides with Grignard Reagents

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**S** Supporting Information

**ABSTRACT:** A highly efficient method for the copper-catalyzed asymmetric allylic alkylation of ortho-substituted cinnamyl bromides with Grignard reagents is reported. The use of a catalytic system comprising CuBr·SMe<sub>2</sub> and TaniaPhos as chiral ligands gives rise to a range of branched products with excellent regio- and enantioselectivity.



## INTRODUCTION

Copper-catalyzed asymmetric allylic alkylation (AAA) has become a powerful tool for the introduction of configurationally defined stereogenic carbon atoms.<sup>1</sup> Since the pioneering work of Bäckvall and van Koten,<sup>2</sup> in which they described the use of an arenethiolatocopper complex for the AAA of allyl esters with Grignard reagents, several highly efficient methods based on phosphoramidite,<sup>3</sup> diphosphine,<sup>4</sup> phosphine–phosphite,<sup>5</sup> and NHC ligands<sup>6</sup> have been reported for the AAA of different allyl substrates with these organometallic compounds. While these methodologies usually afford the corresponding branched products with very high regio- and enantioselectivity, the use of important ortho-substituted cinnamyl substrates still represents a challenge in this field, especially when the AAA is performed with MeMgBr, as the regio- and enantioselectivity reached decreases significantly (Scheme 1a,b).<sup>3b,5a</sup>

The resulting ortho-substituted chiral allyl compounds are of particular importance for synthetic applications as they can be versatile precursors of carbo- and heterocycles through various cyclization reactions.<sup>7</sup> Therefore, the development of an efficient and highly selective catalytic method for the AAA of ortho-substituted substrates remains an important goal.

The combination of CuBr·SMe<sub>2</sub> with TaniaPhos L3 has emerged as an excellent catalyst for the introduction of the methyl unit via copper-catalyzed AAA.<sup>4</sup> However, the use of this catalytic system has not been reported for the copper-catalyzed AAA of ortho-substituted cinnamyl substrates. Herein, we present a highly regio- and enantioselective CuBr·SMe<sub>2</sub>/TaniaPhos-catalyzed AAA of ortho-substituted cinnamyl bromides with MeMgBr (Scheme 1c). This transformation is also extended to the use of other Grignard reagents.

## RESULTS AND DISCUSSION

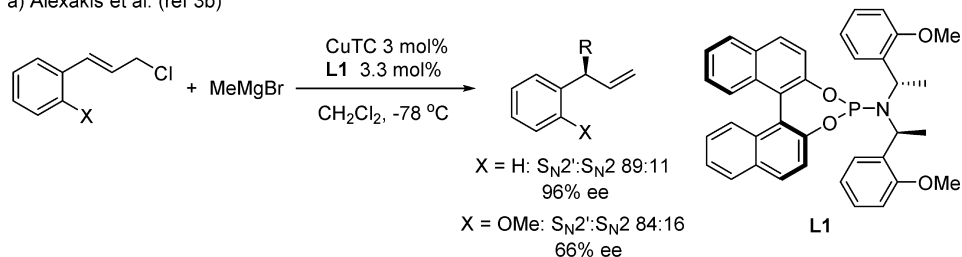
We started our investigation by carrying out the reaction between *o*-bromocinnamyl bromide **1a** and MeMgBr in CH<sub>2</sub>Cl<sub>2</sub> at –78 °C (Table 1). When we performed the reaction at this temperature using 1.5 equiv of MeMgBr, branched product **2a** was formed with very good regioselectivity but with incomplete conversion (entry 1). A longer reaction time slightly improved the conversion but not sufficiently (entry 2). Complete conversion could be achieved by the use of 3 equiv of MeMgBr at –78 °C, which allowed us to obtain **2a** with a near-perfect  $S_N2'/S_N2$  ratio and enantiomeric excess (99% ee) (entry 4). A higher temperature (–70 °C) also helped to reach full conversion using only 1.5 equiv of MeMgBr; however, product **2a** was obtained with slightly lower regio- and enantioselectivity in this case (entry 3).

Having established the optimized conditions for the copper-catalyzed AAA of **1a**, we set out to investigate the compatibility of this method with substrates bearing different ortho substituents (Table 2). To our delight, the CuBr·SMe<sub>2</sub>/TaniaPhos system proved to be very efficient for the enantioselective methylation of chloro-, methyl-, and alkoxy-substituted substrates **1b–e**, leading in all cases to the formation of the corresponding branched product **2b–e** with excellent regio- and enantioselectivity (entries 2–5). Different alkyl Grignard reagents were also used in this transformation. Similarly, the use of EtMgBr and *n*-HexMgBr in combination with bromo- and methoxy-substituted substrates **1a** and **1d** gave rise to the corresponding products **2** with excellent selectivities (entries 6–12). We found that reactions involving EtMgBr proceed with better selectivities when a solution of 1.1 equiv of this Grignard reagent (reverse addition) is added to the mixture of catalyst and allyl bromide (entries 6, 7 and 11, 12). Finally, a decrease in the regioselectivity of the reaction was observed when EtMgBr was used for the AAA of methyl-substituted substrate **1c**, although product **2j** was still obtained with excellent enantioselectivity (entry 12).<sup>8</sup> To illustrate the synthetic utility of the current methodology, we performed the synthesis of **2g** on a larger scale (0.98 mmol), obtaining the title compound with similar yield and selectivity.

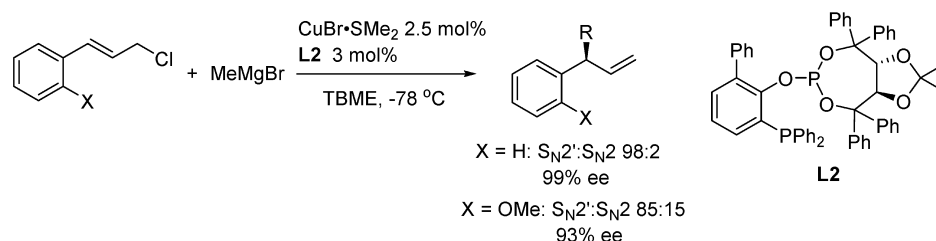
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## Scheme 1. Copper-Catalyzed AAA of Ortho-Substituted Cinnamyl Substrates with MeMgBr

a) Alexakis et al. (ref 3b)



b) Schmalz et al. (ref 5a)



c) This work

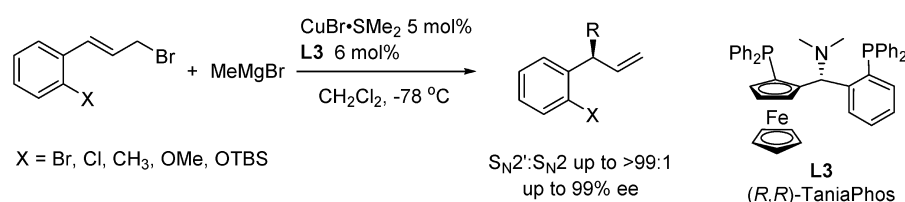
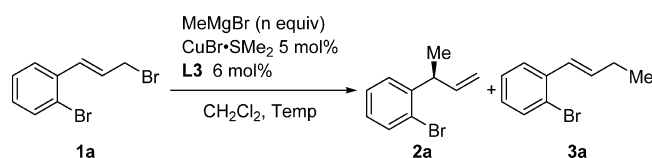


Table 1. Optimization of the Copper-Catalyzed AAA of 1a



entry <sup>a</sup>	MeMgBr (equiv)	temp (°C)	conv <sup>b,c</sup> (%)	2a:3a <sup>d</sup>	ee of 2a <sup>d</sup> (%)
1	1.5	-78	80	94:6	n.d. <sup>f</sup>
2 <sup>e</sup>	1.5	-78	90	>99:1	n.d. <sup>f</sup>
3	1.5	-70	full (70)	96:4	98
4	3.0	-78	full (71)	99:1	99

<sup>a</sup>Reaction conditions: A solution of **1a** (1.0 equiv, 0.25 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (1 mL) was added to a solution of catalyst and MeMgBr in CH<sub>2</sub>Cl<sub>2</sub> (2 mL); reaction run over 16 h. <sup>b</sup>Determined by <sup>1</sup>H NMR analysis. <sup>c</sup>Yield of isolated product shown in parentheses. <sup>d</sup>Determined by GC analysis. <sup>e</sup>Reaction stirred for 48 h. <sup>f</sup>n.d. = not determined.

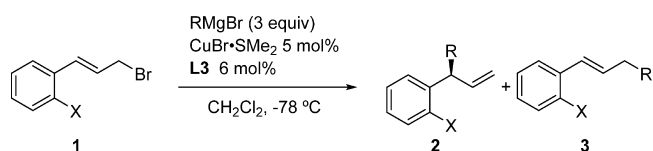
## CONCLUSION

In summary, we have shown that CuBr·SMe<sub>2</sub>/TaniaPhos is an efficient catalyst for the AAA of ortho-substituted cinnamyl substrates. The reaction with MeMgBr proceeds with excellent regio- and enantioselectivity independent of the nature of the ortho substituent. Longer alkyl Grignard reagents are also tolerated by this catalytic system, and the corresponding branched products are also obtained with excellent chemo-, regio-, and enantioselectivities.

## EXPERIMENTAL SECTION

**General Procedures.** Chromatography was performed on silica gel (230–400 mesh). Thin-layer chromatography was performed on

Table 2. Scope of the Reaction



entry <sup>a</sup>	1, X	R	yield <sup>b</sup> (%)	2:3 <sup>c</sup>	ee of 2 <sup>d</sup> (%)
1	1a, Br	Me	71	99:1	2a, 99
2	1b, Cl	Me	69	>99:1	2b, 98
3	1c, CH <sub>3</sub>	Me	87	98:2	2c, 98
4	1d, OMe	Me	53 <sup>f</sup>	>99:1	2d, 96
5	1e, OTBS	Me	77	97:3	2e, >99
6	1a, Br	Et	40	90:10	2f, 99
7 <sup>e</sup>	1a, Br	Et	76	92:8	2f, 99
8	1a, Br	<i>n</i> -Hex	87 (76) <sup>g</sup>	93:7 (91:9) <sup>g</sup>	2g, 98 (98) <sup>g</sup>
9	1d, OMe	Et	46 <sup>f</sup>	92:8	2h, 93
10	1d, OMe	<i>n</i> -Hex	45 <sup>f</sup>	94:6	2i, 99
11	1c, CH <sub>3</sub>	Et	90	75:25	2j, 92
12 <sup>e</sup>	1c, CH <sub>3</sub>	Et	88	78:22	2j, 96

<sup>a</sup>Reaction conditions: see Table 1, entry 4. <sup>b</sup>Yield of isolated product. <sup>c</sup>Determined by GC analysis. <sup>d</sup>Determined by GC or HPLC analysis. <sup>e</sup>1.1 equiv of EtMgBr; reverse addition. <sup>f</sup>Lower yields are due to instability of substrate **1d**. <sup>g</sup>Reaction performed on a 0.98 mmol scale.

silica plates. Compounds were visualized by UV and cerium/molybdenum or potassium permanganate staining. Progress and conversion of the reaction were determined by GC–MS. Mass spectra were recorded on a mass spectrometer using an orbitrap analyzer. <sup>1</sup>H and <sup>13</sup>C NMR were recorded on 400 and 100.59 MHz using CDCl<sub>3</sub> as solvent. Chemical shift values are reported in ppm with the solvent resonance as the internal standard (CHCl<sub>3</sub>: δ 7.26 for <sup>1</sup>H, δ 77.0 for <sup>13</sup>C). Data are reported as follows: chemical shifts, multiplicity (*s* =

singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), and integration. Optical rotations were measured on a polarimeter with a 10 cm cell ( $c$  given in g/100 mL). Enantiomeric excess values were determined by chiral HPLC analysis using a diode array detector.

All reactions were carried out under a nitrogen atmosphere using oven-dried glassware and using standard Schlenk techniques. All reagents, CuBr-SMe<sub>2</sub>, and TaniaPhos (L3) were purchased from commercial sources and used without further purification. Dichloromethane was used from a solvent purification system. Allyl bromides **1** were synthesized from the corresponding benzaldehydes following a three-step Horner–Wadsworth–Emmons/DIBAL-H reduction/PBr<sub>3</sub> bromination sequence according to literature procedures.<sup>9</sup>

**General Procedure for the Copper-Catalyzed AAA of Ortho-Substituted Cinnamyl Bromides 1.** A Schlenk tube equipped with septum and stirring bar was charged with CuBr-SMe<sub>2</sub> (0.01 mmol, 2.05 mg, 5 mol %) and (*R<sub>p</sub>*,*R*)-TaniaPhos (L3) (0.012 mmol, 8.24 mg, 6 mol %). CH<sub>2</sub>Cl<sub>2</sub> (2.0 mL) was added, and the solution was stirred for 15 min at room temperature. The mixture was cooled to -78 °C, and the corresponding Grignard reagent (solution in Et<sub>2</sub>O, 3 equiv) was added dropwise. The corresponding allyl bromide **1** (0.2 mmol) was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (0.8 mL) and added dropwise to the reaction mixture over 1 h via a syringe pump. Once the addition was complete, the resulting mixture was further stirred at -78 °C overnight. The reaction was quenched with MeOH (0.5 mL) and the mixture allowed to reach room temperature. Aqueous NH<sub>4</sub>Cl solution (2 mL) was added to the mixture, and the organic phase was separated. The resulting aqueous layer was extracted with Et<sub>2</sub>O (3 × 5 mL), and the combined organic layers were dried over MgSO<sub>4</sub>. The solvent was removed under reduced pressure to yield a yellow oil, which was purified by flash chromatography (pentane) to yield the corresponding products **2**.

Note: Regioselectivity was measured by GC analysis carried out on a sample obtained after aqueous extraction with Et<sub>2</sub>O, which had been passed through a short plug of silica gel to remove transition-metal residues.

**(-)-(S)-1-Bromo-2-(but-3-en-2-yl)benzene (2a).** Obtained as a 99:1 mixture of **2a** and **3a** as a colorless oil (71% yield, **2a** 99% ee,  $[\alpha]_D^{20} = -33.5$  ( $c = 1.0$ , CHCl<sub>3</sub>)). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.55 (d,  $J = 7.9$  Hz, 1H), 7.32–7.18 (m, 2H), 7.06 (td,  $J = 2.1, 8.3$  Hz, 1H), 6.01 (ddd,  $J = 5.6, 10.8, 16.8$  Hz, 1H), 5.17–5.05 (m, 2H), 3.99 (quin,  $J = 6.8$  Hz, 1H), 1.34 (d,  $J = 7.0$  Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  144.4, 141.5, 132.9, 128.2, 127.6, 127.6, 124.4, 113.9, 41.1, 19.5. Enantiomeric excess determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m × 0.25 mm × 0.25  $\mu$ m), initial temp 40 °C, then 10 °C/min to 95 °C (final temp) for 45 min, retention times (min): 32.7 (major) and 33.8 (minor); retention time **3a**: 53.4 min. HRMS (APCI+,  $m/z$ ): calcd for C<sub>10</sub>H<sub>11</sub> [M(-HBr) + H] 131.0855, found 131.0853

**(-)-(S)-1-Chloro-2-(but-3-en-2-yl)benzene (2b).** Obtained as a colorless oil (69% yield, 98% ee,  $[\alpha]_D^{20} = -33.8$  ( $c = 0.7$ , CHCl<sub>3</sub>)). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.36 (d,  $J = 7.9$  Hz, 1H), 7.27–7.19 (m, 2H), 7.14 (td,  $J = 2.6, 7.9$  Hz, 1H), 6.01 (ddd,  $J = 5.7, 10.8, 16.9$  Hz, 1H), 5.16–5.05 (m, 2H), 4.01 (quin,  $J = 6.6$  Hz, 1H), 1.35 (d,  $J = 7.0$  Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  142.8, 141.5, 133.5, 129.5, 128.1, 127.3, 126.9, 113.9, 38.8, 19.3. Enantiomeric excess determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m × 0.25 mm × 0.25  $\mu$ m), initial temp 40 °C, then 10 °C/min to 95 °C (final temp) for 40 min, retention times (min): 20.9 (major) and 21.5 (minor). HRMS (APCI+,  $m/z$ ): calcd for C<sub>10</sub>H<sub>11</sub> [M(-HCl) + H] 131.0855, found 131.0853.

**(-)-(S)-1-Methyl-2-(but-3-en-2-yl)benzene (2c).** Obtained as a 98:2 mixture of **2c** and **3c** as a colorless oil (87% yield, 94% conversion, **2c** 98% ee),  $[\alpha]_D^{20} = -5.8$  ( $c = 1.0$ , CHCl<sub>3</sub>) (lit.<sup>10</sup> (99% ee)  $[\alpha]_D^{20} = -6.99$  ( $c = 1.0$ , CHCl<sub>3</sub>)). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.24–7.06 (m, 4H), 6.00 (ddd,  $J = 6.2, 10.6, 16.9$  Hz, 1H), 5.11–4.94 (m, 2H), 3.71 (quin,  $J = 6.6$  Hz, 1H), 2.36 (s, 3H), 1.36 (d,  $J = 7.0$  Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  143.4, 142.8, 135.5, 130.3, 126.2, 126.2, 125.9, 113.0, 38.6, 19.9, 19.4. Enantiomeric excess determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m × 0.25

mm × 0.25  $\mu$ m), initial temp 40 °C, then 10 °C/min to 95 °C (final temp) for 40 min, retention times (min): 14.8 (minor) and 15.0 (major); retention time **3c**: 18.3 min. HRMS (APCI+,  $m/z$ ): calcd for C<sub>11</sub>H<sub>15</sub> [M + H] 147.1168, found 147.1166

**(-)-(S)-1-Methoxy-2-(but-3-en-2-yl)benzene (2d).** Obtained as a colorless oil (53% yield, 96% ee,  $[\alpha]_D^{20} = -34.2$  ( $c = 0.6$ , CHCl<sub>3</sub>) (lit.<sup>5a</sup> (93% ee, 85:15 S<sub>N</sub>2':S<sub>N</sub>2)  $[\alpha]_D^{20} = -1.9$  ( $c = 0.6$ , CHCl<sub>3</sub>)). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.23–7.12 (m, 2H), 6.92 (t,  $J = 7.5$  Hz, 1H), 6.87 (d,  $J = 8.2$  Hz, 1H), 6.06 (ddd,  $J = 6.2, 10.3, 16.5$  Hz, 1H), 5.11–4.97 (m, 2H), 3.93 (quin,  $J = 6.6$  Hz, 1H), 3.84 (s, 3H), 1.32 (d,  $J = 7.0$  Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  156.7, 142.8, 134.0, 134.0, 127.4, 127.0, 125.6, 112.8, 110.5, 35.5, 19.4. Enantiomeric excess determined by chiral GC analysis, Beta DEX tm 225 (30 m × 0.25 mm × 0.25  $\mu$ m), initial temp 40 °C, then 10 °C/min to 95 °C for 5 min, then 0.2 °C/min to 150 °C (final temp) for 20 min, retention times (min): 20.3 (minor) and 20.6 (major). HRMS (APCI+,  $m/z$ ): calcd for C<sub>11</sub>H<sub>15</sub>O [M + H] 163.1117, found 163.1116.

**(-)-(S)-1-((tert-Butyldimethylsilyloxy)-2-(but-3-en-2-yl)benzene (2e).** Obtained as a 97:3 mixture of **2e** and **2e** as a colorless oil (77% yield, **5e** >99% ee,  $[\alpha]_D^{20} = -26.6$  ( $c = 2.5$ , CHCl<sub>3</sub>)). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.15 (d,  $J = 7.6$  Hz, 1H), 7.08 (t,  $J = 7.3$  Hz, 1H), 6.93 (t,  $J = 7.3$  Hz, 1H), 6.81 (d,  $J = 7.9$  Hz, 1H), 6.06 (ddd,  $J = 5.5, 11.1, 16.4$  Hz, 1H), 5.09–5.00 (m, 2H), 3.95 (quin,  $J = 6.4$  Hz, 1H), 1.31 (d,  $J = 7.0$  Hz, 3H), 1.04 (s, 9H), 0.26 (d,  $J = 4.1$  Hz, 6H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  152.7, 142.8, 136.0, 127.7, 126.7, 121.1, 118.4, 112.8, 35.2, 25.8, 19.5, 18.3, -4.1. Enantiomeric excess determined by chiral HPLC analysis, Chiralcel OD-H column, *n*-heptane/*i*-PrOH 100:0, 40 °C, 210 nm, retention times (min): 8.5 (major) and 9.2 (minor). HRMS (ESI+,  $m/z$ ): calcd for C<sub>16</sub>H<sub>27</sub>OSi [M + H] 263.1826, found 263.1816.

**(-)-(S)-1-Bromo-2-(pent-1-en-3-yl)benzene (2f).** Obtained as a 92:8 mixture of **2f** and **3f** as a colorless oil (76% yield, **2f** 99% ee,  $[\alpha]_D^{20} = -7.3$  ( $c = 1.0$ , CHCl<sub>3</sub>)). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.55 (dd,  $J = 1.0, 8.1$  Hz, 1H), 7.26 (t,  $J = 3.5$  Hz, 1H), 7.20 (dd,  $J = 1.4, 4.6$  Hz, 1H), 7.05 (td,  $J = 1.8, 8.3$  Hz, 1H), 5.91 (ddd,  $J = 7.2, 10.3, 17.1$  Hz, 1H), 5.14–5.01 (m, 2H), 3.75 (q,  $J = 7.3$  Hz, 1H), 1.82–1.68 (m, 2H), 0.90 (t,  $J = 7.3$  Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  143.4, 140.5, 132.9, 128.4, 127.5, 127.5, 125.0, 115.0, 49.4, 27.9, 11.9. Enantiomeric excess determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m × 0.25 mm × 0.25  $\mu$ m), initial temp 40 °C, then 10 °C/min to 75 °C, then 0.5 °C/min to 120 °C (final temp), retention times (min): 54.3 (major) and 54.8 (minor); retention time **3f**: 83.3 min. HRMS (APCI+,  $m/z$ ): calcd for C<sub>11</sub>H<sub>13</sub> [M(-HBr) + H] 145.1012, found 145.1011.

**(-)-(S)-1-Bromo-2-(non-1-en-3-yl)benzene (2g).** Obtained as a 93:7 mixture of **2g** and **3g** as a colorless oil (87% yield, **2g** 98% ee,  $[\alpha]_D^{20} = -2.4$  ( $c = 1.0$ , CHCl<sub>3</sub>)). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.56 (d,  $J = 7.9$  Hz, 1H), 7.32–7.20 (m, 2H), 7.05 (td,  $J = 1.8, 8.2$  Hz, 1H), 5.93 (ddd,  $J = 7.3, 9.7, 16.5$  Hz, 1H), 5.16–5.02 (m, 2H), 3.87 (q,  $J = 7.2$  Hz, 1H), 1.72 (q,  $J = 7.3$  Hz, 2H), 1.43–1.20 (m, 8H), 0.97–0.81 (m, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  143.6, 140.8, 132.9, 128.4, 127.5, 127.4, 124.9, 114.8, 47.7, 35.0, 31.8, 29.3, 27.3, 22.7, 14.1. Enantiomeric excess determined by chiral GC analysis, Chiraldex G-TA (30 m × 0.25 mm × 0.25  $\mu$ m), initial temp 40 °C, then 10 °C/min to 95 °C for 5 min, then 2 °C/min to 150 °C (final temp) for 20 min, retention times (min): 37.2 (minor) and 38.3 (major); retention time **3g**: 38.6 min. HRMS (APCI+,  $m/z$ ): calcd for C<sub>15</sub>H<sub>21</sub> [M(-HBr) + H] 201.1638, found 201.1634.

**(+)-(S)-1-Methoxy-2-(pent-1-en-3-yl)benzene (2h).** Obtained as a 92:8 mixture of **2h** and **3h** as a colorless oil (46% yield, **2h** 93% ee,  $[\alpha]_D^{20} = +7.5$  ( $c = 0.9$ , CHCl<sub>3</sub>)). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.23–7.10 (m, 2H), 6.93 (t,  $J = 7.3$  Hz, 1H), 6.87 (d,  $J = 8.2$  Hz, 1H), 5.99 (ddd,  $J = 7.6, 10.0, 17.2$  Hz, 1H), 5.07–4.97 (m, 2H), 3.82 (s, 3H), 3.65 (q,  $J = 7.3$  Hz, 1H), 1.81–1.63 (m, 2H), 0.88 (t,  $J = 7.5$  Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  157.1, 141.8, 132.9, 127.8, 126.9, 120.6, 113.9, 55.5, 43.9, 27.4, 12.2. Enantiomeric excess determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m × 0.25 mm × 0.25  $\mu$ m), initial temp 40 °C, then 10 °C/min to 95 °C (final temp) for 40 min, retention times (min): 21.9 (major) and 22.1 (minor);

retention time **3h**: 32.0 min. HRMS (APCI+,  $m/z$ ): calcd for  $C_{12}H_{17}O$  [ $M + H$ ] 177.1274, found 177.1272.

(+)-(*S*)-1-Methoxy-2-(*non-1-en-3-yl*)benzene (**2i**). Obtained as a 94:6 mixture of **2i** and **3i** as a colorless oil (45% yield, **2i** 99% ee,  $[\alpha]_D^{20} = +10.5$  ( $c = 1.0$ ,  $CHCl_3$ )).  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  7.22–7.10 (m, 2H), 6.95–6.89 (m, 1H), 6.86 (d,  $J = 7.9$  Hz, 1H), 5.98 (ddd,  $J = 7.7, 10.3, 17.1$  Hz, 1H), 5.05–4.94 (m, 2H), 3.82 (s, 3H), 3.73 (q,  $J = 7.4$  Hz, 1H), 1.72–1.63 (m, 2H), 1.33–1.20 (m, 8H), 0.92–0.83 (m, 3H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  157.0, 142.0, 133.1, 127.8, 126.8, 120.6, 113.6, 110.7, 55.5, 42.11, 34.6, 31.9, 31.8, 29.7, 29.3, 27.5, 22.7, 14.1. Enantiomeric excess determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m  $\times$  0.25 mm  $\times$  0.25  $\mu$ m), initial temp 40  $^\circ$ C, then 10  $^\circ$ C/min to 95  $^\circ$ C for 5 min, then 2  $^\circ$ C/min to 150  $^\circ$ C (final temp) for 20 min, retention times (min): 40.7 (minor) and 40.8 (major); retention time **3i**: 68.1 min. HRMS (ESI+,  $m/z$ ): calcd for  $C_{16}H_{22}O$  [ $M + H$ ] 233.1900, found 233.1890.

(+)-(*S*)-1-Methyl-2-(*pent-1-en-3-yl*)benzene (**2j**). Obtained as a 78:22 mixture of **2j** and **3j** as a colorless oil (88% yield, **2j** 96% ee,  $[\alpha]_D^{20} = +6.3$  ( $c = 0.2$ ,  $CHCl_3$ ), (lit.<sup>11</sup> (83% ee)  $[\alpha]_D^{20} = +19.6$  ( $c = 0.8$   $CHCl_3$ )).  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  7.21–7.05 (m, 4H), 5.88 (ddd,  $J = 7.7, 10.3, 17.3$  Hz, 1H), 5.05–4.91 (m, 2H), 3.40 (q,  $J = 7.4$  Hz, 1H), 2.33 (s, 3H), 1.85–1.66 (m, 2H), 0.96 (t,  $J = 7.3$  Hz, 3H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  142.4, 141.8, 135.9, 130.3, 126.7, 126.1, 125.4, 114.0, 46.7, 27.9, 19.6, 12.2. Enantiomeric excess determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m  $\times$  0.25 mm  $\times$  0.25  $\mu$ m), initial temp 40  $^\circ$ C, then 10  $^\circ$ C/min to 75  $^\circ$ C, then 0.5  $^\circ$ C/min to 120  $^\circ$ C (final temp), retention times (min): 31.1 (major) and 31.6 (minor); retention time **3j**: 52.2 min. MS:  $m/z$  160.1 (21.2,  $M^+$ ), 131.0 (100), 115.0 (29.4), 91.0 (24.3).

## ■ ASSOCIATED CONTENT

### Supporting Information

$^1H$  and  $^{13}C$  spectra and GC and HPLC traces for compounds **2**. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00371.

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### Notes

The authors declare no competing financial interest.

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