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

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#### Abstract

A highly efficient method for the copper-catalyzed asymmetric alylic 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 ligand 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 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 arenethiolato-copper complex for the AAA of allyl esters with Grignard reagents, several highly efficient methods based on phosphoramidite,<sup>3</sup> diphosphine,<sup>4</sup> phosphinephosphite<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>

# Scheme 1. Copper-catalyzed AAA of ortho-substituted cinnamyl substrates with MeMgBr



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-catalysed AAA.<sup>4</sup> However, the use of this catalytic system has not been reported for the copper-catalyzed AAA of ortho-substituted cinammyl substrates. Herein, we present a highly regio- and enantioselective CuBr•SMe<sub>2</sub>/TaniaPhos catalyzed AAA of ortho-substituted cinammyl 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 ortho-bromo cinnamyl 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 to obtained **2a** with 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).



Table 1. Optimization of the copper-catalyzed AAA of 1a.

Entry <sup>a</sup>	N° equiv MeMgBr	Temp (°C)	<b>Conv (%)</b> <sup>b,c</sup>	2a:3a <sup>d</sup>	<b>2a ee</b> (%) <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  $CH_2Cl_2$  (1 mL) added to a solution of catalyst and MeMgBr in  $CH_2Cl_2$  (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 brackets. <sup>*d*</sup>Determined by GC analysis. <sup>*e*</sup>Reaction stirred for 48 h. <sup>*f*</sup>n.d. = not determined. Once 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 also very efficient for the enantioselective methylation of chloro-, methyland 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.

#### Table 2. Scope of the reaction



2	<b>1b</b> , Cl	Me	69	>99:1	<b>2b</b> , 98
3	1c, CH3	Me	87	98:2	<b>2c</b> , 98
4	1d, OMe	Me	53 <sup>f</sup>	>99:1	<b>2d</b> , 96
5	1e, OTBS	Me	77	97:3	2e, >99
6	<b>1a</b> , Br	Et	40	90:10	<b>2f</b> , 99
$7^e$	<b>1a</b> , Br	Et	76	92:8	<b>2f</b> , 99
8	<b>1a</b> , Br	n-Hex	87 (76) <sup>g</sup>	93:7 (91:9) <sup>g</sup>	<b>2g</b> , 98 (98) <sup>g</sup>
9	1d, OMe	Et	46 <sup>f</sup>	92:8	<b>2h</b> , 93
10	1d, OMe	n-Hex	45 <sup>t</sup>	94:6	<b>2i</b> , 99
11	<b>1c</b> , CH <sub>3</sub>	Et	90	75:25	<b>2j</b> , 92
$12^e$	1c, CH <sub>3</sub>	Et	88	78:22	<b>2j</b> , 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.

#### 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 silica plates. Compounds were visualized by UV and cerium/molybdenum or potassium permanganate staining. Progress and conversion

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of the reaction were determined by GC-MS. Mass spectra were recorded on a mass spectrometer using orbitrap analyzer. <sup>1</sup>H- and <sup>13</sup>C-NMR were recorded on 400 MHz 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>:  $\delta$  7.26 for <sup>1</sup>H,  $\delta$  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-steps 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 cinammyl 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  $R_{p}$ ,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  $Et_2O$  (3 x 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 has 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 x 0.25 mm x 0.25 µm), 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,

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19.3. Enantiomeric excess determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m x 0.25 mm x 0.25  $\mu\mu$ 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 x 0.25 mm x 0.25 µm), 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 x 0.25 mm x 0.25 µm), 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*-butyl)dimethylsilyl)oxy)-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,  $[\alpha]_D = -26.6$  (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,  $[\alpha]_D = -7.3$  (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 x 0.25 mm x 0.25 µm), 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, [α]<sub>D</sub> = -2.4 (*c* = 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 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>) δ 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 x 0.25 mm x 0.25 µm), 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,  $[\alpha]_D = +7.5$  (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 x 0.25 x 0.25 µm), 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<sub>12</sub>H<sub>17</sub>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,  $[\alpha]_D = +10.5$  (c = 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  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). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  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 x 0.25 mm x 0.25 µm), initial temp. 40 °C,

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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): 40.7 (minor) and 40.8 (major); retention time **3i**: 68.1 min.

HRMS (ESI+, *m/z*): calcd. for C<sub>16</sub>H<sub>25</sub>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,  $[\alpha]_D = +6.3$  (c = 0.2, CHCl<sub>3</sub>), (lit.<sup>11</sup> (83% ee)  $[\alpha]_D^{20} = +19.6$  (c = 0.8 CHCl<sub>3</sub>)). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  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). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  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 x 0.25 mm x 0.25 µm), initial temp. 40 °C, then 10 °C/min to 75°C, then 0.5 °C/min to 120 °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<sup>+</sup>), 131.0 (100), 115.0 (29.4), 91.0 (24.3).

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**Supporting Information** <sup>1</sup>H, <sup>13</sup>C spectra and GC and HPLC traces for compounds **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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