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Enhanced anti-Diastereo- and Enantioselectivity in Alcohol-Mediated Carbonyl Crotylation Using an Isolable Single Component Iridium Catalyst

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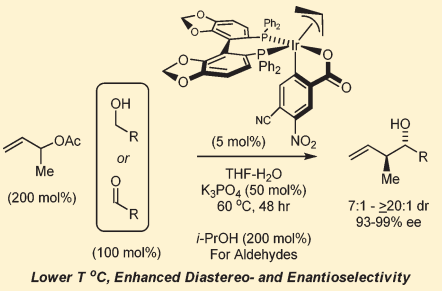
Supporting Information

ABSTRACT: The cyclometalated iridium complex (*S*)-**I** derived from [Ir(cod)Cl]$_2$, 4-cyano-3-nitrobenzoic acid, allyl acetate, and (*S*)-SEGPHOS is conveniently isolated by precipitation or through conventional silica gel flash chromatography. This single-component precatalyst allows alcohol mediated carbonyl crotylations to be performed at significantly lower temperature, resulting in enhanced levels of *anti*-diastereo- and enantioselectivity. Most significantly, the chromatographically isolated precatalyst (*S*)-**I** enables carbonyl crotylations that are not possible under previously reported conditions involving in situ generation of (*S*)-**I**.



In the course of developing C−C bond-forming hydrogenations and transfer hydrogenations,[1] it was found that *ortho*-cyclometalated iridium *C*,*O*-benzoates serve as catalysts for diverse carbonyl allylation processes wherein primary alcohol dehydrogenation triggers reductive generation of allyliridium nucleophiles from allylic carboxylates, thus enabling asymmetric carbonyl allylation directly from the alcohol oxidation level. Under nearly identical conditions, carbonyl allylation is achieved from the aldehyde oxidation level employing 2-propanol as terminal reductant.[2] Notably, by harnessing the reductive capability of alcohol mediated transfer hydrogenation, asymmetric carbonyl allylation is achieved in the absence of stoichiometric allylmetal reagents or metallic reductants, representing a significant departure from conventional carbonyl allylation protocols.[3−5]

Our initial investigations into stereoselective carbonyl crotylation employing α-methyl allyl acetate as the crotyl donor were achieved using the *ortho*-cyclometalated iridium *C*,*O*-benzoate prepared in situ from [Ir(cod)Cl]$_2$, allyl acetate, 4-cyano-3-nitrobenzoic acid, and the chiral phosphine ligand (*S*)-SEGPHOS.[2c,6,7] Although in situ assembly of the catalyst proved convenient and exceptional enantioselectivities typically were observed (>95% ee), only moderate levels of *anti*-diastereoselectivity were evident (5:1−11:1 dr). In subsequent work, conditions for preparation of the discrete *ortho*-cyclometalated iridium *C*,*O*-benzoate precatalyst and its isolation via precipitation were identified.[2d] Notably, using such single-component precatalysts, alcohol-mediated carbonyl allylation processes were found to proceed at considerably lower temperatures. This fact prompted the present reinvestigation of alcohol-mediated carbonyl crotylation. Here, we report that the *ortho*-cyclometalated iridium *C*,*O*-benzoate derived from [Ir(cod)Cl]$_2$, allyl acetate, 4-cyano-3-nitrobenzoic acid, and (*S*)-SEGPHOS, termed (*S*)-**I**, is subject to conventional silica gel flash chromatographic purification, and that use of (*S*)-**I** purified in this manner enables low-temperature (60 °C) alcohol-mediated carbonyl crotylation, resulting in enhanced levels of *anti*-diastereo- and enantioselectivity.

Purification of the *ortho*-cyclometalated iridium *C*,*O*-benzoate precatalyst (*S*)-**I** by conventional flash silica gel chromatographically was motivated by the fact that isolation of (*S*)-**I** by direct precipitation from the parent reaction mixture failed to exclude small quantities of inorganic byproducts, which contribute to batch dependent variability in catalytic performance. To remove such inorganic impurities, the precatalyst (*S*)-**I** was subjected to flash silica gel chromatographically and was found to exhibit excellent chromatographic stability. Thus, using (*S*)-SEGPHOS as the limiting reagent, the iridium precatalyst (*S*)-**I** is obtained in 85% isolated as a yellow powder after purification by silica gel

Scheme 1. Synthesis and Isolation of the Cyclometalated Iridium Complex (*S*)-I

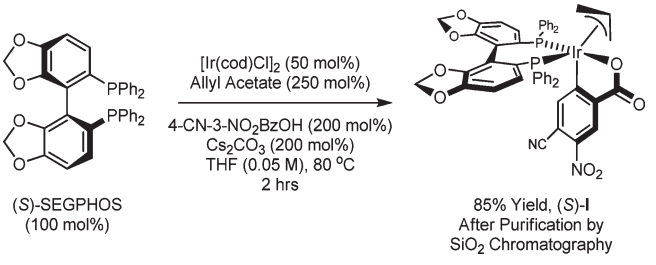


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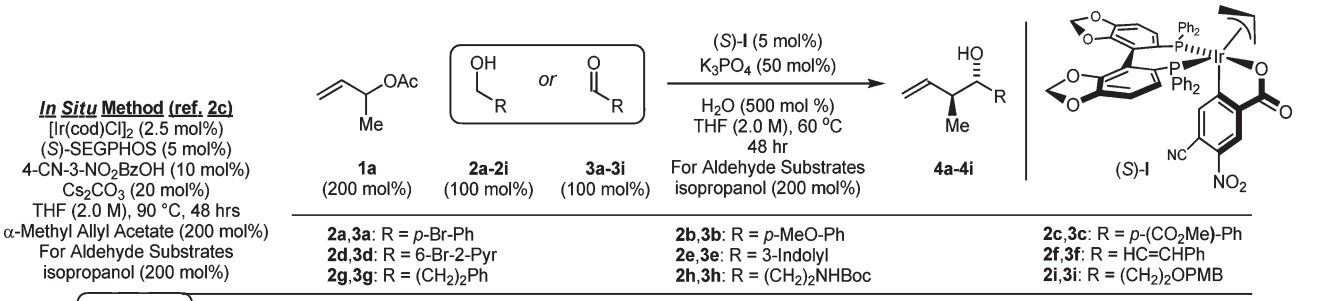
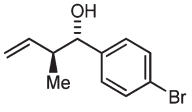
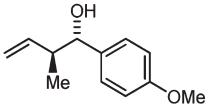
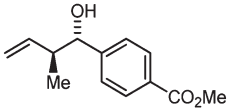
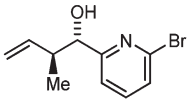
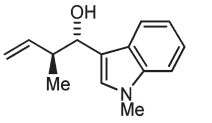
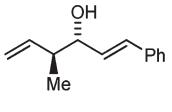
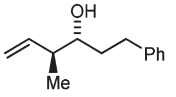
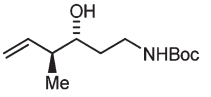
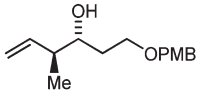
Table 1. Enhanced Levels of *anti*-Diastereo- And Enantioselectivity in Alcohol-Mediated Carbonyl Crotylations Using the Chromatographically Isolated Single Component Iridium Catalyst (*S*)-I.[a]



Oxidation Level			
Alcohol	Preformed (*S*)-I 78% Yield **4a**, 16:1 dr, 97% ee	Preformed (*S*)-I 91% Yield **4b**, 10:1 dr, 95% ee	Preformed (*S*)-I 78% Yield **4c**, 11:1 dr, 98% ee
Aldehyde	82% Yield **4a**, 17:1 dr, 98% ee	89% Yield **4b**, 12:1 dr, 98% ee)	81% Yield **4c**, 13:1 dr, 98% ee
Alcohol	*In Situ* (*S*)-I 73% Yield **4a**, 8:1 dr, 95% ee	*In Situ* (*S*)-I 67% Yield **4b**, 5:1 dr, 90% ee	*In Situ* (*S*)-I 70% Yield **4c**, 7:1 dr, 95% ee
Aldehyde	78% Yield **4a**, 11:1 dr, 97% ee	75% Yield **4b**, 7:1 dr, 97% ee	80% Yield **4c**, 11:1 dr, 96% ee
			
Alcohol	Preformed (*S*)-I 50% Yield **4d**, 14:1 dr, 98% ee	Preformed (*S*)-I 75% Yield **4e**, 7:1 dr, 98% ee	Preformed (*S*)-I[b] 72% Yield **4f**, 10:1 dr, 93% ee
Aldehyde	75% Yield **4d**, >20:1 dr, 97% ee	74% Yield **4e**, 10:1 dr, 98% ee	77% Yield **4f**, 10:1 dr,98% ee
Alcohol	*In Situ* (*S*)-I no product observed	*In Situ* (*S*)-I 73% Yield **4e**, 5:1 dr, 95% ee	*In Situ* (*S*)-I 61% Yield **4f**, 7:1 dr, 86% ee
Aldehyde		78% Yield **4e**, 6:1 dr, 97% ee	66% Yield **4f**, 8:1 dr, 98% ee
			
Alcohol	Preformed (*S*)-I 71% Yield **4g**, >20:1 dr, 99% ee	Preformed (*S*)-I[b] 71% Yield **4h**, >20:1 dr, 96% ee	Preformed (*S*)-I 76% Yield **4i**, 15:1 dr, 97% ee
Aldehyde	71% Yield **4g**, >20:1 dr, 98% ee	66% Yield **4h**, >20:1 dr, 99% ee	76% Yield **4i**, >20:1 dr, 99% ee
Alcohol	*In Situ* (*S*)-I 69% Yield **4g**, 7:1 dr, 98% ee	*In Situ* (*S*)-I no product observed	*In Situ* (*S*)-I 73% Yield **4i**, 7:1 dr, 95% ee
Aldehyde	71% Yield **4g**, 11:1 dr, 98% ee		88% Yield **4i**, 7:1 dr, 95% ee

[a] Cited yields are of material isolated by silica gel chromatography. Enantiomeric excess was determined by chiral stationary-phase HPLC analysis through comparison of reaction products to racemic diastereomeric mixtures. For assignment of relative and absolute stereochemistry, see ref 2c. See the Experimental Section for further details. [b] 70 °C.

chromatography and subsequent precipitation, as described in the Experimental Section (Scheme 1).

The performance of the chromatographically isolated precatalyst (*S*)-**I** was evaluated in carbonyl crotylations from the alcohol or aldehyde oxidation level via transfer hydrogenation, and a comparison with results obtained in reactions involving generation of (*S*)-**I** in situ was made.[2c] Whereas reaction temperatures of 90 °C were necessary using the catalyst generated in situ, the chromatographically isolated precatalyst (*S*)-**I** functioned at 60 °C without extending reaction time. A considerable improvement in the level of *anti*-diastereoselectivity (7:1 to >20:1 dr) was accompanied by a modest but consistent improvement in enantioselectivity (93−99% ee). As demonstrated by the conversion of alcohols **2a**−**i** to adducts **4a**−**i** and the conversion of aldehydes **3a**−**i** to adducts **4a**−**i**, these favorable trends in selectivity were evident in carbonyl crotylations from the alcohol or aldehyde oxidation level. Most significantly, as illustrated by the formation of adducts **4d** and **4h**, the chromatographically isolated precatalyst (*S*)-**I** enables carbonyl crotylations that are not possible under previously reported conditions involving in situ generation of (*S*)-**I**, perhaps due to thermal instability of these particular aldehydes or cross reactivity of these aldehydes with the catalyst at higher temperatures. As established in prior mechanistic studies,[2c] diastereomeric ratios are generally higher in crotylations conducted from the aldehyde oxidation level, as capture of the kinetically formed (*E*)-σ-allyliridium via carbonyl addition is more rapid due to higher concentrations of aldehyde (Table 1).

In summary, we report that the iridium precatalyst (*S*)-**I** is subject to chromatographic purification and that the single-component precatalyst (*S*)-**I** promotes alcohol-mediated carbonyl crotylation at significantly lower temperature, resulting in

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enhanced levels of *anti*-diastereo- and enantioselectivity.[2c] Future studies will focus on the development of related C−C bond-forming processes that occur in the absence of stoichiometric organometallic reagents, including butadiene-mediated carbonyl crotylations from the alcohol oxidation level.[7]

EXPERIMENTAL SECTION

Preparation of the Single-Component Iridium Precatalyst (*S*)-I. To a mixture of $[Ir(cod)Cl]_2$ (87.3 mg, 0.13 mmol, 100 mol %), (*S*)-SEGPHOS (159 mg, 0.26 mmol, 200 mol %), Cs_2CO_3 (169 mg, 0.52 mmol, 400 mol %), 4-CN-3-NO_2BzOH (100 mg, 0.52 mmol, 400 mol %), and allyl acetate (65 mg, 0.65 mmol, 500 mol %) in a sealed tube under an atmosphere of N_2 was added THF (2.6 mL, 0.05 M). The reaction mixture was stirred for 30 min at ambient temperature and heated for 1.5 h at 80 °C. Upon cooling to ambient temperature, the reaction mixture was diluted with CH_2Cl_2 (10 mL), filtered through a Celite plug, washed with CH_2Cl_2 (50 mL), and concentrated in vacuo. The residue was purified by flash chromatography (SiO_2, 20% Et_2O/CH_2Cl_2) and concentrated in vacuo. The light yellow gum was dissolved in THF (3 mL). Rapid addition of hexanes (50 mL) to the stirred solution resulted in precipitation of a bright yellow powder, which was collected by gravity filtration. Removal of trace solvents in vacuo delivered (*S*)-**I** (228 mg, 0.221 mmol) in 85% yield.

General Procedure for Carbonyl Crotylation from the Alcohol Oxidation Level. An oven-dried sealed tube under an atmosphere of N_2 was charged with alcohols **2a**−**i**, (*S*)-**I** (10.3 mg, 0.01 mmol, 5 mol %), K_3PO_4 (21.5 mg, 0.10 mmol, 50 mol %), THF (0.1 mL, 2.0 M), and H_2O (18 μL, 1.0 mmol, 500 mol %). But-3-en-2-yl acetate **1** (45.6 mg, 0.40 mmol, 200 mol %) was added, and the mixture was allowed to stir at ambient temperature for 0.5 h, at which point the reaction vessel was placed in an oil bath at 60 °C and was allowed to stir for 48 h. The reaction mixture was concentrated in vacuo. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes) provided **4a**−**i**.

General Procedure for Carbonyl Crotylation from the Aldehyde Oxidation Level. An oven-dried sealed tube under an atmosphere of N_2 was charged with aldehydes **3a**−**i**, (*S*)-**I** (10.3 mg, 0.01 mmol, 5 mol %), K_3PO_4 (21.5 mg, 0.10 mmol, 50 mol %), THF (0.1 mL, 2.0 M), 2-propanol (31 μL, 0.4 mmol, 200 mol %), and H_2O (18 μL, 1.0 mmol, 500 mol %). But-3-en-2-yl acetate **1** (45.6 mg, 0.40 mmol, 200 mol %) was added, and the mixture was allowed to stir at ambient temperature for 0.5 h, at which point the reaction vessel was placed in an oil bath at 60 °C and was allowed to stir for 48 h. The reaction mixture was concentrated in vacuo. Purification of the residue by column chromatography (SiO_2; ethyl acetate/hexanes, 1:20 with 0.1% TEA) provided **4a**−**i**.

(1*S*,2*S*)-1-(4-Bromophenyl)-2-methylbut-3-en-1-ol, 4a. The reaction was performed in accordance with the general experimental procedure for carbonyl crotylation from the alcohol oxidation level. Purification of the residue by column chromatography (SiO_2; ethyl acetate/hexanes, 1:20 with 0.1% TEA) provided **4a** (37.6 mg, 0.156 mmol) as a colorless oil in 78% yield (16:1 dr, 95% ee).

(1*S*,2*S*)-1-(4-Bromophenyl)-2-methylbut-3-en-1-ol, 4a. The reaction was performed in accordance with the general experimental procedure for carbonyl crotylation from the aldehyde oxidation level. Purification of the residue by column chromatography (SiO_2; ethyl acetate/hexanes, 1:20 with 0.1% TEA) provided **4a** (39.5 mg, 0.164 mmol) as a colorless oil in 82% yield (17:1 dr, 98% ee). TLC (SiO_2): R_f = 0.4 (ethyl acetate/hexanes, 1:5). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 5.81−5.71 (m, 1H), 5.22−5.16 (m, 2H), 4.32 (d, J = 7.6 Hz, 1H), 2.45−2.37 (m, 1H), 2.20 (br s, 1H), 0.87 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ141.4, 140.1, 131.3, 128.6, 121.4, 117.3, 77.1, 46.4, 16.4. HPLC (Chiralpak AS-H/AS-H column, hexanes/*i*-PrOH = 98:2, 0.5 mL/min, 230 nm): t_{minor} = 27.9 min, t_{major} = 31.8 min.

(1*S*,2*S*)-1-(4-Methoxyphenyl)-2-methylbut-3-en-1-ol, 4b. The reaction was performed in accordance with the general experimental procedure for carbonyl crotylation from the alcohol oxidation level. Purification of the residue by column chromatography (SiO_2; ethyl acetate/hexanes, 1:20 with 0.1% TEA) provided **4b** (35.0 mg, 0.182 mmol) as a colorless oil in 91% yield (10:1 dr, 94% ee).

(1*S*,2*S*)-1-(4-Methoxyphenyl)-2-methylbut-3-en-1-ol, 4b. The reaction was performed in accordance with the general experimental procedure for carbonyl crotylation from the aldehyde oxidation level. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **4b** (34.2 mg, 0.178 mmol) as a colorless oil in 89% yield (12:1 dr, 98% ee). TLC (SiO_2): R_f = 0.4 (ethyl acetate/hexanes, 1:5). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 (d, J = 8.0 Hz, 2H), 6.87 (d, J = 8.0 Hz, 2H), 5.86−5.76 (m, 1H), 5.23−5.16 (m, 2H), 4.29 (d, J = 8.4 Hz, 1H), 3.80 (s, 3H), 2.48−2.42 (m, 1H), 2.15 (br s, 1H), 0.83 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ159.3, 141.2, 134.8, 128.2, 117.0, 113.9, 77.7, 55.5, 46.7, 16.8. HPLC (Chiralpak AD-H/AD-H column, hexanes/*i*-PrOH = 95:5, 0.5 mL/min, 230 nm): t_{minor} = 41.2 min, t_{major} = 48.9 min.

Methyl 4-((1*S*,2*S*)-1-Hydroxy-2-methylbut-3-enyl)benzoate, 4c. The reaction was performed in accordance with the general experimental procedure for carbonyl crotylation from the alcohol oxidation level. Purification of the residue by column chromatography (SiO_2; ethyl acetate/hexanes, 1:20 with 0.1% TEA) provided **4c** (34.4 mg, 0.156 mmol) as a colorless oil in 78% yield (11:1 dr, 97% ee).

Methyl 4-((1*S*,2*S*)-1-Hydroxy-2-methylbut-3-enyl)benzoate, 4c. The reaction was performed in accordance with the general experimental procedure for carbonyl crotylation from the aldehyde oxidation level. Purification of the residue by column chromatography (SiO_2; ethyl acetate/hexanes, 1:20 with 0.1% TEA) provided **4c** (35.7 mg, 0.162 mmol) as a colorless oil in 81% yield (13:1 dr, 98% ee). TLC (SiO_2): R_f = 0.4 (ethyl acetate/hexanes, 1:5). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, J = 8.0 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 5.79−5.69 (m, 1H), 5.17−5.12 (m, 2H), 4.40 (d, J = 7.2 Hz, 1H), 3.88 (s, 3H), 2.49−2.36 (m, 2H), 0.86 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.2, 147.9, 140.1, 129.7, 129.6, 127.0, 117.5, 77.3, 52.3, 46.5, 16.6. HPLC (Chiralpak AD-H column, hexanes/*i*-PrOH = 95:5, 0.5 mL/min, 254 nm): t_{minor} = 27.1 min, t_{major} = 32.3 min.

(1*S*,2*S*)-1-(6-Bromopyridin-2-yl)-2-methylbut-3-en-1-ol, 4d. The reaction was performed in accordance with the general experimental procedure for carbonyl crotylation from the alcohol oxidation level. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **4d** (24.2 mg, 0.100 mmol) as a colorless oil in 50% yield (14:1 dr, 98% ee).

(1*S*,2*S*)-1-(6-Bromopyridin-2-yl)-2-methylbut-3-en-1-ol, 4d. The reaction was performed in accordance with the general experimental procedure for carbonyl crotylation from the aldehyde oxidation level. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **4d** (36.3 mg, 0.150 mmol) as a colorless oil in 75% yield (>20:1 dr, 97% ee). TLC (SiO_2): R_f = 0.3 (ethyl acetate/hexanes, 1:5). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (t, J = 7.6 Hz, 1H), 7.38 (d, J = 7.6 Hz, 1H), 7.25 (d, J = 8.0 Hz, 1H), 5.73 (dt, J = 17.2, 10.4, 1H), 5.10−4.99 (m, 2H), 4.58 (t, J = 5.2 Hz, 1H), 3.28 (d, J = 6.0 Hz, 1H), 2.72−2.64 (m, 1H), 1.06 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.8, 141.0, 138.7, 138.6, 126.7, 120.0, 116.5, 44.6, 16.1. HPLC (Chiralcel OD-H column, hexanes/*i*-PrOH = 95:5, 0.5 mL/min, 210 nm): t_{major} = 12.1 min, t_{minor} = 16.8 min.

(1*S*,2*S*)-2-Methyl-1-(1-methyl-1*H*-indol-3-yl)but-3-en-1-ol, 4e. The reaction was performed in accordance with the general experimental procedure for carbonyl crotylation from the aldehyde oxidation level. Purification of the residue by column chromatography (SiO_2; ethyl

acetate: hexanes, 1:20 with 0.1% TEA) provided **4e** (32.3 mg, 0.150 mmol) as a colorless oil in 75% yield (7:1 dr, 98% ee).

(1*S*,2*S*)-2-Methyl-1-(1-methyl-1*H*-indol-3-yl)but-3-en-1-ol, 4e. The reaction was performed in accordance with the general experimental procedure for carbonyl crotylation from the aldehyde oxidation level. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **4e** (31.9 mg, 0.148 mmol) as a colorless oil in 74% yield (10:1 dr, 98% ee). TLC (SiO_2): R_f = 0.4 (ethyl acetate/hexanes, 1:5). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, J = 8.0 Hz, 1H), 7.34 (d, J = 8.4 Hz, 1H), 7.26 (t, J = 8.0 Hz, 1H), 7.14 (t, J = 8.0 Hz, 1H), 6.48 (s, 1H), 5.98−5.88 (m, 1H), 5.33−5.25 (m, 2H), 4.60 (d, J = 8.4 Hz, 1H), 3.81 (s, 3H), 2.86−2.78 (m, 1H), 2.22 (br s, 1H), 1.03 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.7, 140.3, 138.2, 127.5, 121.9, 120.9, 119.8, 117.4, 109.4, 100.8, 71.4, 44.3, 30.7, 17.5. HPLC (Chiralcel OJ-H column, hexanes/*i*-PrOH = 93:7, 0.5 mL/min, 254 nm): t_{major} = 53.3 min, t_{minor} = 60.0 min

(3*R*,4*S*,*E*)-4-Methyl-1-phenylhexa-1,5-dien-3-ol, 4f. The reaction was performed in accordance with the general experimental procedure for carbonyl crotylation from the alcohol oxidation level. Purification of the residue by column chromatography (SiO_2; ethyl acetate/hexanes, 1:20 with 0.1% TEA) provided **4f** (27.1 mg, 0.144 mmol) as a colorless oil in 72% yield (10:1 dr, 93% ee).

(3*R*,4*S*,*E*)-4-Methyl-1-phenylhexa-1,5-dien-3-ol, 4f. The reaction was performed in accordance with the general experimental procedure for carbonyl crotylation from the aldehyde oxidation level. Purification of the residue by column chromatography (SiO_2; ethyl acetate/hexanes, 1:20 with 0.1% TEA) provided **4f** (29.0 mg, 0.154 mmol) as a colorless oil in 77% yield (10:1 dr, 98% ee). TLC (SiO_2): R_f = 0.3 (ethyl acetate/hexanes, 1:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41−7.23 (m, 5H), 6.61 (d, J = 16.0 Hz, 1H), 6.21 (dd, J = 16.0, 7.2 Hz, 1H), 5.88−5.78 (m, 1H), 5.21−5.16 (m, 2H), 4.06 (t, J = 6.8 Hz, 1H), 2.41−2.35 (m, 1H), 1.99 (br s, 1H), 1.06 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.4, 136.9, 132.0, 130.4, 128.8, 127.9, 126.8, 117.0, 76.4, 44.9, 16.3. HPLC (Chiralpak AS-H/AS-H column, hexanes/*i*-PrOH = 98:2, 0.5 mL/min, 254 nm): t_{minor} = 26.8 min, t_{major} = 31.5 min.

(3*R*,4*S*)-4-Methyl-1-phenylhex-5-en-3-ol, 4g. The reaction was performed in accordance with the general experimental procedure for carbonyl crotylation from the alcohol oxidation level. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **4g** (27.0 mg, 0.142 mmol) as a colorless oil in 71% yield (>20:1 dr, 99% ee).

(3*R*,4*S*)-4-Methyl-1-phenylhex-5-en-3-ol, 4g. The reaction was performed in accordance with the general experimental procedure for carbonyl crotylation from the aldehyde oxidation level. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **4g** (27.0 mg, 0.142 mmol) as a colorless oil in 71% yield (>20:1 dr, 98% ee). TLC (SiO_2): R_f = 0.4 (ethyl acetate/hexanes, 1:5). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31−7.17 (m, 5H), 5.80−5.70 (m, 1H), 5.15−5.10 (m, 2H), 3.43−3.40 (m, 1H), 2.89−2.81 (m, 1H), 2.72−2.64 (m, 1H), 2.26−2.20 (m, 1H), 1.89−1.80 (m, 1H), 1.75−1.62 (m, 2H), 1.03 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.6, 140.4, 128.7, 128.6, 126.0, 116.8, 74.2, 44.6, 36.4, 32.4, 16.5. HPLC (Chiralcel OD-H column, hexanes/*i*-PrOH = 97:3, 0.7 mL/min, 254 nm): t_{minor} = 11.5 min, t_{major} = 18.7 min.

***tert*-Butyl (3*R*,4*S*)-3-Hydroxy-4-methylhex-5-enylcarbamate, 4h.** The reaction was performed in accordance with the general experimental procedure for carbonyl crotylation from the alcohol oxidation level. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **4h** (32.6 mg, 0.142 mmol) as a colorless oil in 71% yield (>20:1 dr, 96% ee).

***tert*-Butyl (3*R*,4*S*)-3-Hydroxy-4-methylhex-5-enylcarbamate, 4h.** The reaction was performed in accordance with the general experimental procedure for carbonyl crotylation from the aldehyde oxidation level. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **4h** (30.3 mg, 0.142 mmol) as a colorless oil in 66% yield (>20:1 dr, 99% ee). TLC (SiO_2): R_f = 0.5 (ethyl acetate/hexanes, 1:3). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.76 (dtd, J = 17.2, 10.0, 0.4 Hz, 1H), 5.12−5.05 (m, 2H), 4.91 (br, 1H), 3.48−3.41 (m, 2H), 3.20−3.11 (m, 1H), 2.58 (d, J = 2.8 Hz, 1H), 2.30−2.17 (m, 1H), 1.72−1.64 (m, 1H), 1.54−1.45 (m, 1H), 1.44 (s, 9H), 1.03 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.7, 140.4, 116.1, 79.3, 72.6, 44.2, 37.7, 34.2, 28.4, 16.2. HPLC enantiomeric excess was determined by HPLC analysis of the 4-nitrobenzoate derivative of the product (Chiralcel OJ-H column, hexanes/*i*-PrOH = 98:2, 0.75 mL/min, 254 nm): t_{minor} = 24.4 min, t_{major} = 28.1 min.

(3*R*,4*S*)-1-(4-Methoxybenzyloxy)-4-methylhex-5-en-3-ol, 4i. The reaction was performed in accordance with the general experimental procedure for carbonyl crotylation from the alcohol oxidation level. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **4i** (38.1 mg, 0.152 mmol) as a colorless oil in 76% yield (15:1 dr, 97% ee).

(3*R*,4*S*)-1-(4-Methoxybenzyloxy)-4-methylhex-5-en-3-ol, 4i. The reaction was performed in accordance with the general experimental procedure for carbonyl crotylation from the aldehyde oxidation level. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **4i** (38.1 mg, 0.152 mmol) as a colorless oil in 76% yield (>20:1 dr, 99% ee). TLC (SiO_2): R_f = 0.5 (ethyl acetate/hexanes, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26−7.24 (m, 2H), 6.90−6.86 (m, 2H), 5.80 (dt, J = 17.2, 10.0 Hz, 1H), 5.09−5.02 (m, 2H), 4.45 (s, 2H), 3.80 (s, 3H), 3.71−3.61 (m, 3H), 2.79 (d, J = 2.8, 1H), 2.23 (qt, J = 6.8, 0.8 Hz, 1H), 1.74−1.70 (m, 2H), 1.03 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.2, 140.5, 130.1, 129.3, 115.4, 113.8, 74.3, 73.0, 68.9, 55.3, 44.0, 33.5, 15.8. HPLC enantiomeric excess was determined by HPLC analysis of the 4-nitrobenzoate derivative of the product (Chiralcel AD-H column, hexanes/*i*-PrOH = 98:2, 1.0 mL/min, 210 nm): t_{minor} = 15.4 min, t_{major} = 24.8 min.

■ ASSOCIATED CONTENT

Supporting Information. Spectral data for adducts **4a**−**i**, including scanned images of ^{1}H and ^{13}C NMR spectra and chiral stationary phase HPLC traces. This material is available free of charge via the Internet at http://pubs.acs.org.

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