Regio- and Stereospecfic Rhodium-Catalyzed Allylic Alkylation with an Acyl Anion Equivalent: An Approach to Acyclic α-Ternary β,γ-Unsaturated Aryl Ketones

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1. General Information

All reactions were carried out under an argon atmosphere in anhydrous solvent using commercially available reagents that were purchased and used as received. Tetrahydrofuran was freshly distilled from sodium benzophenone ketyl. Analytical thin layer chromatography (TLC) was performed on pre-coated 0.25 mm thick silica gel 60-F₂₅₄ plates (*Merck* or *Whatman PE SIL G/UV*); visualized using UV light and by treatment with a KMnO₄, followed by heating. All compounds were purified by flash chromatography using silica gel 60 (40-63 µm, *Silicycle* or *FluoroChem*) and gave spectroscopic data consistent with being \geq 95% the assigned structure. Melting points (uncorrected) were obtained from a Büchi M560 melting point instrument.

Optical rotations ($[\alpha]_{D}^{\circ C}$) were measured on a *Anton Parr MCP 200* polarimeter with a tungsten halogen lamp (589 nm) at the stated temperature (indicated in °C as superscript) using a 0.7 mL quartz cell of 100 mm length; solution concentrations (c) are given in g/100 mL. ¹H NMR and ¹³C NMR spectra were recorded on a *Bruker Avance DRX-500* spectrometer in CDCl₃ at ambient temperature; chemical shifts (δ) are given in ppm and calibrated using the signal of residual undeuterated solvent as internal reference ($\delta_{\rm H}$ = 7.26 ppm and $\delta_{\rm C}$ = 77.16 ppm). ¹H NMR data are reported as follows: chemical shift (multiplicity, 1st order spin system if available, coupling constant, integration). Coupling constants (J) are reported in Hz and apparent splitting patterns are designated using the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad), app. (apparent) and the appropriate combinations. ¹³C NMR spectra with complete proton decoupling were described with the aid of an APT sequence, separating methylene and quaternary carbons (e, even), from methyl and methine carbons (o, odd). IR spectra were recorded on an Agilent Technologies Cary 630 FT-IR (ATR); wavenumbers (v) are given in cm^{-1} ; and the abbreviations w (weak, <33%), m (medium, 33-66%), s (strong, >66%), vs (very strong, $\geq 95\%$) and br (broad) are used to describe the relative intensities of the IR absorbance bands. Mass spectra were obtained through the Queen's University Mass Spectrometry and Proteomics Services Unit. All liquid chromatographs were obtained on an Agilent 1260 Infinity series HPLC equipped with a variable wavelength UV detector. The instrument was fitted with a CHIRALPAK AS-H[™] column (Diacel, 4.6 mm × 25cm).

2. Representative Experimental Procedure for the Preparation of Secondary Allylic Carbonates 1a-i.

Lithium bis(trimethylsilyl)amide (6.50 mL, 6.50 mmol; 1M solution in THF) was added dropwise to a stirred solution 5-phenylpent-1-en-3-ol (811 mg, 5.0 mmol) in anhydrous tetrahydrofuran (50 mL) at 0 °C under an atmosphere of argon. The mixture was stirred for *ca.* 15 minutes at this temperature and 2-(boc-oxyimino)-2-phenylacetonitrile (1.85 g, 7.5 mmol) was added. The reaction was then allowed to slowly warm to room temperature, stirred for *ca.* 16 hours and quenched by the dropwise addition of saturated aqueous ammonium chloride solution (10 mL). The reaction mixture was then partitioned between diethyl ether and saturated aqueous ammonium chloride solution. The combined organic layers were dried (anhyd. MgSO₄), filtered and concentrated *in vacuo* to afford the crude product. Purification by flash column chromatography (silica gel, eluting with 2-6% diethyl ether/hexane) afforded the *carbonate* **1a** (1.18 g, 90%) as a pale yellow oil.

3. Spectral Data for the Secondary Allylic Carbonates 1a-i

OCO₂^tBu *tert*-Butyl 5-phenylpent-1-en-3-yl carbonate (1a)

Color and State: Pale yellow oil

Ph ²

Ph 、

¹**H NMR** (500 MHz, CDCl₃) δ 7.30-7.27 (m, 2H), 7.21-7.18 (m, 3H), 5.84 (ddd, J = 17.2, 10.6, 6.7 Hz, 1H), 5.31 (d, J = 17.3 Hz, 1H), 5.23 (d, J = 10.5 Hz, 1H), 5.04 (app. q, J = 6.7 Hz, 1H), 2.72 (ddd, A of ABXY, $J_{AB} = 14.0$ Hz, $J_{AX} = 10.1$ Hz, $J_{AY} = 6.0$ Hz, 1H), 2.67 (ddd, B of ABXY, $J_{AB} = 13.9$ Hz, $J_{BX} = 9.9$ Hz, $J_{BY} = 6.3$ Hz, 1H), 2.05 (dddd, A of ABXYZ, $J_{AB} = 13.8$ Hz, $J_{AX} = 10.0$ Hz, $J_{AY} = 7.6$ Hz, $J_{AZ} = 6.1$ Hz, 1H), 1.91 (ddt, B of ABXYZ, $J_{AB} = 13.9$ Hz, $J_{BX} = 10.0$ Hz, $J_{BY} = J_{BZ} = 6.1$ Hz, 1H), 1.51 (s, 9H).

¹³C NMR (125 MHz, CDCl₃) δ 153.08 (e), 141.38 (e), 136.30 (o), 128.56 (o), 128.50 (o), 126.11 (o), 117.43 (e), 82.14 (e), 77.44 (o), 36.03 (e), 31.51 (e), 27.94 (o).

IR (Neat) 3087 (w), 3065 (w), 3028 (w), 2981 (w), 2935 (w), 2866 (w), 1736 (s), 1647 (w), 1604 (w), 1498 (w), 1369 (m), 1272 (s), 1252 (vs), 1156 (s), 928 (m), 699 (s) cm⁻¹.

HRMS (ESI, $[M+Na]^+$) calcd for C₁₆H₂₂O₃Na 285.1461, found 285.1467.

OCO₂^tBu *tert*-Butyl 1-phenylbut-3-en-2-yl carbonate (1b)

Color and State: Pale yellow oil

¹**H NMR** (500 MHz, CDCl₃) δ 7.30-7.27 (m, 2H), 7.23-7.20 (m, 3H), 5.83 (ddd, J = 17.2, 10.6, 6.5 Hz, 1H), 5.25 (app. q, J = 6.8 Hz, 1H), 5.23 (d, J = 17.1 Hz, 1H), 5.17 (d, J = 10.6 Hz, 1H), 3.04 (dd, A of ABX, $J_{AB} = 13.7$ Hz, $J_{AX} = 7.2$ Hz, 1H), 2.89 (dd, B of ABX, $J_{AB} = 13.7$ Hz, $J_{BX} = 6.4$ Hz, 1H), 1.44 (s, 9H).

¹³C NMR (125 MHz, CDCl₃) δ 152.89 (e), 136.86 (e), 135.71 (o), 129.72 (o), 128.44 (o), 126.67 (o), 117.44 (e), 82.14 (e), 78.28 (o), 41.18 (e), 27.88 (o).

IR (Neat) 3088 (w), 3065 (w), 3031 (w), 2982 (w), 2935 (w), 1736 (s), 1648 (w), 1604 (w), 1498 (w), 1369 (m), 1272 (s), 1251 (vs), 1156 (s), 929 (m), 699 (s) cm⁻¹.

HRMS (ESI, $[M+Na]^+$) calcd for C₁₅H₂₀O₃Na 271.1305, found 271.1296.

OCO₂^tBu *tert*-Butyl hex-1-en-3-yl carbonate (1c)

Color and State: Colorless oil

¹**H NMR** (500 MHz, CDCl₃) δ 5.77 (ddd, J = 17.3, 10.5, 6.7 Hz, 1H), 5.24 (d, J = 17.1 Hz, 1H), 5.15 (d, J = 10.4 Hz, 1H), 4.97 (app. q, J = 6.7 Hz, 1H), 1.69-1.62 (m, 1H), 1.58-1.50 (m, 1H), 1.46 (s, 9H), 1.41-1.29 (m, 2H), 0.90 (t, J = 7.3 Hz, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 153.18 (e), 136.60 (o), 116.96 (e), 81.90 (e), 77.92 (o), 36.47 (e), 27.91 (o), 18.47 (e), 13.88 (o).

IR (Neat) 3088 (w), 2963 (w), 2937 (w), 2876 (w), 1738 (s), 1648 (w), 1369 (m), 1273 (s), 1251 (vs), 1162 (s), 929 (m) cm⁻¹.

HRMS (ESI, $[M+Na]^+$) calcd for $C_{11}H_{20}O_3Na$ 223.1305, found 223.1310.

OCO₂^tBu But-3-en-2-yl *tert*-butyl carbonate (1d)

Me *Color and State:* Colorless oil

¹**H** NMR (500 MHz, CDCl₃) δ 5.86 (ddd, J = 17.1, 10.7, 6.3 Hz, 1H), 5.27 (app. dt, J = 17.3, 1.2 Hz, 1H), 5.15 (app. dt, J = 10.5, 1.5 Hz, 1H), 5.13 (app. pentet, J = 6.4 Hz, 1H), 1.49 (s, 9H), 1.35 (d, J = 6.6 Hz, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 152.96 (e), 137.62 (o), 116.17 (e), 81.97 (e), 74.11 (o), 27.91 (o), 20.14 (o).

IR (Neat) 3091 (w), 2982 (w), 2937 (w), 1736 (s), 1647 (w), 1370 (m), 1273 (s), 1252 (vs), 1162 (s) cm⁻¹.

HRMS (ESI, $[M+H]^+$) calcd for C₉H₁₇O₃ 173.1172, found 173.1169.

OCO₂/Bu *tert*-Butyl 5-methylhex-1-en-3-yl carbonate (1e)

Color and State: Colorless oil

¹**H** NMR (500 MHz, CDCl₃) δ 5.79 (ddd, J = 17.3, 10.5, 6.8 Hz, 1H), 5.28 (app. dt, J = 17.3, 1.2 Hz, 1H), 5.17 (app. dt, J = 10.5, 1.1 Hz, 1H), 5.07 (app. qq, J = 6.9, 0.9 Hz, 1H), 1.67 (nonet, J = 6.6 Hz, 1H), 1.63 (app. dt, A of ABXY, $J_{AB} = 13.4$ Hz, $J_{AX} = J_{AY} = 6.8$ Hz, 1H), 1.48 (s, 9H), 1.39 (app. dt, B of ABXY, $J_{AB} = 13.2$ Hz, $J_{BX} = J_{BY} = 6.2$ Hz, 1H), 0.93 (d, J = 6.3 Hz, 3H), 0.92 (d, J = 6.6 Hz, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 153.17 (e), 136.89 (o), 116.93 (e), 81.95 (e), 76.64 (o), 43.38 (e), 27.95 (o), 24.49 (o), 22.75 (o), 22.53 (o).

IR (Neat) 3088 (w), 2959 (w), 2935 (w), 2873 (w), 1738 (s), 1648 (w), 1369 (m), 1274 (s), 1252 (vs), 1161 (s), 931 (m) cm⁻¹.

HRMS (ESI, $[M+Na]^+$) calcd for $C_{12}H_{22}O_3Na$ 237.1461, found 237.1464.

tert-Butyl 6-methylhept-1-en-3-yl carbonate (1f)



Color and State: Pale yellow oil

¹**H NMR** (500 MHz, CDCl₃) δ 5.79 (ddd, J = 17.3, 10.5, 6.8 Hz, 1H), 5.26 (app. dt, J = 17.3, 1.2 Hz, 1H), 5.18 (app. dt, J = 10.5, 1.1 Hz, 1H), 4.96 (app. q, J = 6.7 Hz, 1H), 1.74-1.65 (m, 1H), 1.62-1.52 (m, 2H), 1.48 (s, 9H), 1.29-1.15 (m, 2H), 0.88 (d, J = 6.6 Hz, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 153.18 (e), 136.63 (o), 117.08 (e), 81.94 (e), 78.44 (o), 34.17 (e), 32.30 (e), 27.95 (o), 22.64 (o), 22.58 (o).

IR (Neat) 3085 (w), 2957 (w), 2936 (w), 2872 (w), 1737 (s), 1648 (w), 1369 (m), 1273 (vs), 1252 (s), 1161 (s), 930 (m) cm⁻¹.

HRMS (ESI, $[M+Na]^+$) calcd for C₁₃H₂₄O₃Na 251.1618, found 251.1612.

OCO2ⁱBu *tert*-Butyl hepta-1,6-dien-3-yl carbonate (1g)

Color and State: Colorless oil.

¹**H NMR** (500 MHz, CDCl₃) δ 5.80 (ddt, J = 17.3, 10.4, 6.8 Hz, 1H), 5.79 (ddd, J = 17.3, 10.4, 6.8 Hz, 1H), 5.28 (app. dt, J = 17.3, 1.1 Hz, 1H), 5.20 (app. dt, J = 10.5, 1.1 Hz, 1H), 5.03 (app. dq, J = 17.2, 1.7 Hz, 1H), 5.01 (app. q, J = 6.4 Hz, 1H), 4.98 (app. dq, J = 10.1, 1.4 Hz, 1H), 2.14-2.10 (m, 2H), 1.81 (app. dq, A of ABXY₂, $J_{AB} = 13.8$ Hz, $J_{AX} = J_{AY} = 7.4$ Hz, 1H), 1.68 (ddt, B of ABXY₂, $J_{AB} = 13.7$ Hz, $J_{BX} = 8.4$ Hz, $J_{BY} = 6.5$ Hz, 1H), 1.48 (s, 9H).

¹³C NMR (125 MHz, CDCl₃) δ 153.05 (e), 137.54 (o), 136.30 (o), 117.28 (e), 115.34 (e), 82.00 (e), 77.41 (o), 33.49 (e), 29.40 (e), 27.91 (o).

IR (Neat) 3080 (w), 2981 (w), 2935 (w), 2870 (w), 1738 (s), 1643 (w), 1369 (m), 1272 (s), 1253 (vs), 1160 (s) cm⁻¹.

HRMS (ESI, $[M+H]^+$) calcd for C₁₂H₂₁O₃ 213.1485, found 213.1475.

OCO₂^{*i*}Bu 1-(Benzyloxy)but-3-en-2-yl *tert*-butyl carbonate (1h)

Color and State: Pale yellow oil.

BnO

¹**H NMR** (500 MHz, CDCl₃) δ 7.36-7.32 (m, 4H), 7.30-7.27 (m, 1H), 5.85 (ddd, J = 17.2, 10.7, 6.4 Hz, 1H), 5.37 (app. dt, J = 17.4, 1.3 Hz, 1H), 5.29-5.25 (m, 2H), 4.59 (d, A of AB, $J_{AB} = 12.1 \text{ Hz}, 1\text{H}$), 4.56 (d, B of AB, $J_{AB} = 12.2 \text{ Hz}, 1\text{H}$), 3.61 (dd, A of ABX, $J_{AB} = 10.6 \text{ Hz}, J_{AX} = 7.0 \text{ Hz}, 1\text{H}$), 3.57 (dd, B of ABX, $J_{AB} = 10.7 \text{ Hz}, J_{BX} = 4.4 \text{ Hz}, 1\text{H}$), 1.49 (s, 9H)

¹³C NMR (125 MHz, CDCl₃) δ 152.99 (e), 138.06 (e), 133.34 (o), 128.47 (o), 127.76 (o), 127.74 (o), 118.36 (e), 82.30 (e), 76.23 (o), 73.31 (e), 71.48 (e), 27.91 (o).

IR (Neat) 3090 (w), 3067 (w), 3031 (w), 2982 (w), 2936 (w), 2865 (w), 1740 (s), 1648 (w), 1369 (m), 1273 (s), 1252 (s), 1160 (s), 910 (m), 697 (s) cm⁻¹.

HRMS (ESI, $[M+H]^+$) calcd for C₁₆H₂₃O₄ 279.1591, found 279.1579.

OCO₂^tBu 5-(Benzyloxy)pent-1-en-3-yl *tert*-butyl carbonate (1i)

BnO *Color and State:* Pale yellow oil.

¹**H NMR** (500 MHz, CDCl₃) δ 7.36-7.32 (m, 4H), 7.30-7.27 (m, 1H), 5.81 (ddd, *J* = 17.2, 10.5, 6.7 Hz, 1H), 5.29 (app. dt, *J* = 17.2, 1.1 Hz, 1H), 5.21 (app. q, *J* = 6.7 Hz, 1H), 5.19 (app. dt,

10.5, 1.0 Hz, 1H), 4.51 (d, A of AB, $J_{AB} = 12.0$ Hz, 1H), 4.48 (d, B of AB, $J_{AB} = 11.9$ Hz, 1H), 3.55 (ddd, A of ABXY, $J_{AB} = 12.9$ Hz, $J_{AX} = 6.9$ Hz, $J_{AY} = 6.1$ Hz, 1H), 3.52 (dt, B of ABXY, $J_{AB} = 12.5$ Hz, $J_{BX} = J_{BY} = 6.3$ Hz, 1H), 2.02 (ddt, A of ABXY₂, $J_{AB} = 14.0$ Hz, $J_{AX} = 7.8$ Hz, $J_{AY} = 6.2$ Hz, 1H), 1.91 (app. dq, B of ABXY₂, $J_{AB} = 12.9$ Hz, $J_{BX} = J_{BY} = 6.4$ Hz, 1H), 1.48 (s, 9H).

¹³C NMR (125 MHz, CDCl₃) δ 152.98 (e), 138.48 (e), 136.27 (o), 128.49 (o), 127.78 (o), 127.68 (o), 117.22 (e), 82.07 (e), 75.32 (o), 73.22 (e), 66.26 (e), 34.63 (e), 27.94 (o).

IR (Neat) 3067 (w), 3030 (w), 2981 (w), 2936 (w), 2865 (w), 1737 (s), 1648 (w), 1369 (m), 1273 (s), 1252 (vs), 1155 (s), 930 (m), 698 (s) cm⁻¹.

HRMS (ESI, $[M+Na]^+$) calcd for $C_{17}H_{24}O_4Na$ 315.1567, found 315.1554.

4. Spectral Data for the Aryl Cyanohydrins 2a-d

The aryl cyanohydrins **2a-d** were prepared from the corresponding aldehydes according to the previously reported procedure.^{1,2} The spectral data for the cyanohydrins **2a'** and **2aa'** has been previously reported.^{2b}

OTBS 2-(*tert*-Butyldimethylsilyloxy)-2-(4-(dimethylamino)phenyl)acetonitrile CN (2a)

Me₂N [^]

Color and State: Yellow oil.

¹**H NMR** (500 MHz, CDCl₃) δ 7.32-7.29 (m, 2H), 6.72-6.69 (m, 2H), 5.41 (s, 1H), 2.98 (s, 6H), 0.92 (s, 9H), 0.19 (s, 3H), 0.11 (s, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 151.16 (e), 127.63 (o), 124.06 (e), 119.90 (e), 112.29 (o), 64.16 (o), 40.48 (o), 25.71 (o), 18.30 (e), -4.90 (o).

IR (Neat) 2932 (w), 2889 (w), 2859 (w), 2813 (w), 1613 (m), 1524 (m), 1255 (m), 1063 (s), 835 (s), 777 (s) cm⁻¹.

HRMS (EI, M^+) calcd for $C_{16}H_{26}N_2OSi$ 290.1814, found 290.1819.



2-(*tert*-Butyldimethylsilyloxy)-2-(4-pyrrolidin-1-yl)phenyl)acetonitrile (2b)

Color and State: Yellow oil.

¹**H NMR** (500 MHz, CDCl₃) δ 7.30-7.27 (m, 2H), 6.56-6.53 (m, 2H), 3.40 (s, 1H), 3.31-3.28 (m, 4H), 2.03-2.00 (m, 4H), 0.92 (s, 9H), 0.18 (s, 3H), 0.10 (s, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 148.60 (e), 127.80 (o), 123.11 (e), 119.99 (e), 111.67 (o), 64.34 (o), 47.70 (e), 25.73 (o), 25.60 (e), 18.30 (e), -4.87 (o), -4.89 (o).

IR (Neat) 2955 (w), 2932 (w), 2857 (w), 1612 (m), 1524 (s), 1254 (m), 1180 (m), 1066 (m), 835 (s), 778 (s) cm⁻¹.

HRMS (EI, M^+) calcd for $C_{18}H_{28}N_2OSi$ 316.1971, found 316.1978.

OTBS **2-(***tert***-Butyldimethylsilyloxy)-2-(4-(piperidin-1-yl)phenyl)acetonitrile**



Color and State: Yellow oil.

¹**H NMR** (500 MHz, CDCl₃) δ 7.33-7.30 (m, 2H), 6.93-6.90 (m, 2H), 5.43 (s, 1H), 3.20 (t, J = 5.5 Hz, 4H), 1.70 (pentet, J = 5.6 Hz, 4H), 1.62-1.57 (m, 2H), 0.93 (s, 9H), 0.20 (s, 3H), 0.12 (s, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 152.73 (e), 127.46 (o), 126.38 (e), 119.75 (e), 116.00 (o), 64.05 (o), 50.10 (e), 25.77 (e), 25.71 (o), 24.41 (e), 18.30 (e), -4.90 (o), -4.93 (o).

IR (Neat) 2932 (m), 2858 (w), 2809 (w), 1611 (m), 1516 (m), 1254 (m), 1238 (m), 1073 (m), 836 (s), 778 (s) cm⁻¹.

HRMS (EI, M^+) calcd for $C_{19}H_{30}N_2OSi$ 330.2127, found 330.2120.

OTBS **2-(tert-Butyldimethylsilyloxy)-2-(4-morpholinophenyl)acetonitrile (2d)** Color and State: Yellow oil.

¹**H** NMR (500 MHz, CDCl₃) δ 7.35 (d, J = 8.7 Hz, 2H), 6.91 (d, J = 8.7 Hz, 2H), 5.44 (s, 1H), 3.86 (t, J = 4.8 Hz, 4H), 3.19 (t, J = 4.9 Hz, 4H),

0.92 (s, 9H), 0.20 (s, 3H), 0.12 (s, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 151.98 (e), 127.61 (e), 127.53 (o), 119.64 (e), 115.50 (o), 66.91 (e), 63.91 (o), 48.92 (e), 25.69 (o), 18.30 (e), -4.91 (o), -4.96 (o).

IR (Neat) 2956 (w), 2930 (w), 2889 (w), 2857 (m), 1611 (m), 1518 (m), 1255 (m), 1235 (s), 1070 (s), 835 (vs), 779 (s) cm⁻¹.

HRMS (EI, M^+) calcd for $C_{18}H_{28}N_2O_2Si$ 332.1920, found 332.1928.

5. Representative Experimental Procedure for the Rhodium-Catalyzed Allylic Alkylation with an Acyl Anion Equivalent

Lithium bis(trimethylsilyl)amide (0.90 mL, 0.90 mmol; 1M solution in THF) was added dropwise to a stirred solution of 2-(*tert*-butyldimethylsilyloxy)-2-(4-(dimethylamino)phenyl)acetonitrile **2a** (189 mg, 0.65 mmol) in anhydrous tetrahydrofuran (2.5 mL) and DMPU (0.5 mL) at -10 °C under an atmosphere of argon. The anion was allowed to form over *ca*. 30 minutes, resulting in a green homogeneous solution. In a separate flask, [RhCl(COD)]₂ (6.20 mg, 0.013 mmol) and tris(*tert*-butyldimethylsilyl) phosphite (23.0 µL, 0.050 mmol) were dissolved in anhydrous tetrahydrofuran (2 mL) at room temperature under an atmosphere of argon. The mixture was stirred for *ca*. 5 minutes, resulting in a light yellow homogeneous solution, and then cooled to -10 °C. The catalyst solution was then added to the anion *via* Teflon[®] cannula, followed immediately by the addition of *tert*-butyl 5-phenylpent-1-en-3-yl carbonate **1a** (131 mg, 0.50 mmol) *via* tared 500 µL gastight syringe. The mixture was allowed to stir for *ca*. 16 hours and then cooled to -40 °C (dry ice/acetonitrile bath). TBAF (2.00 mL, 2.00 mmol; 1M solution in THF) was then added dropwise and the solution was allowed to stir for *ca*. 1 hour at -40 °C. The reaction mixture was quenched with saturated aqueous ammonium chloride solution (2 mL), allowed to warm to room temperature and then partitioned between diethyl ether and saturated aqueous ammonium chloride solution. The combined organic layers were dried (anhyd. MgSO₄), filtered and concentrated *in vacuo* to give the crude product. Purification by flash column chromatography (silica gel, eluting with 3-9% diethyl ether/hexane) afforded the *ketone* **3a** (131 mg, 89%) as a white solid.

6. Spectral Data for the α-Ternary β,γ-Unsaturated Aryl Ketones 3a-l



1-(4-(Dimethylamino)phenyl)-2-phenethylbut-3-en-1-one (3a) *Color and State:* White solid; $\mathbf{mp} = 43-44$ °C; $b:l \ge 19:1$

^O ¹**H NMR** (500 MHz, CDCl₃) δ 7.85-7.82 (m, 2H), 7.28-7.25 (m, 2H), 7.20-7.16 (m, 3H), 6.65-6.62 (m, 2H), 5.95 (ddd, J = 17.1, 10.3, 8.6 Hz, 1H), 5.16 (app. dt, J = 17.3, 1.1 Hz, 1H), 5.15 (app. dt, J = 10.3, 1.4 Hz, 1H), 3.99 (app. q, J = 7.5 Hz, 1H), 3.05 (s, 6H), 2.69-2.60 (m, 2H), 2.23 (ddt, A of ABXY₂, $J_{AB} = 13.6$ Hz, $J_{AX} = 8.6$ Hz, $J_{AY} = 6.8$ Hz, 1H), 1.91 (ddt, B of ABXY₂, $J_{AB} = 13.8$ Hz, $J_{BX} = 8.3$ Hz, $J_{BY} = 7.0$ Hz, 1H).

¹³C NMR (125 MHz, CDCl₃) δ 198.67 (e), 153.52 (e), 142.06 (e), 138.03 (o), 130.80 (o), 128.70 (o), 128.42 (o), 125.92 (o), 124.65 (e), 117.14 (e), 110.80 (o), 50.08 (o), 40.09 (o), 33.84 (e), 33.45 (e).

IR (Neat) 3078 (w), 3058 (w), 3024 (w), 2915 (w), 2854 (w), 2816 (w), 1655 (m), 1590 (vs), 1548 (s), 1525 (m), 1367 (s), 1163 (s), 991 (m), 937 (m), 824 (m), 698 (s) cm⁻¹.

HRMS (EI, M^+) calcd for C₂₀H₂₃NO 293.1780, found 293.1791.



2-Benzyl-1-(4-(dimethylamino)phenyl)but-3-en-1-one (3b)

Color and State: White solid; $\mathbf{mp} = 40-42 \text{ °C}; b:l \ge 19:1$

^b ¹**H NMR** (500 MHz, CDCl₃) δ 7.90-7.87 (m, 2H), 7.27-7.21 (m, 4H), 7.18-7.14 (m, 1H), 6.64-6.62 (m, 2H), 5.96 (ddd, J = 17.2, 10.1, 8.5 Hz, 1H), 5.10 (d, J = 10.5Hz, 1H), 5.07 (d, J = 17.3 Hz, 1H), 4.31 (app. q, J = 7.5 Hz, 1H), 3.28 (dd, A of ABX, $J_{AB} = 13.8$ Hz, $J_{AX} = 6.9$ Hz, 1H), 3.04 (s, 6H), 2.91 (dd, B of ABX, $J_{AB} = 13.8$ Hz, $J_{BX} = 7.4$ Hz, 1H). ¹³**C NMR** (125 MHz, CDCl₃) δ 198.13 (e), 153.49 (e), 140.05 (e), 137.54 (o), 130.84 (o), 129.34 (o), 128.29 (o), 126.11 (o), 124.55 (e), 117.45 (e), 110.76 (o), 52.80 (o), 40.09 (o), 38.32 (e). **IR** (Neat) 3078 (w), 3032 (w), 2999 (w), 2912 (m), 2850 (w), 2744 (w), 1653 (m), 1591 (vs), 1549 (s), 1530 (m), 1374 (s), 1167 (s), 999 (s), 933 (s), 819 (s), 698 (s) cm⁻¹. **HRMS** (EI, M⁺) calcd for C₁₉H₂₁NO 279.1623, found 279.1615.



1-(4-(Dimethylamino)phenyl)-2-vinylpentan-1-one (3c)

Color and State: White solid; $\mathbf{mp} = 39-41 \text{ °C}; b:l \ge 19:1$

^b ¹**H NMR** (500 MHz, CDCl₃) δ 7.93-7.90 (m, 2H), 6.67-6.64 (m, 2H), 5.92 (ddd, *J* = 17.3, 10.0, 8.6 Hz, 1H), 5.13 (app. dt, *J* = 17.3, 0.6 Hz, 1H), 5.09 (dd, *J* = 10.2, 1.3 Hz, 1H), 4.00 (app. q, *J* = 7.6 Hz, 1H), 3.04 (s, 6H), 1.85 (ddt, A of ABXYZ, *J*_{AB} = 13.2 Hz, *J*_{AX} = 9.8 Hz, *J*_{AY} = *J*_{AZ} = 6.5 Hz, 1H), 1.58 (dddd, B of ABXYZ, *J*_{AB} = 13.1 Hz, *J*_{BX} = 10.0 Hz, *J*_{BY} = 7.6 Hz, *J*_H), 1.42-1.25 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 199.23 (e), 153.46 (e), 138.42 (o), 130.73 (o), 124.76 (e), 116.48 (e), 110.79 (o), 50.78 (o), 40.09 (o), 34.65 (e), 20.61 (e), 14.15 (o).

IR (Neat) 3079 (w), 2956 (w), 2930 (w), 2870 (w), 2819 (w), 1655 (m), 1591 (vs), 1551 (m), 1527 (m), 1367 (s), 1185 (s), 1167 (s), 994 (m), 823 (s) cm⁻¹.

HRMS (EI, M^+) calcd for C₁₅H₂₁NO 231.1623, found 231.1630.

NMe₂ 1-(4-(Dimethylamino)phenyl)-2-methylbut-3-en-1-one (3d)

Color and State: Yellow solid; $\mathbf{mp} = 45-47 \text{ }^\circ\text{C}; b:l \ge 19:1$

^b ¹**H NMR** (500 MHz, CDCl₃) δ 7.93-7.90 (m, 2H), 6.67-6.64 (m, 2H), 6.01 (ddd, J = 17.4, 10.1, 7.5 Hz, 1H), 5.15 (app. dt, J = 17.2, 1.3 Hz, 1H), 5.09 (app. dt, J = 10.2, 1.0 Hz, 1H), 4.11 (app. pentet, J = 7.1 Hz, 1H), 3.05 (s, 6H), 1.31 (d, J = 6.8 Hz, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 199.32 (e), 153.45 (e), 139.34 (o), 130.84 (o), 124.19 (e), 115.66 (e), 110.78 (o), 44.77 (o), 40.10 (o), 17.41 (o).

IR (Neat) 3079 (w), 2974 (w), 2929 (w), 2870 (w), 2816 (w), 1659 (m), 1634 (w), 1591 (vs), 1550 (s), 1526 (s), 1366 (s), 1187 (s), 1160 (s), 944 (s), 825 (s) cm⁻¹.

HRMS (EI, M^+) calcd for $C_{13}H_{17}NO 203.1310$, found 203.1312.



1-(4-(Dimethylamino)phenyl)-4-methyl-2-vinylpentan-1-one (3e) Color and State: Pale yellow solid; $\mathbf{mp} = 61-63 \text{ °C}$; $b:l \ge 19:1$

¹**H NMR** (500 MHz, CDCl₃) δ 7.93-7.90 (m, 2H), 6.68-6.65 (m, 2H),

5.90 (ddd, J = 17.2, 10.1, 8.7 Hz, 1H), 5.13 (app. dt, J = 17.2, 1.1 Hz, 1H), 5.09 (dd, J = 10.2, 1.4

Hz, 1H), 4.10 (app. q, J = 7.7 Hz, 1H), 3.06 (s, 6H), 1.74 (ddd, A of ABXY, $J_{AB} = 13.3$ Hz, $J_{AX} = 7.6$ Hz, $J_{AY} = 6.7$ Hz, 1H), 1.65-1.57 (m, 1H), 1.50 (ddd, B of ABXY, $J_{AB} = 13.4$ Hz, $J_{BX} = 7.6$ Hz, $J_{BY} = 6.0$ Hz, 1H), 0.92 (d, J = 6.5 Hz, 3H), 0.90 (d, J = 6.6 Hz, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 199.21 (e), 153.48 (e), 138.55 (o), 130.74 (o), 124.69 (e), 116.45 (e), 110.84 (o), 48.96 (o), 41.46 (e), 40.13 (o), 25.75 (o), 23.15 (o), 22.40 (o).

IR (Neat) 3079 (w), 2954 (m), 2930 (m), 2870 (m), 2808 (w), 1649 (m), 1596 (vs), 1548 (s), 1529 (m), 1368 (s), 1187 (s), 1169 (s), 999 (m), 826 (s) cm⁻¹.

HRMS (EI, M^+) calcd for C₁₆H₂₃NO 245.1780, found 245.1768.



1-(4-(Dimethylamino)phenyl)-5-methyl-2-vinylhexan-1-one (3f) *Color and State:* Yellow oil; *b:l*≥19:1

¹**H NMR** (500 MHz, CDCl₃) δ 7.93-7.90 (m, 2H), 6.68-6.65 (m, 2H), 5.91 (ddd, J = 17.2, 10.1, 8.6 Hz, 1H), 5.13 (app. dt, J = 17.3, 1.1 Hz, 1H), 5.10 (dd, J = 10.2, 1.4 Hz, 1H), 3.94 (app. q, J = 7.6 Hz, 1H), 3.06 (s, 6H), 1.91-1.83 (m, 1H), 1.59 (dddd, A of ABXYZ, $J_{AB} = 13.1$ Hz, $J_{AX} = 11.3$ Hz, $J_{AY} = 7.6$ Hz, $J_{AZ} = 5.3$ Hz, 1H), 1.55 (nonet, J = 6.7 Hz, 1H), 1.25-1.12 (m, 2H), 0.87 (d, J = 6.6 Hz, 3H), 0.86 (d, J = 6.6 Hz, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 199.28 (e), 153.48 (e), 138.50 (o), 130.75 (o), 124.80 (e), 116.55 (e), 110.80 (o), 51.32 (o), 40.11 (o), 36.68 (e), 30.39 (e), 28.21 (o), 22.75 (o), 22.58 (o).

IR (Neat) 3079 (w), 2952 (m), 2904 (w), 2868 (w), 1658 (m), 1633 (w), 1592 (vs), 1551 (m), 1527 (m), 1366 (s), 1185 (s), 1167 (s), 994 (m), 824 (m) cm⁻¹.

HRMS (EI, M^+) calcd for $C_{17}H_{25}NO 259.1936$, found 259.1939.



2 1-(4-(Dimethylamino)phenyl)2-vinylhex-5-en-1-one (3g)

Color and State: Pale yellow oil; $b:l \ge 19:1$

^O ¹**H NMR** (500 MHz, CDCl₃) δ 7.92-7.89 (m, 2H), 6.67-6.64 (m, 2H), 5.90 (ddd, J = 17.2, 10.2, 8.7 Hz, 1H), 5.80 (ddt, J = 17.0, 10.3, 6.7 Hz, 1H), 5.15 (app. dt, J = 17.0, 1.0 Hz, 1H), 5.12 (dd, J = 10.2, 1.4 Hz, 1H), 5.00 (app. dq, J = 17.2, 1.7 Hz, 1H), 4.97 (ddt, J = 10.1, 2.0, 1.1 Hz, 1H), 4.03 (app. q, J = 7.5 Hz, 1H), 3.06 (s, 6H), 2.11-2.06 (m, 2H), 1.98 (ddt, A of ABXY₂, $J_{AB} = 13.3$ Hz, $J_{AX} = 8.7$ Hz, $J_{AY} = 6.6$ Hz, 1H), 1.69 (app. dq, B of ABXY₂, $J_{AB} = 13.5$ Hz, $J_{BX} = J_{BY} = 7.2$ Hz, 1H).

¹³C NMR (125 MHz, CDCl₃) δ 198.89 (e), 153.50 (e), 138.36 (o), 138.07 (o), 130.79 (o), 124.68
(e), 116.97 (e), 115.19 (e), 110.79 (o), 50.10 (o), 40.11 (o), 31.43 (e), 31.37 (e).

IR (Neat) 3076 (w), 2976 (w), 2920 (w), 2855 (w), 2818 (w), 1655 (m), 1591 (vs), 1551 (m), 1527 (m), 1368 (s), 1185 (s), 1166 (s), 993 (m), 821 (s) cm⁻¹.

HRMS (EI, M^+) calcd for C₁₆H₂₁NO 243.1623, found 243.1631.



¹**H NMR** (500 MHz, CDCl₃) δ 7.93-7.90 (m, 2H), 7.32-7.23 (m, 5H), 6.67-6.64 (m, 2H), 5.92 (ddd, J = 17.4, 10.1, 8.0 Hz, 1H), 5.22 (d, J = 17.3 Hz, 1H), 5.17 (d, J = 10.2 Hz, 1H), 4.56 (d, A of AB, $J_{AB} = 12.1$ Hz, 1H), 4.51 (d, B of AB, $J_{AB} = 12.1$ Hz, 1H), 4.39 (app. q, J = 7.3 Hz, 1H), 3.97 (dd, A of ABX, $J_{AB} = 9.1$ Hz, $J_{AX} = 7.4$ Hz, 1H), 3.66 (dd, B of ABX, $J_{AB} = 9.1$ Hz, $J_{BX} = 6.4$ Hz, 1H), 3.06 (s, 6H).

¹³C NMR (125 MHz, CDCl₃) δ 197.02 (e), 153.55 (e), 138.43 (e), 135.04 (o), 130.92 (o), 128.36 (o), 127.68 (o), 127.54 (o), 124.73 (e), 118.35 (e), 110.75 (o), 73.41 (e), 71.44 (e), 51.20 (o), 40.07 (o).

IR (Neat) 3082 (w), 3061 (w), 3029 (w), 2900 (w), 2857 (w), 1654 (m), 1590 (vs), 1550 (m), 1527 (m), 1368 (s), 1186 (s), 1168 (s), 1093 (s), 994 (m), 825 (s), 697 (s) cm⁻¹.

HRMS (EI, M^+) calcd for $C_{20}H_{23}NO_2$ 309.1729, found 309.1721.

¹**H NMR** (500 MHz, CDCl₃) δ 7.95-7.92 (m, 2H), 7.33-7.24 (m, 5H), 6.66-6.63 (m, 2H), 5.90 (ddd, *J* = 17.2, 10.1, 8.6 Hz, 1H), 5.14 (ddd, *J* = 17.3, 1.4, 0.9 Hz, 1H), 5.11 (ddd, *J* = 10.1, 1.4, 0.5 Hz, 1H), 4.46 (d, A of AB, *J*_{AB} = 12.0 Hz, 1H), 4.44 (d, B of AB, *J*_{AB} = 12.0 Hz, 1H), 4.30 (app. q, *J* = 7.6 Hz, 1H), 3.54 (ddd, A of ABXY, *J*_{AB} = 9.5 Hz, *J*_{AX} = 7.2 Hz, *J*_{AY} = 5.2 Hz, 1H), 3.47 (ddd, B of ABXY, *J*_{AB} = 9.5 Hz, *J*_{BX} = 6.4 Hz, *J*_{BY} = 5.3 Hz, 1H), 3.06 (s, 6H), 2.23 (dtd, A of ABXYZ, *J*_{AB} = 14.1 Hz, *J*_{AX} = *J*_{AY} = 7.1 Hz, *J*_{AZ} = 5.3 Hz, 1H), 1.87 (dddd, B of ABXYZ, *J*_{AB} = 14.0 Hz, *J*_{BY} = 6.6 Hz, *J*_{BZ} = 5.3 Hz, 1H).

¹³C NMR (125 MHz, CDCl₃) δ 198.76 (e), 153.50 (e), 138.66 (e), 137.62 (o), 130.92 (o), 128.39 (o), 127.73 (o), 127.55 (o), 124.63 (e), 117.19 (e), 110.77 (o), 72.99 (e), 67.88 (e), 47.29 (o), 40.10 (o), 32.26 (e).

IR (Neat) 3078 (w), 3030 (w), 2919 (w), 2856 (w), 1655 (m), 1591 (vs), 1551 (m), 1527 (m), 1366 (s), 1185 (s), 1167 (s), 1099 (s), 994 (m), 823 (s), 697 (s) cm^{-1} .

HRMS (EI, M^+) calcd for $C_{21}H_{25}NO_2$ 323.1885, found 323.1880.



2-Phenethyl-1-(4-(pyrrolidine-1-yl)phenyl)but-3-en-1-one (3j)

Color and State: White solid; **mp** = 80-82 °C; *b:l*≥19:1 ¹**H NMR** (500 MHz, CDCl₃) δ 7.85-7.82 (m, 2H), 7.29-7.26 (m, 2H), 7.20-7.17 (m, 3H), 6.51-6.48 (m, 2H), 5.95 (ddd, *J* = 17.2, 10.2, 8.6

Hz, 1H), 5.16 (dd, J = 17.3, 0.9 Hz, 1H), 5.14 (dd, J = 10.2, 1.2, 1H), 3.99 (app. q, J = 7.1 Hz, 1H), 3.38-3.35 (m, 4H), 2.66-2.63 (m, 2H), 2.23 (ddt, A of ABXY₂, $J_{AB} = 13.6$ Hz, $J_{AX} = 8.6$ Hz, $J_{AY} = 6.9$ Hz, 1H), 2.05-2.02 (m, 4H), 1.91 (ddt, B of ABXY₂, $J_{AB} = 13.8$ Hz, $J_{BX} = 8.2$ Hz, $J_{BY} = 7.0$ Hz, 1H).

¹³C NMR (125 MHz, CDCl₃) δ 198.62 (e), 151.11 (e), 142.11 (e), 138.14 (o), 130.98 (o), 128.72 (o), 128.42 (o), 125.91 (o), 124.14 (e), 117.06 (e), 110.85 (o), 50.00 (o), 47.66 (e), 33.88 (e), 33.47 (e), 25.56 (e).

IR (Neat) 3058 (w), 3023 (w), 2964 (w), 2944 (w), 2925 (w), 2848 (w), 1654 (m), 1588 (vs), 1546 (m), 1524 (m), 1388 (s), 1244 (m), 1177 (s), 1118 (m), 699 (m) cm⁻¹.

HRMS (EI, M⁺) calcd for C₂₂H₂₅NO 319.1936, found 319.1931.



2-Phenethyl-1-(4-piperidin-1-yl)but-3-en-1-one (3k)

Color and State: White solid; $\mathbf{mp} = 81-82^{\circ}\text{C}; \ b:l \ge 19:1$

¹**H NMR** (500 MHz, CDCl₃) δ 7.83-7.80 (m, 2H), 7.29-7.26 (m, 2H), 7.20-7.16 (m, 3H), 6.84-6.81 (m, 2H), 5.98-5.91 (m, 1H), 5.16 (d, *J* =

16.7 Hz, 1H), 5.16 (dd, J = 10.2, 1.1 Hz, 1H), 3.99 (app. q, J = 7.5 Hz, 1H), 3.37-3.35 (m, 4H), 2.66 (dt, A of ABX₂, $J_{AB} = 13.9$ Hz, $J_{AX} = 6.6$ Hz, 1H), 2.63 (dt, B of ABX₂, $J_{AB} = 13.7$ Hz, $J_{BX} = 7.1$ Hz, 1H), 2.22 (dtd, A of ABX₂Y, $J_{AB} = 13.6$ Hz, $J_{AX} = 6.8$ Hz, $J_{AY} = 1.8$ Hz, 1H), 1.91 (dtd, B of ABX₂Y, $J_{AB} = 13.9$ Hz, $J_{BX} = 6.8$ Hz, $J_{AY} = 1.6$ Hz, 1H), 1.68-1.64 (m, 6H).

¹³C NMR (125 MHz, CDCl₃) δ 198.71 (e), 154.47 (e), 142.00 (e), 137.86 (o), 130.77 (o), 128.69 (o), 128.43 (o), 125.94 (o), 125.83 (e), 117.27 (e), 113.29 (o), 50.12 (o), 48.60 (e), 33.80 (e), 33.42 (e), 25.46 (e), 24.47 (e).

IR (Neat) 3076 (w), 3024 (w), 2931 (m), 2853 (w), 1659 (m), 1592 (vs), 1557 (m), 1516 (m), 1451 (m), 1387 (m), 1223 (s), 1188 (s), 1124 (s), 699 (m) cm⁻¹.

HRMS (EI, M⁺) calcd for C₂₃H₂₇NO 333.2093, found 333.2099.



1-(4-Morpholinophenyl)-2-phenethylbut-3-en-1-one (3l) *Color and State:* White solid; **mp** = 86-88 °C; *b:l*≥19:1 ¹**H NMR** (500 MHz, CDCl₃) δ 7.85-7.82 (m, 2H), 7.29-7.26 (m, 2H), 7.20-7.16 (m, 3H), 6.85-6.82 (m, 2H), 5.94 (ddd, *J* = 17.4, 2H), 7.20-7.16 (m, 3H), 6.85-6.82 (m, 2H), 5.94 (ddd, *J* = 17.4, 2H), 7.20-7.16 (m, 3H), 6.85-6.82 (m, 2H), 5.94 (ddd, *J* = 17.4, 2H), 7.20-7.16 (m, 3H), 6.85-6.82 (m, 2H), 5.94 (ddd, *J* = 17.4, 2H), 7.20-7.16 (m, 3H), 6.85-6.82 (m, 2H), 5.94 (ddd, *J* = 17.4, 2H), 7.20-7.16 (m, 3H), 6.85-6.82 (m, 2H), 5.94 (ddd, *J* = 17.4, 2H), 7.20-7.16 (m, 3H), 6.85-6.82 (m, 2H), 5.94 (ddd, *J* = 17.4, 2H), 5.94 (ddd, *J* = 17.4, 2H), 7.20-7.16 (m, 3H), 6.85-6.82 (m, 2H), 5.94 (ddd, *J* = 17.4, 2H), 5.94 (ddd, J = 17.4), 5.94 (ddd, J 10.0, 8.5 Hz, 1H), 5.18-5.15 (m, 2H), 3.98 (app. q, J = 7.5 Hz, 1H), 3.85 (br. t, J = 4.9 Hz, 4H), 3.30 (br. t, J = 4.9 Hz, 4H), 2.69-2.60 (m, 2H), 2.22 (ddt, A of ABXY₂, $J_{AB} = 13.5$ Hz, $J_{AX} = 8.6$ Hz, $J_{AY} = 6.8$ Hz, 1H), 1.92 (ddt, B of ABXY₂, $J_{AB} = 13.7$ Hz, $J_{BX} = 8.4$ Hz, $J_{BY} = 6.9$ Hz, 1H).

¹³C NMR (125 MHz, CDCl₃) δ 198.92 (e), 154.31 (e), 141.91 (e), 137.63 (o), 130.66 (o), 128.70 (o), 128.47 (o), 127.46 (e), 126.00 (o), 117.50 (e), 113.40 (o), 66.68 (e), 50.26 (o), 47.62 (e), 33.74 (e), 33.38 (e).

IR (Neat) 3078 (w), 3060 (w), 3023 (w), 2958 (w), 2919 (w), 2854 (w), 1662 (m), 1596 (vs), 1516 (w), 1449 (w), 1381 (w), 1223 (m), 1190 (m), 1122 (m), 701 (w) cm⁻¹. **HRMS** (EI, M^+) calcd for C₂₂H₂₅NO₂ 335.1885, found 335.1891.

7. Stereospecific Rhodium-Catalyzed Allylic Alkylation/CBS reduction

$OCO_2^{t}Bu$ (*R*)-But-3-en-2-yl *tert*-butyl carbonate ((*R*)-1d)

Me Prepared according to the general procedure.

Color and State: Colorless oil.; $[\alpha]_D^{20}$ +15.4 (c = 1.0, CHCl₃).

¹**H NMR** (500 MHz, CDCl₃) δ 5.86 (ddd, J = 17.1, 10.7, 6.3 Hz, 1H), 5.27 (d, J = 17.1 Hz, 1H), 5.15 (d, J = 10.5 Hz, 1H), 5.12 (app. q, J = 6.3 Hz, 1H), 1.48 (s, 9H), 1.35 (d, J = 6.6 Hz, 3H). **IR** (Neat) 2982 (w), 2935 (w), 1736 (s), 1647 (w), 1369 (m), 1273 (s), 1252 (vs), 1162 (s) cm⁻¹.



(*R*)-1-(4-(Dimethylamino)phenyl)-2-methylbut-3-en-1-one ((*R*)-3d). Lithium bis(trimethylsilyl)amide (12.6 mL, 12.6 mmol; 1M solution in THF) was added dropwise to a stirred solution of 2-(*tert*-butyldimethylsilyloxy)-2-(4-(dimethylamino)phenyl)acetonitrile **2a** (2.64

g, 9.10 mmol) and lithium chloride (594 mg, 14.0 mmol) in anhydrous tetrahydrofuran (22.5 mL) at -10 °C under an atmosphere of argon. The anion was allowed to form over *ca*. 30 minutes, resulting in a dark green homogeneous solution. In a separate flask, [RhCl(COD)]₂ (86.0 mg, 0.175 mmol) and tris(2,2,2-trifluoroethyl) phosphite (154 µL, 0.70 mmol) were dissolved in anhydrous tetrahydrofuran (12.5 mL) at room temperature under an atmosphere of argon. The mixture was stirred for *ca*. 5 minutes, resulting in a light yellow homogeneous solution, and then cooled to -10 °C. The catalyst solution was then added to the anion *via* Teflon[®] cannula, followed immediately by the addition of (*R*)-but-3-en-2-yl *tert*-butyl carbonate (*R*)-**1e** (1.21 g, 7.0 mmol). The mixture was allowed to stir for *ca*. 16 hours and then cooled to -40 °C (dry ice/acetonitrile bath). TBAF (35.0 mL, 35.0 mmol; 1M solution in THF) was then added dropwise and the solution was allowed to stir for *ca*. 1 hour at -40 °C. The reaction mixture was

quenched with saturated aqueous ammonium chloride solution (20 mL), allowed to warm to room temperature and then partitioned between diethyl ether and saturated aqueous ammonium chloride solution. The combined organic layers were dried (anhyd. MgSO₄), filtered and concentrated *in vacuo* to give the crude product. Purification by flash column chromatography (silica gel, eluting with 10-30% diethyl ether/hexane) afforded the *α-ternary ketone* **7** (1.15 g, 81%) as a white solid: **mp** = 46-48 °C; *b:l*≥19:1; $[\alpha]_D^{20}$ –17.4 (*c* = 1.0, CHCl₃); Chiral HPLC analysis (CHIRALPAK AS-H column), 95:5 hexane/isopropanol at 1.0 mL/min flow rate; *t*_R (*R*)enantiomer (major) = 13.4 min., *t*_R (*S*)-enantiomer (minor) = 14.8 min.; 94% *ee*; 95% *cee*.

¹**H** NMR (500 MHz, CDCl₃) δ 7.93-7.90 (m, 2H), 6.67-6.64 (m, 2H), 6.01 (ddd, J = 17.5, 10.2, 7.6 Hz, 1H), 5.15 (app. dt, J = 17.2, 1.3 Hz, 1H), 5.09 (ddd, J = 10.2, 1.3, 1.0 Hz, 1H), 4.11 (app. pentet of triplets, J = 6.8, 1.0 Hz, 1H), 3.06 (s, 6H), 1.31 (d, J = 6.8 Hz, 3H).

IR (Neat) 3083 (w), 3052 (w), 2975 (w), 2931 (w), 2870 (w), 2818 (w), 1659 (m), 1593 (vs), 1551 (m), 1527 (m), 1368 (s), 1188 (s), 1168 (s), 944 (m), 827 (m) cm⁻¹.



(1*R*,2*R*)-1-(4-(Dimethylamino)phenyl)-2-methylbut-3-en-1-ol (7). (*S*)-CBS (1.39 g, 5.0 mmol) was dissolved in anhydrous tetrahydrofuran (12.5 mL) and cooled with stirring to -30 °C under an atmosphere of argon. Borane dimethylsulfide complex (0.95 mL, 10 mmol) was added to the

solution and the mixture was stirred for *ca*. 30 minutes. A solution of (*R*)-1-(4-(dimethylamino)phenyl)-2-methylbut-3-en-1-one (*R*)-3d (1.02 g, 5.0 mmol) in anhydrous tetrahydrofuran (12.5 mL) was then added dropwise and the reaction mixture was stirred for *ca*. 16 hours. The reaction mixture was quenched with methanol (5 mL) and partitioned between ethyl acetate and saturated aqueous sodium chloride solution. The combined organic layers were the sequentially washed with a saturated aqueous sodium bicarbonate and sodium chloride, dried (anhyd. MgSO₄), filtered and concentrated *in vacuo* to give the crude product. Purification by flash column chromatography (silica gel, eluting with 20-30% ethyl acetate/hexane) afforded the *alcohol* **8** (854 mg, 83%) as a pale yellow oil: $dr \ge 19:1$; $[\alpha]_D^{20} + 91.2$ (c = 1.0, CHCl₃).

¹**H** NMR (500 MHz, CDCl₃) δ 7.22-7.19 (m, 2H), 6.73-6.70 (m, 2H), 5.85 (ddd, J = 17.4, 10.1, 8.1 Hz, 1H), 5.20 (app. dt, J = 17.3, 0.9 Hz, 1H), 5.16 (dd, J = 10.2, 1.8 Hz, 1H), 4.26 (dd, J = 8.2, 1.7 Hz, 1H), 2.95 (s, 6H), 2.48 (sextet, J = 7.4 Hz, 1H), 2.00 (br. d, J = 2.4 Hz, 1H), 0.85 (d, J = 6.8 Hz, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 150.35 (e), 141.51 (o), 130.54 (e), 127.79 (o), 116.26 (e), 112.49 (o), 77.88 (o), 46.28 (o), 40.76 (o), 16.79 (o).

IR (Neat) 3397 (br, w), 3076 (w), 2962 (w), 2879 (m), 2800 (w), 1614 (s), 1521 (s), 1345 (s), 1187 (m), 1162 (s), 1003 (s), 947 (m), 814 (s) cm⁻¹.

HRMS (ESI, $[M+H]^+$) calcd for C₁₃H₂₀NO 206.1539, found 206.1539.

Me₂N

4-((1R,2R)-1-(Benzyloxy)-2-methylbut-3-enyl)-*N*,*N*-dimethylaniline (8a). A solution of (1R,2R)-1-(4-(Dimethylamino)phenyl)-2-methylbut-3-en-1-ol 7 (115 mg, 0.560 mmol) in dimethylformamide (1.4 mL) was added dropwise to a stirred suspension of sodium hydride (25.0 mg, 0.616

mmol; 60% dispersion in mineral oil) in dimethylformamide (4.2 mL) at 0 °C under an atmosphere of argon. The mixture was stirred for *ca*. 15 minutes before benzyl bromide (73.0 μ L, 0.616 mmol) was added and the solution was allowed to warm to room temperature and stirred for *ca*. 16 hours. The reaction mixture was cooled to 0 °C and quenched with saturated aqueous ammonium chloride solution (5 mL), allowed to warm to room temperature and then partitioned between diethyl ether and saturated aqueous ammonium chloride solution. The combined organic layers were washed with water, dried (anhyd. MgSO₄), filtered and concentrated *in vacuo* to give the crude product. Purification by flash column chromatography (silica gel, eluting with 5-15% diethyl ether/hexane) afforded the *benzyl ether* **8a** (136 mg, 82%) as a pale yellow oil: $[\alpha]_D^{20}$ +99.7 (*c* = 1.0, CHCl₃).

¹**H NMR** (500 MHz, CDCl₃) δ 7.35-7.29 (m, 4H), 7.27-7.23 (m, 1H), 7.18-7.15 (m, 2H), 6.74-6.72 (m, 2H), 5.96 (ddd, J = 17.1, 10.6, 7.3 Hz, 1H), 5.04 (ddd, J = 17.1, 1.8, 1.3 Hz, 1H), 5.03 (ddd, J = 10.6, 1.8, 1.0 Hz, 1H), 4.46 (d, A of AB, $J_{AB} = 12.3$ Hz, 1H), 4.20 (d, B of AB, $J_{AB} = 12.1$ Hz, 1H), 4.00 (d, J = 7.6 Hz, 1H), 2.97 (s, 6H), 2.56 (app. sextet of triplets, J = 7.1, 1.1 Hz, 1H), 0.83 (d, J = 6.9 Hz, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 150.22 (e), 142.09 (o), 139.20 (e), 128.70 (o), 128.35 (e), 128.30 (o), 127.79 (o), 127.33 (o), 113.98 (e), 112.24 (o), 85.29 (o), 70.09 (e), 44.45 (o), 40.72 (o), 16.62 (o).

IR (Neat) 3065 (w), 3027 (w), 2962 (w), 2929 (w), 2863 (w), 2800 (w), 1613 (s), 1521 (s), 1453 (m), 1346 (m), 1186 (m), 1164 (m), 1088 (m), 1065 (s), 947 (m), 814 (s), 696 (vs) cm⁻¹. **HRMS** (ESI, $[M+H]^+$) calcd for C₂₀H₂₆NO 296.2009, found 296.2003.



4-((1R,2R)-1-Methoxy-2-methylbut-3-enyl)-*N*,*N*-dimethylaniline (8b). A solution of (1R,2R)-1-(4-(Dimethylamino)phenyl)-2-methylbut-3-en-1ol 7 (123 mg, 0.60 mmol) in dimethylformamide (1.5 mL) was added

dropwise to a stirred suspension of sodium hydride (26.0 mg, 0.66 mmol; 60% dispersion in

mineral oil) in dimethylformamide (4.5 mL) at 0 °C under an atmosphere of argon. The mixture was stirred for *ca*. 15 minutes before iodomethane (41.0 μ L, 0.66 mmol) was added and the solution was allowed to warm to room temperature and stirred for *ca*. 16 hours. The reaction mixture was cooled to 0 °C and quenched with saturated aqueous ammonium chloride solution (5 mL), allowed to warm to room temperature and then partitioned between diethyl ether and saturated aqueous ammonium chloride solution. The combined organic layers were washed with water, dried (anhyd. MgSO₄), filtered and concentrated *in vacuo* to give the crude product. Purification by flash column chromatography (silica gel, eluting with 5-15% diethyl ether/hexane) afforded the *methyl ether* **8b** (101 mg, 77%) as a colorless oil: $[\alpha]_D^{20}$ +51.4 (*c* = 1.0, CHCl₃).

¹**H** NMR (500 MHz, CDCl₃) δ 7.14-7.11 (m, 2H), 6.73-6.70 (m, 2H), 5.91 (ddd, J = 17.4, 10.2, 7.3 Hz, 1H), 5.05 (ddd, J = 17.2, 1.8, 1.3 Hz, 1H), 5.03 (ddd, J = 10.4, 1.8, 1.0 Hz, 1H), 3.81 (d, J = 7.7 Hz, 1H), 3.16 (s, 3H), 2.96 (s, 6H), 4.00 (sextet, J = 7.1 Hz, 1H), 0.82 (d, J = 6.9 Hz, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 150.20 (e), 142.06 (o), 128.52 (o), 128.21 (e), 114.00 (e), 112.21 (o), 88.09 (o), 56.68 (o), 44.51 (o), 40.71 (o), 16.68 (o).

IR (Neat) 3079 (w), 2961 (w), 2925 (m), 2853 (m), 2818 (w), 1614 (s), 1521 (s), 1347 (s), 1185 (m), 1164 (m), 1090 (vs), 948 (m), 814 (s) cm⁻¹.

HRMS (ESI, $[M+H]^+$) calcd for $C_{14}H_{22}NO$ 220.1696, found 220.1688.

8. Preparation of Biaryl 9



4-((1*R***,2***R***)-1-(Benzyloxy)-2-methylbut-3-enyl)biphenyl (9).³** Methyl trifluoromethanesulfonate (23.0 μ L, 0.21 mmol) was added dropwise to a stirred solution of 4-((1*R*,2*R*)-1-(benzyloxy)-2-methylbut-3-enyl)-*N*,*N*-dimethylaniline **8a** (59.0 mg, 0.20 mmol) in dichloromethane (0.67 mL)

at 0 °C under an atmosphere of argon. The resulting mixture was allowed to warm to room for 3 hours. temperature and stirred ca. Tetrahydrofuran (1.33)mL) and bis(triphenylphosphine)palladium(II) dichloride (7.0 mg, 10 µmmol) were then added and the flask was evacuated and backfilled with argon $(3\times)$. Phenylmagnesium bromide (0.22 mL, 0.22 mL)mmol; 1M solution in THF) was then added dropwise and the light brown, heterogeneous solution was stirred at room temperature for ca. 16 hours. The reaction mixture was quenched with water (0.75 mL) and partitioned between ether and a 2M hydrochloric acid solution. The combined organic layers were dried (anhyd. MgSO₄), filtered and concentrated in vacuo to give the crude product. Purification by flash column chromatography (silica gel, eluting with 1-3%)

diethyl ether/hexane) afforded the *biaryl* **9** (51.0 mg, 78%) as a white solid: $\mathbf{mp} = 71-73 \text{ °C}$; [α] $_{\mathrm{D}}^{20}$ +112.3 (c = 1.0, CHCl₃).

¹**H NMR** (500 MHz, CDCl₃) δ 7.65-7.60 (m, 4H), 7.48-7.44 (m, 2H), 7.39-7.33 (m, 7H), 7.31-7.27 (m, 1H), 5.98 (ddd, J = 17.2, 10.5, 7.4 Hz, 1H), 5.08-5.04 (m, 2H), 4.53 (d, A of AB, $J_{AB} = 12.1$ Hz, 1H), 4.29 (d, B of AB, $J_{AB} = 12.1$ Hz, 1H), 4.19 (d, J = 7.2 Hz, 1H), 2.63 (sextet, J = 7.0 Hz, 1H), 0.92 (d, J = 6.9 Hz, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 141.32 (o), 141.02 (e), 140.55 (e), 139.81 (e), 138.82 (e), 128.91 (o), 128.40 (o), 128.23 (o), 127.82 (o), 127.54 (o), 127.38 (o), 127.19 (o), 126.99 (o), 114.56 (e), 85.28 (o), 70.64 (e), 44.43 (o), 16.55 (o).

IR (Neat) 3064 (w), 3029 (w), 2964 (w), 2926 (w), 2863 (w), 1600 (w), 1487 (m), 1454 (m), 1089 (m), 1070 (s), 913 (m), 734 (m), 696 (vs) cm⁻¹.

HRMS (ESI, $[M+Na]^+$) calcd for C₂₄H₂₄ONa 351.1719, found 351.1706.

9. Formal Synthesis of Trichostatic Acid

 $\underbrace{(2S,3R)-3-(4-(Dimethylamino)phenyl)-3-methoxy-2-methylpropanal}_{Me_2N} (10).^4 2,6-lutidine (47 muL, 0.40 mmol), osmium tetroxide (31 muL, 4.0 mumol; 4% aqueous solution) and sodium periodate (171 mg, 0.80 mumol).$

mmol) were added to a stirred solution of 4-((1*R*,2*R*)-1-Methoxy-2-methylbut-3-enyl)-*N*,*N*-dimethylaniline **8b** in dioxane (1.5 mL) and water (0.5 mL) at room temperature under an atmosphere of argon. The resulting hetereogenous mixture was allowed to stir for *ca*. 3 hours before being partitioned between dichloromethane and water. The combined organic layers were washed with saturated aqueous sodium chloride solution, dried (anhyd. MgSO₄), filtered and concentrated *in vacuo* to give the crude product. Purification by flash column chromatography (silica gel, eluting with 10-20% ethyl acetate/hexane) afforded the *aldehyde* **10** (34 mg, 78%) as a yellow oil: $[\alpha]_D^{20}$ +90.0 (*c* = 0.76, CHCl₃), [lit.⁵: $[\alpha]_D^{20}$ +63.4 (*c* = 0.76, CHCl₃)].

¹**H NMR** (500 MHz, CDCl₃) δ 9.81 (d, J = 3.1 Hz, 1H), 7.17-7.14 (m, 2H), 6.74-6.71 (m, 2H), 4.16 (d, J = 9.2 Hz, 1H), 3.15 (s, 3H), 2.97 (s, 6H), 2.70 (dqd, A of AMX₃Y, $J_{AM} = 9.3$ Hz, $J_{AX} = 7.1$ Hz, $J_{AY} = 3.1$ Hz, 1H), 0.83 (d, J = 7.1 Hz, 3H).

IR (Neat) 2979 (w), 2928 (w), 2893 (w), 2851 (w), 2819 (m), 2711 (w), 1724 (s), 1670 (w), 1612 (s), 1522 (s), 1446 (m), 1349 (s), 1081 (s), 944 (m), 815 (s) cm⁻¹.

10. References

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11. Proton and Carbon NMR Spectra








































OTBS











OTBS



























NMe₂














































210 200 190 180 170 160 150 140 130 120 110 100 and and and a second - Journe 90 80 70 60 50 40 <u>30</u> 20 10 ppm





210 200 190 180 170 160 150 140 130 120 110 100 and and and a second 90 80 70 60 50 40 <u>30</u> 20 10 ppm











12. HPLC Chromatograms

(R)-1-(4-(Dimethylamino)phenyl)-2-methylbut-3-en-1-one ((R)-3d)



#	[min]		[min]	[mAU*s]	[mAU]	%
1	13.372	MM	0.3917	1.25158e4	532.60858	97.2187
2	14.759	MM	0.3979	358.05652	14.99719	2.7813

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