Lewis Base Activation of Lewis Acids. Catalytic Enantioselective Addition of Silyl Enol Ethers of Achiral Methyl Ketones to Aldehydes.

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SUPPORTING INFORMATION

General Experimental

All reactions were performed in oven-dried (140 ^{o}C) or flame dried glassware under an atmosphere of dry N_2. The following reaction solvents were distilled from the indicated drying agents: dichloromethane (P_2O_5) and tetrahydrofuran (Na/benzophenone). The solvents for recrystallization were: benzene (Fisher ACS grade), and hexanes (Fisher ACS grade). The solvents for chromatography and filtration were: diethylether (Mallinckrodt), pentane (Fisher ACS grade), and dichloromethane ($CaCl_2$). Column chromatography was performed using EM Science 230-400-mesh silica gel. Benzaldehyde, 1-naphthaldehyde, 4-anisaldehyde, 4-trifluoromethylbenzaldehyde, (*E*)-cinnamaldehyde, (*E*)-2-methylcinnamaldehyde, furfural, 2-thiophenecarboxaldehyde and hydrocinnamaldehyde were freshly distilled before use. 2-Naphthaldehyde (Aldrich) was sublimed prior to use. Silicon tetrachloride (Gelest) was heated at reflux for 24 h and then distilled prior to use unless otherwise noted. Chlolrotrimethylsilane (TMSCl, Aldrich) was distilled from CaH_2 prior to use. Acetophenone, 2-hexanone, 4-methyl-2-pentanone, 3-methyl-2-butanone, and 3,3-dimethyl-2-butanone (Aldrich) were distilled and stored over 3Å molecular sieves. Diisopropylamine and diisopropylethylamine were freshly distilled from CaH_2 prior to use. Tetrabutylammonium iodide and tetrabutylammonium triflate were recrystallized from toluene and dried under vacuum prior to use. All reaction temperatures

correspond to internal temperatures measured be Teflon-coated thermocouples unless otherwise noted.

^{1}H NMR, ^{13}C NMR ^{19}F NMR spectra were recorded on Varian Unity 400 (400 MHz, ^{1}H; 100 MHz, ^{13}C; 376 MHz, ^{19}F) and Unity 500 (500 MHz, ^{1}H; 126 MHZ, ^{13}C) spectrometers. Spectra were referenced to residual chloroform (7.26 ppm, ^{1}H, 77.23 ppm, ^{13}C), ^{19}F spectra was referenced internally to C_6F_6. Chemical shifts are reported in ppm, multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), m (multiplet) and br (broad). Coupling Constants, J, are reported in Hertz. Mass Spectrometry was performed by the University of Illinois Mass Spectrometer Center. EI mass spectra were performed on a 70-VSE spectrometer. CI mass spectra were performed on a 70-VSE-B spectrometer. Data are reported in the form of (*m*/*z*). Infared spectra (IR) were recorded on a Mattson Galaxy 5020 spectrophotometer in NaCl cells. Peaks are recorded in cm^{-1} with indicated relative intensities: s (strong, 67-100%); m (medium, 34-66%); and w (weak, 0-33%). Elemental analyses were performed by the University of Illinois Microanalytical Service Laboratory. Melting points (mp) were determined on a Thomas-Hoover capillary melting point apparatus in sealed tubes and are corrected. Kugelrohr distillations were performed on a Büchi GKR-50 Kugelrohr and temperatures are air bath temperatures. Analytical thin-layer chromatography was performed on Merck silica gel plates with QF-254 indicator. Visualization was accomplished with UV(254) and 4-anisaldehyde.

Optical rotation data was obtained on a JASCO DIP-360 digital polarimeter and are reported as follows: (c = g/100 mL), and solvent. Analytical supercritical fluid chromatography (SFC) was performed on a Berger Instruments packed-column SFC with built-in photometric detector (220 nm) using Daicel Chiralpak AD, AS, OD, OJ, and Welko columns.

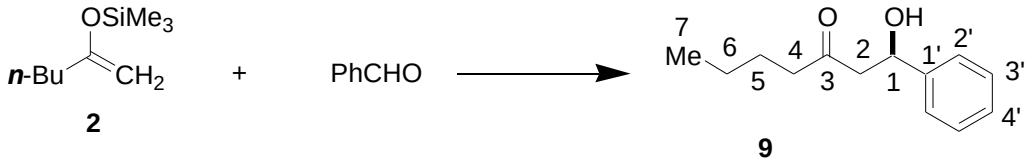
Literature Preparations

The preparation of 2-trimethylsilyloxy-1-hexene (**2**), 4-methyl-2-trimethylsilyloxy-1-pentene (**3**) 3-methyl-2-trimethylsilyloxy-1-butene (**4**) 2-phenyl-2-trimethylsilyloxy-1-ethene,

and (**6**) followed the procedure described by Enders *et. a*l.[1] Preparation of 2-trimethylsilyloxy-1-propene (**1**) and 3,3-dimethyl-2-trimethylsilyloxy-1-butene (**5**) and followed the procedure described by Myles and Bigham.[2] The preparation of (*R*,*R*)-*N*,*N*'-bis[4,5-dihydro-3,5-dimethyl-4-(3H-dinaphtho[2,1-d:1',2'-f][1,3,2]-2-oxo-diazaphosphephepino)]-*N*,*N*'-dimethyl-1,5-pentanediamine (*R*,*R*)-**7** followed the procedure described by Denmark and Wynn.[3]

Initial Studies

Reaction between 2 and Benzaldehyde (9) [JRH-I-27]



Benzaldehyde (102 μL, 1.0 mmol) was added to a flame-dried, 5-mL, 2-neck flask under N_2 containing a solution of 42 mg (0.05 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** in CH_2Cl_2 (2 mL). To this solution was added 126 μL (1.1 mmol, 1.1 equiv) of $SiCl_4$ in one portion, and the reaction mixture was cooled to –78 °C (bath temperature) over 15 min. Then, 206 mg (1.2 mmol, 1.2 equiv) of **2** was added dropwise neat over 5 min. The resulting mixture was stirred at –78 °C for 2 h whereupon the cold reaction mixture was poured into a rapidly stirring solution of 1/1 1.0 M KH_2PO_4 / sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 83 mg (81%) of **9** as a clear, colorless oil.[4]

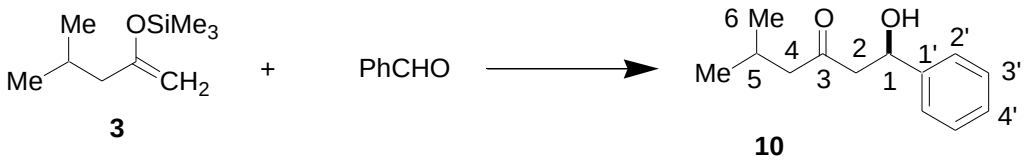
Data for **9**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.36-7.26 (m, 5 H, H(aryl)), 5.16 (dt, J = 8.8, 3.5, 1 H, HC(1)), 3.43 (d, J = 3.3, 1 H, OH), 2.88 (ABX, J_{AB} = 17.3, J_{AX} = 9.4, 1 H, H_aC(2)), 2.81 (ABX, J_{AB} = 17.3, J_{BX} = 2.8, 1 H, H_bC(2)), 2.43 (t, J = 7.3, 2 H, H_2C(4)), 1.57 (quint, J = 7.3, 2 H, H_2C(5)), 1.30 (sext, J = 7.3, 2 H, H_2C(6)), 0.90 (t, J = 7.3, 3 H, H_3C(7))

SFC: (*R*)-**9** t_R 4.08 min (99.0%); (*S*)-**9** t_R 3.32 min (1.0%) (AD column, 125 bar, 3.0 mL/min, 7.0% MeOH)

Reaction between 3 and Benzaldehyde (10) [JRH-I-36]



Benzaldehyde (51 μL, 0.5 mmol) was added to a flame-dried, 5-mL, 2-neck flask under N_2 containing a solution of 21 mg (0.025 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** in CH_2Cl_2 (1 mL). To this solution was added 63 μL (0.55 mmol, 1.1 equiv) of $SiCl_4$ in one portion, and the reaction mixture was cooled to –78 °C (bath temperature) over 15 min. Then, 103 mg (0.6 mmol, 1.2 equiv) of **3** was added dropwise neat over 5 min. The resulting mixture was stirred at –78 °C for 2 h whereupon the cold reaction mixture was poured into a rapidly stirring solution of 1/1 1.0 M KH_2PO_4 / sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 72 mg (70%) of **10** as a clear, colorless oil.[4]

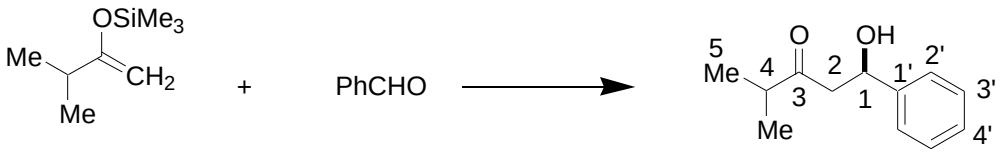
Data for **10**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.36-7.27 (m, 5 H, H(aryl)), 5.16 (dt, J = 9.0, 3.4, 1 H, HC(1)), 3.41 (d, J = 3.3, 1 H, OH), 2.85 (ABX, J_{AB} = 17.5, J_{AX} = 9.5, 1 H, H_aC(2)), 2.78 (ABX, J_{AB} = 17.5, J_{BX} = 2.8, 1 H, H_bC(2)), 2.34 (d, J = 7.0, 2 H, H_2C(4)), 2.14 (septet, J = 6.7, 1 H, H_2C(5)), 0.96 (d, J = 6.7, 6 H, 2 x H_3C(6))

SFC: (*R*)-**10** t_R 2.57 min (99.0%); (*S*)-**10** t_R 3.16 min (1.0%) (AD column, 125 bar, 3.0 mL/min, 7.0% MeOH)

Reaction between 4 and Benzaldehyde (11) [JRH-I-31]



4 **11**

Benzaldehyde (51 μL, 0.5 mmol) was added to a flame-dried, 5-mL, 2-neck flask under N_2 containing a solution of 21 mg (0.025 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** in CH_2Cl_2 (1 mL). To this solution was added 63 μL (0.55 mmol, 1.1 equiv) of $SiCl_4$ in one portion, and the reaction mixture was cooled to –78 °C (bath temperature) over 15 min. Then, 118 μL (95 mg, 0.6 mmol, 1.2 equiv) of **4** was added dropwise over 5 min. The resulting mixture was stirred at –78 °C for 2 h whereupon the cold reaction mixture was poured into a rapidly stirring solution of 1/1 1.0 M KH_2PO_4 / sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 69 mg (72%) of **11** as a clear, colorless oil.[4]

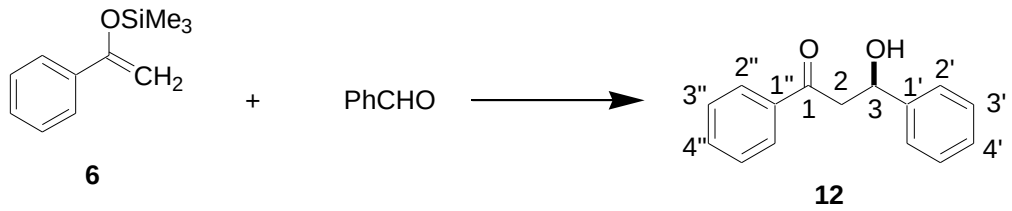
Data for **11**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.38-7.25 (m, 5 H, H(aryl)), 5.15 (dt, *J* = 8.3, 3.3, 1 H, HC(1)), 3.44 (d, *J* = 3.2, 1 H, OH), 2.87 (m, 2 H, HC(2)), 2.59 (sept, *J* = 7.1, 1 H, H_2C(4)), 1.11 (d, *J* = 6.8, 6 H, 2 x H_3C(5))

SFC: (*R*)-**11** t_R 2.46 min (99.5%); (*S*)-**11** t_R 2.71min (1.5%) (AD column, 125 bar, 3.0 mL/min, 7.0% MeOH)

Reaction between 6 and Benzaldehyde (12) [JRH-I-34]



6 **12**

Benzaldehyde (51 μL, 0.5 mmol) was added to a flame-dried, 5-mL, 2-neck flask under N_2 containing a solution of 21 mg (0.025 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** in CH_2Cl_2 (1 mL). To this solution was added 63 μL (0.55 mmol, 1.1 equiv) of $SiCl_4$ in one portion, and the reaction mixture was cooled to –78 °C (bath temperature) over 15 min. Then, 102 μL (115 mg, 0.6 mmol, 1.2 equiv) of **6** was added dropwise over 5 min. The resulting mixture was to stirred at –78 °C for 2 h whereupon the cold reaction mixture was poured into a rapidly stirring solution of 1/1 1.0 M KH_2PO_4 / sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 73 mg (76%) of **12** as a clear, colorless oil.[4]

Data for **12**:

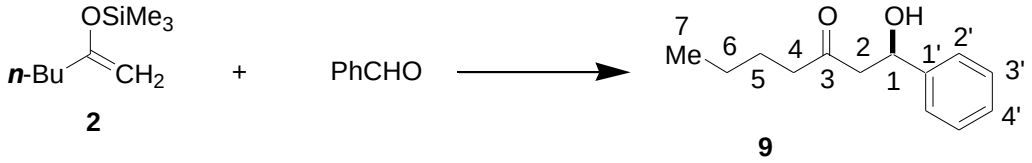
^{1}H NMR: (500 MHz, $CHCl_3$)

7.96 (d, *J* = 8.3, 2 H, 2 x HC(2")), 7.59 (t, *J* = 7.3, 1 H, HC(4")), 7.48-7.44 (m, 4 H, 2 x HC(3"')) + 2 x HC(2')), 7.39 (t, *J* = 7.8, 2 H, 2 x HC(3')), 7.31 (t, *J* = 7.1, 1 H, HC(4')), 5.35 (dt, *J* = 6.1, 2.9, 1 H, HC(1)), 3.62 (d, *J* = 3.2, 1 H, OH), 3.39 (d, *J* = 6.6, 1 H, H_2C(2))

SFC: (*R*)-**12** t_R 6.53 min (97.0%); (*S*)-**12** t_R 6.82min (3.0%) (AD column, 225 bar, 3.0 mL/min, 6.0% MeOH)

$SiCl_4$ Loading Study

Reaction of 2 and Benzaldehyde with 1.5 equiv of $SiCl_4$ (9) [JRH-I-47]



Benzaldehyde (51 μL, 0.5 mmol) was added to a flame-dried, 5 mL, 2-neck flask under N_2 containing a solution of 21 mg (0.025 mmol, 0.05 equiv) of bisphosphoramide (*R,R*)-**7** in CH_2Cl_2 (1 mL). To this solution was added 86 μL (0.75 mmol, 1.5 equiv) of $SiCl_4$ in one portion, and the reaction mixture was cooled to –78 °C (bath temperature) over 15 min. Then, 103 mg (0.6 mmol, 1.2 equiv) of **2** was added dropwise neat over 5 min. The resulting mixture was stirred at –78 °C for 2.5 h whereupon the cold reaction mixture was poured into a rapidly stirring solution of 1/1 1.0 M KH_2PO_4 / sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 89 mg (86%) of **9** as a clear, colorless oil.[4]

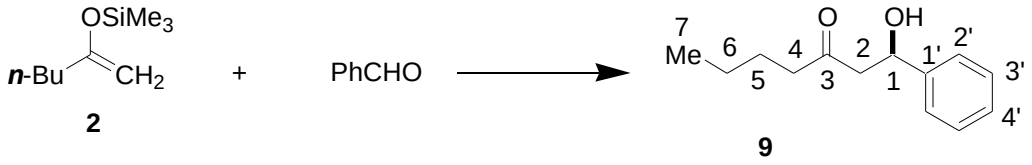
Data for **9**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.37-7.26 (m, 5 H, H(aryl)), 5.16 (dt, J = 8.7, 3.4, 1 H, HC(1)), 3.43 (d, J = 3.2, 1 H, OH), 2.88 (ABX, J_{AB} = 17.3, J_{AX} = 9.1, 1 H, H_aC(2)), 2.81 (ABX, J_{AB} = 17.3, J_{BX} = 3.1, 1 H, H_bC(2)), 2.45 (t, J = 7.3, 2 H, H_2C(4)), 1.58 (quint, J = 7.3, 2 H, H_2C(5)), 1.30 (sext, J = 7.3, 2 H, H_2C(6)), 0.90 (t, J = 7.3, 3 H, H_3C(7))

SFC: (*R*)-**9** t_R 3.24 min (99.5%); (*S*)-**9** t_R 3.47 min (0.5%) (AD column, 125 bar, 3.0 mL/min, 7.0% MeOH)

Reaction of 2 and Benzaldehyde with 2.0 equiv of $SiCl_4$ (9) [JRH-I-44]



Benzaldehyde (51 μL, 0.5 mmol) was added to a flame-dried, 5-mL, 2-neck flask under N_2 containing a solution of 21 mg (0.025 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** in CH_2Cl_2 (1 mL). To this solution was added 115 μL (1.0 mmol, 2.0 equiv) of $SiCl_4$ in one portion, and the reaction mixture was cooled to –78 °C (bath temperature) over 15 min. Then, 103 mg (0.6 mmol, 1.2 equiv) of **2** was added dropwise over 5 min. The resulting mixture was stirred at –78 °C for 2.5 h whereupon the cold reaction mixture was poured into a rapidly stirring solution of 1/1 1.0 M KH_2PO_4 / sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 83 mg (81%) of **9** as a clear, colorless oil.[7b]

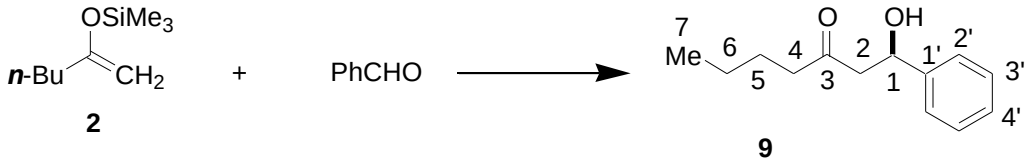
Data for **9**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.38-7.26 (m, 5 H, H(aryl)), 5.15 (dd, J = 8.9, 3.4, 1 H, HC(1)), 3.43 (d, J = 3.1, 1 H, OH), 2.86 (ABX, J_{AB} = 17.3, J_{AX} = 9.4, 1 H, $H_aC(2)$), 2.80 (ABX, J_{AB} = 17.3, J_{BX} = 2.8, 1 H, $H_bC(2)$), 2.42 (t, J = 7.33 2 H, $H_2C(4)$), 1.58 (quint, J = 7.2, 2 H, $H_2C(5)$), 1.31 (sext, J = 7.3, 2 H, $H_2C(6)$), 0.93 (t, J = 7.3, 3 H, $H_3C(7)$)

SFC: (*R*)-**9** t_R 2.98 min (99.5%); (*S*)-**9** t_R 3.22 min (0.5%) (AD column, 125 bar, 3.0 mL/min, 7.0% MeOH)

Reaction of 2 and Benzaldehyde with 3.0 equiv of $SiCl_4$ (9) [JRH-I-46]



2 **9**

Benzaldehyde (51 μL, 0.5 mmol) was added to a flame-dried, 5-mL, 2-neck flask under N_2 containing a solution of 21 mg (0.025 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** in CH_2Cl_2 (1 mL). To this solution was added 172 μL (1.5 mmol, 3.0 equiv) of $SiCl_4$ in one portion, and the reaction mixture was cooled to –78 °C (bath temperature) over 15 min. Then, 103 mg (0.6 mmol, 1.2 equiv) of **2** was added dropwise neat over 5 min. The resulting mixture was stirred at –78 °C for 2.5 h whereupon the cold reaction mixture was poured into a rapidly stirring solution of 1/1 1.0 M KH_2PO_4 / sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 83 mg (81%) of **9** as a clear, colorless oil.[4]

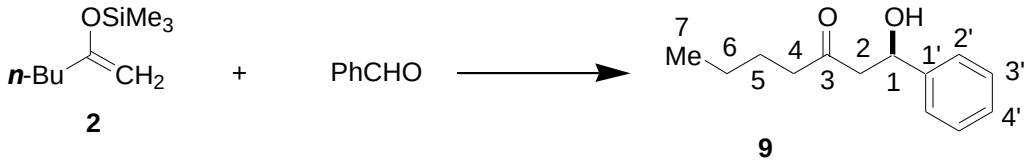
Data for **9**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.37-7.26 (m, 5 H, H(aryl)), 5.15 (dt, J = 8.5, 3.1, 1 H, HC(1)), 3.38 (d, J = 2.9, 1 H, OH), 2.85 (ABX, J_{AB} = 17.3, J_{AX} = 9.2, 1 H, H_aC(2)), 2.79 (ABX, J_{AB} = 17.3, J_{BX} = 2.7, 1 H, H_bC(2)), 2.42 (t, J = 7.3, 2 H, H_2C(4)), 1.54 (quint, J = 7.3, 2 H, H_2C(5)), 1.30 (sext, J = 7.3, 2 H, H_2C(6)), 0.91 (t, J = 7.32, 3 H, H_3C(7))

SFC: (*R*)-**9** t_R 3.18 min (99.5%); (*S*)-**9** t_R 3.38 min (0.5%) (AD column, 125 bar, 3.0 mL/min, 7.0% MeOH)

Reaction of 2 and Benzaldehyde with 4.0 equiv of $SiCl_4$ (9) [JRH-I-45]



Benzaldehyde (51 μL, 0.5 mmol) was added to a flame-dried, 5-mL, 2-neck flask under N_2 containing a solution of 21 mg (0.025 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** in CH_2Cl_2 (1 mL). To this solution was added 86 μL (2.0 mmol, 4.0 equiv) of $SiCl_4$ in one portion, and the reaction mixture was cooled to –78 °C (bath temperature) over 15 min. Then, 103 mg (0.6 mmol, 1.2 equiv) of **2** was added dropwise over 5 min. The resulting mixture was stirred at –78 °C for 2.5 h whereupon the cold reaction mixture was poured into a rapidly stirring solution of 1/1 1.0 M KH_2PO_4 / sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 84 mg (82%) of **9** as a clear, colorless oil.[4]

Data for **9**:

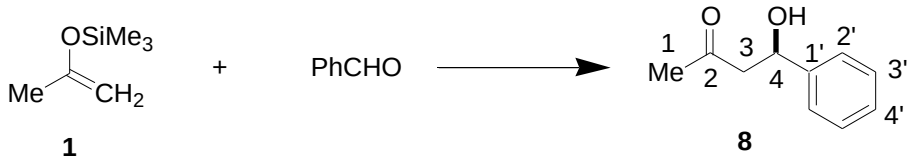
^{1}H NMR: (500 MHz, $CHCl_3$)

7.38-7.25 (m, 5 H, H(aryl)), 5.15 (dt, J = 8.8, 3.3, 1 H, HC(1)), 3.38 (d, J = 3.2, 1 H, OH), 2.87 (ABX, J_{AB} = 17.3, J_{AX} = 9.6, 1 H, H_aC(2)), 2.80 (ABX, J_{AB} = 17.3, J_{BX} = 2.7, 1 H, H_bC(2)), 2.42 (t, J = 7.3, 2 H, H_2C(4)), 1.56 (quint, J = 7.3, 2 H, H_2C(5)), 1.32 (sext, J = 7.4, 2 H, H_2C(6)), 0.92 (t, J = 7.3, 3 H, H_3C(7))

SFC: (*R*)-**9** t_R 2.99 min (99.5%); (*S*)-**9** t_R 3.22 min (0.5%) (AD column, 125 bar, 3.0 mL/min, 7.0% MeOH)

Study of TBAOTf as an additive

Reaction of 1 and Benzaldehyde with 0.05 equiv of TBAOTf (8) [JRH-II-12]



1 **8**

Benzaldehyde (102 μL, 1.0 mmol) was added to a flame-dried, 5-mL, 2-neck flask under N_2 containing a solution of 42 mg (0.05 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** and 20 mg of tetrabutylammonium triflate (0.05 mmol, 0.05 equiv) in CH_2Cl_2 (2 mL). To this solution was added 172 μL (1.5 mmol, 1.5 equiv) of $SiCl_4$ in one portion and the reaction mixture was cooled to –78 °C (bath temperature) over 15 min. Then, 198 μL (156 mg, 1.2 mmol, 1.2 equiv) of **1** was added dropwise over 5 min. The resulting mixture was stirred at –78 °C for 2 h, whereupon 3 mL of chilled CH_2Cl_2 was added before the cold reaction mixture was poured into a rapidly stirring solution of 1/1 sat. aq. $NaHCO_3$/sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 1/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 118 mg (72%) of **8** as a clear, colorless oil.[4]

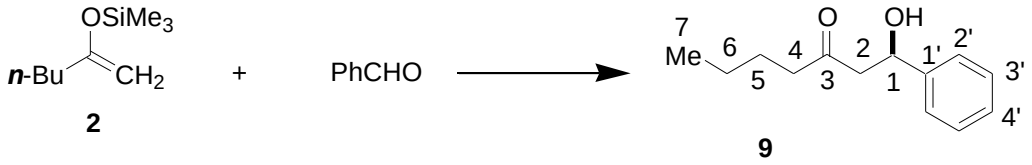
Data for **8**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.37-7.26 (m, 5 H, H(aryl)), 5.16 (dt, J = 9.3, 3.2, 1 H, HC(4)), 3.7 (d, J = 2.93, 1 H, OH), 2.89 (ABX, J_{AB} = 17.8, J_{AX} = 9.6, 1 H H_aC(3)), 2.83 (ABX, J_{AB} = 17.8, J_{BX} = 2.9 1 H, H_bC(4)), 2.20 (s, 3 H H_3C(1))

SFC: (*R*)-**8** t_R 3.16 min (98.0%); (*S*)-**8** t_R 3.47 min (2.0%) (AS column, 125 bar, 2.5 mL/min, 5.0% MeOH)

Reaction of 2 and Benzaldehyde with 0.05 equiv of TBAOTf (9) [JRH-I-92]



Benzaldehyde (102 μL, 1.0 mmol) was added to a flame-dried, 5-mL, 2-neck flask under N_2 containing a solution of 42 mg (0.05 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** and 20 mg of tetrabutylammonium triflate (0.05 mmol, 0.05 equiv) in CH_2Cl_2 (2 mL). To this solution was added 172 μL (1.5 mmol, 1.5 equiv) of $SiCl_4$ in one portion and the reaction mixture was cooled to –78 °C (bath temperature) over 15 min. Then, 206 mg (1.2 mmol, 1.2 equiv) of **2** was added dropwise neat over 5 min. The resulting mixture was stirred at –78 °C for 2 h, whereupon 3 mL of chilled CH_2Cl_2 was added before the cold reaction mixture was poured into a rapidly stirring solution of 1/1 sat. aq. $NaHCO_3$/sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 196 mg (95%) of **9** as a clear, colorless oil.[4]

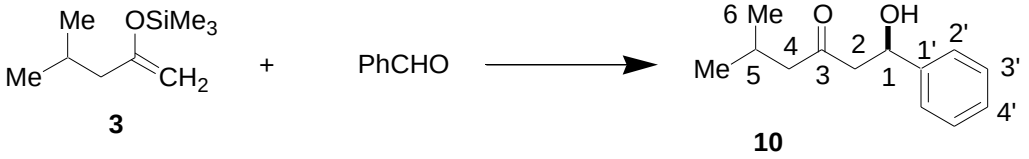
Data for **9**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.37-7.26 (m, 5 H, H(aryl)), 5.16 (dd, J = 9.0, 3.4, 1 H, HC(1)), 3.45 (br s, 1 H, OH), 2.89 (ABX, J_{AB} = 17.3, J_{AX} = 9.7, 1 H, $H_aC(2)$), 2.80 (ABX, J_{AB} = 17.3, J_{BX} = 2.8, 1 H, $H_bC(2)$), 2.43 (t, J = 7.3, 2 H, $H_2C(4)$), 1.57 (quint, J = 7.3, 2 H, $H_2C(5)$), 1.31 (sext, J = 7.3, 2 H, $H_2C(6)$), 0.90 (t, J = 7.3, 3 H, $H_3C(7)$)

SFC: (*R*)-**9** t_R 3.74 min (99.5%); (*S*)-**9** t_R 4.07 min (0.5%) (AD column, 125 bar, 3.0 mL/min, 6.0% MeOH)

Reaction of 3 and Benzaldehyde with 0.05 equiv of TBAOTf (10) [JRH-I-95]



Benzaldehyde (102 μL, 1.0 mmol) was added to a flame-dried, 5-mL, 2-neck flask under N_2 containing a solution of 42 mg (0.05 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** and 20 mg of tetrabutylammonium triflate (0.05 mmol, 0.05 equiv) in CH_2Cl_2 (2 mL). To this solution was added 172 μL (1.5 mmol, 1.5 equiv) of $SiCl_4$ in one portion and the reaction mixture was cooled to –78 °C (bath temperature) over 15 min. Then, 206 mg (1.2 mmol, 1.2 equiv) of **3** was added dropwise over 5 min. The resulting mixture was stirred at –78 °C for 2 h, whereupon 3 mL of chilled CH_2Cl_2 was added before the cold reaction mixture was poured into a rapidly stirring solution of 1/1 sat. aq. $NaHCO_3$/sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 175 mg (85%) of **10** as a clear, colorless oil.[4]

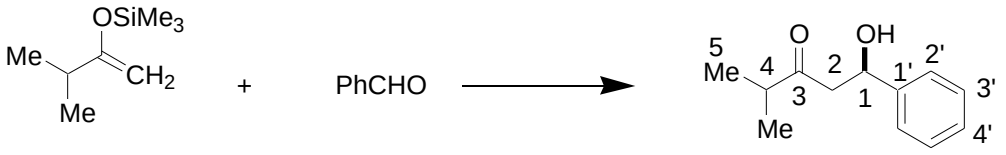
Data for **10**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.37-7.27 (m, 5 H, H(aryl)), 5.16 (dd, J = 9.0, 3.4, 1 H, HC(1)), 3.37 (br s, 1 H, OH), 2.83 (ABX, J_{AB} = 17.6, J_{AX} = 9.7, 1 H, $H_aC(2)$), 2.78 (ABX, J_{AB} = 17.6, J_{BX} = 2.7, 1 H, $H_bC(2)$), 2.31 (d, J = 7.1, 2 H, $H_2C(4)$), 2.15 (septet, J = 6.7, 1 H, $H_2C(5)$), 0.92 (d, J = 6.6, 6 H, 2 x $H_3C(6)$)

SFC: (*R*)-**10** t_R 2.81 min (99.0%); (*S*)-**10** t_R 3.16 min (1.0%) (AD column, 125 bar, 3.0 mL/min, 7.0% MeOH)

Reaction of 4 and Benzaldehyde with 0.05 equiv of TBAOTf (11) [JRH-I-93]



4 **11**

Benzaldehyde (102 μL, 1.0 mmol) was added to a flame-dried, 5-mL, 2-neck flask under N_2 containing a solution of 42 mg (0.05 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** and 20 mg of tetrabutylammonium triflate (0.05 mmol, 0.05 equiv) in CH_2Cl_2 (2 mL). To this solution was added 172 μL (1.5 mmol, 1.5 equiv) of $SiCl_4$ in one portion and the reaction mixture was cooled to –78 °C (bath temperature) over 15 min. Then, 118 μL (95 mg, 0.6 mmol, 1.2 equiv) of **4** was added dropwise over 5 min. The resulting mixture was stirred at –78 °C for 2 h, whereupon 3 mL of chilled CH_2Cl_2 was added before the cold reaction mixture was poured into a rapidly stirring solution of 1/1 sat. aq. $NaHCO_3$/sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 146 mg (76%) of **11** as a clear, colorless oil.[4]

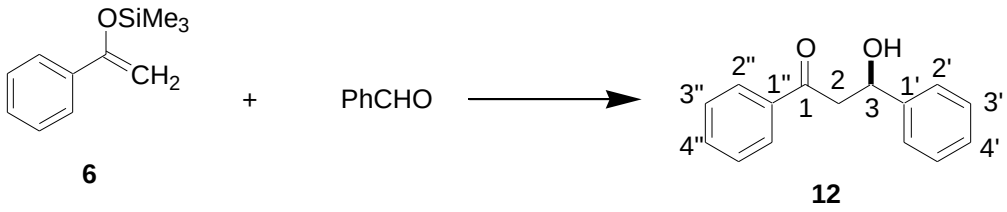
Data for **11**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.38-7.26 (m, 5 H, H(aryl)), 5.11 (dd, *J* = 8.3, 3.9, 1 H, HC(1)), 3.42 (br s, 1 H, OH), 2.88 (m, 2 H, HC(2)), 2.59 (sept, *J* = 6.8, 1 H, H_2C(4)), 1.10 (d, *J* = 6.8, 6 H, 2 x H_3C(5))

SFC: (*R*)-**11** t_R 2.62 min (99.5%); (*S*)-**11** t_R 2.902 min (0.5%) (AD column, 125 bar, 3.0 mL/min, 7.0% MeOH)

Reaction of 6 and Benzaldehyde with 0.05 equiv of TBAOTf (12) [JRH-I-94]



6 **12**

Benzaldehyde (102 μL, 1.0 mmol) was added to a flame-dried, 5-mL, 2-neck flask under N_2 containing a solution of 42 mg (0.05 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** and 20 mg of tetrabutylammonium triflate (0.05 mmol, 0.05 equiv) in CH_2Cl_2 (2 mL). To this solution was added 172 μL (1.5 mmol, 1.5 equiv) of $SiCl_4$ in one portion and the reaction mixture was cooled to –78 °C (bath temperature) over 15 min. Then, 248 μL (231 mg, 1.2 mmol, 1.2 equiv) of **6** was added dropwise over 5 min. The resulting mixture was stirred at –78 °C for 2 h, whereupon the cold reaction mixture was poured into a rapidly stirring solution of 1/1 1.0 M KH_2PO_4/sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 201 mg (89%) of **12** as a white solid.[4]

Data for **12**:

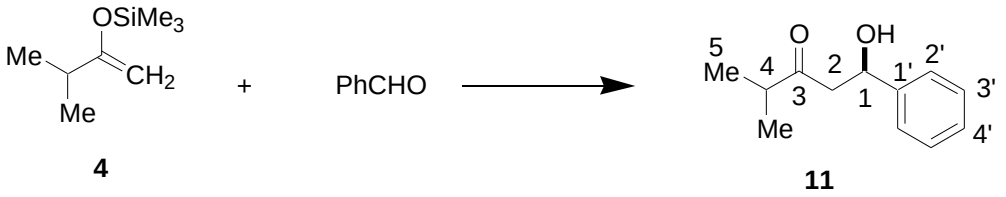
^{1}H NMR: (500 MHz, $CHCl_3$)

7.96 (d, *J* = 7.3, 2 H, 2 x HC(2")), 7.59 (t, *J* = 7.3, 1 H, HC(4")), 7.49-7.44 (m, 4 H, 2 x HC(3"')) + 2 x HC(2')), 7.39 (t, *J* = 7.6, 2 H, 2 x HC(3')), 7.31 (t, *J* = 7.3, 1 H, HC(4')), 5.36 (t, *J* = 6.0, 1 H, HC(1)), 3.79 (br s, 1 H, OH), 3.38 (d, *J* = 5.9, 2 H, H_2C(2))

SFC: (*R*)-**12** t_R 5.23 min (99.5%); (*S*)-**12** t_R 5.85 min (0.5%) (Welko column, 125 bar, 3.0 mL/min, 7.0% MeOH)

Survey of Amine Bases as Additives

Reaction of 4 and Benzaldehyde with 1.0 equiv of 2,4,6-tri-*tert*-Butylpyridine (11) [JRH-II-28]



4 **11**

2,4,6-tri-*tert*-Butylpyridine (124 mg, 0.5 mmol, 1.0 equiv) was added to a flame-dried, 5-mL, 2-neck flask under N_2 containing a solution of 21 mg (0.025 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** in CH_2Cl_2 (0.5 mL). To this solution was added 51 μL (0.5 mmol) of benzaldehyde in one portion. To the resulting mixture was added 86 μL (0.75 mmol, 1.5 equiv) of $SiCl_4$ in one portion and the reaction mixture was cooled to –78 °C (bath temperature) over 15 min. Then, 119 μL (95 mg, 0.6 mmol, 1.2 equiv) of **4** was added dropwise over 5 min. The resulting mixture was stirred at –78 °C for 2 h, whereupon 3 mL of chilled CH_2Cl_2 was added before the cold reaction mixture was poured into a rapidly stirring solution of 1/1 sat. aq. $NaHCO_3$/sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (pentane/Et_2O 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 94 mg (98%) of **11** as a clear, colorless oil.[4]

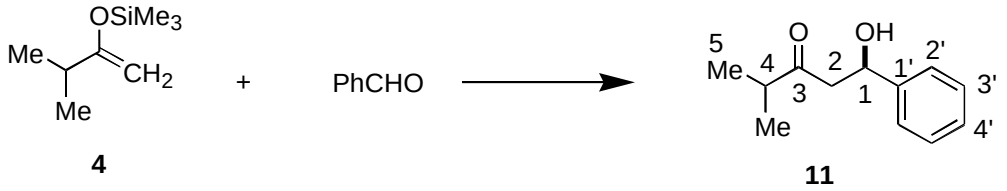
Data for **11**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.38-7.26 (m, 5 H, H(aryl)), 5.11 (dt, *J* = 7.1, 2.9, 1 H, HC(1)), 3.45 (d, *J* = 2.9, 1 H, OH), 2.87 (m, 2 H, HC(2)), 2.59 (sept, *J* = 6.8, 1 H, H_2C(4)), 1.10 (d, *J* = 7.1, 6 H, 2 x H_3C(5))

SFC: (*R*)-**11** t_R 2.52 min (99.0%); (*S*)-**11** t_R 2.80 min (1.0%) (AD column, 125 bar, 3.0 mL/min, 7.0% MeOH)

Reaction of 4 and Benzaldehyde with 0.2 equiv of 2,4,6-tri-*tert*-Butylpyridine (11) [JRH-II-31]



4 **11**

2,4,6-tri-*tert*-Butylpyridine (25 mg, 0.1 mmol, 0.2 equiv) was added to a flame-dried, 5-mL, 2-neck flask under N_2 containing a solution of 21 mg (0.025 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** in CH_2Cl_2 (0.5 mL). Into this reaction mixture 512 μL (0.5 mmol) of benzaldehyde was added in one portion. To this solution was added 86 μL (0.75 mmol, 1.5 equiv) of $SiCl_4$ in one portion and the reaction mixture was cooled to –78 °C (bath temperature) over 15 min. Then, 119 μL (95 mg, 0.6 mmol, 1.2 equiv) of **4** was added dropwise over 5 min. The resulting mixture was stirred at –78 °C for 2 h, whereupon 3 mL of chilled CH_2Cl_2 was added before the cold reaction mixture was poured into a rapidly stirring solution of 1/1 sat. aq. $NaHCO_3$/sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 95 mg (98.5%) of **11** as a clear, colorless oil.[4]

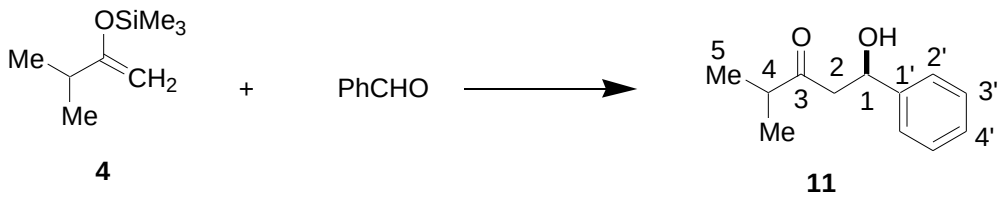
Data for **11**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.38-7.26 (m, 5 H, H(aryl)), 5.15 (dt, *J* = 8.3, 3.4, 1 H, HC(1)), 3.51 (d, *J* = 2.9, 1 H, OH), 2.87 (m, 2 H, HC(2)), 2.59 (sept, *J* = 6.8, 1 H, H_2C(4)), 1.10 (d, *J* = 6.8, 6 H, 2 x H_3C(5))

SFC: (*R*)-**11** t_R 2.59 min (99.0%); (*S*)-**11** t_R 2.88 min (1.0%) (AD column, 125 bar, 3.0 mL/min, 7.0% MeOH)

Reaction of 4 and Benzaldehyde with 0.2 equiv of *i*-Pr_2NEt (11) [JRH-II-34]



4 **11**

Diisopropylethylamine (18 μL, 0.1 mmol, 0.2 equiv) was added via syringe to a flame-dried, 5-mL, 2-neck flask under N_2 containing a solution of 21 mg (0.025 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** in CH_2Cl_2 (0.5 mL). Into this reaction mixture was added 51 μL (0.5 mmol) of benzaldehyde in one portion. To the resulting mixture was added 86 μL (0.75 mmol, 1.5 equiv) of $SiCl_4$ and the reaction mixture was cooled to –78 °C (bath temperature) over 15 min. Then, 119 μL (95 mg, 0.6 mmol, 1.2 equiv) of **4** was added dropwise over 5 min. The resulting mixture was stirred at –78 °C for 3 h whereupon 2.5 mL of chilled CH_2Cl_2 was added before the cold reaction mixture was poured into a rapidly stirring solution of 1/1 sat. aq. $NaHCO_3$/ sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 95 mg (99%) of **11** as a clear, colorless oil.[4]

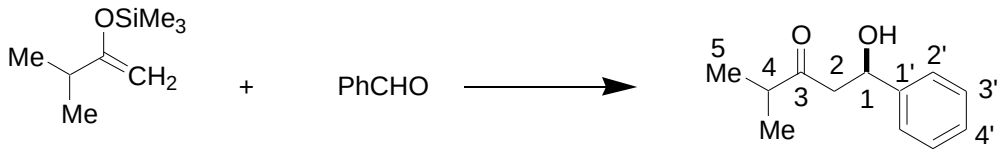
Data for **11**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.38-7.26 (m, 5 H, H(aryl)), 5.16 (dt, *J* = 8.9, 3.2, 1 H, HC(1)), 3.51 (d, *J* = 3.0, 1 H, OH), 2.88 (m, 2H, HC(2)), 2.59 (sept, *J* = 6.8, 1 H, H_2C(4)), 1.10 (d, *J* = 6.8, 6 H, 2 x H_3C(5))

SFC: (*R*)-**11** t_R 2.57 min (99.0%); (*S*)-**11** t_R 2.86 min (1.0%) (AD column, 125 bar, 3.0 mL/min, 7.0% MeOH)

Reaction of 4 and Benzaldehyde with 0.1 equiv of *i*-Pr_2NEt (11) [JRH-II-35]



4 **11**

Diisopropylethylamine (9 μL, 0.05 mmol, 0.1 equiv) was added via syringe to a flame-dried, 5-mL, 2-neck flask under N_2 containing a solution of 21 mg (0.025 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** in CH_2Cl_2 (0.5 mL). Into this reaction mixture was added 51 μL (0.5 mmol) of benzaldehyde in one portion. To this resulting mixture 86 μL (0.75 mmol, 1.5 equiv) of $SiCl_4$ and the reaction mixture was cooled to –78 °C (bath temperature) over 15 min. Then, 119 μL (95 mg, 0.6 mmol, 1.2 equiv) of **4** was added dropwise over 5 min. The resulting mixture was stirred at –78 °C for 3 h whereupon 2.5 mL of chilled CH_2Cl_2 was added before the cold reaction mixture was poured into a rapidly stirring solution of 1/1 sat. aq. $NaHCO_3$/ sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (pentane/Et_2O 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 94 mg (98%) of **11** as a clear, colorless oil.[4]

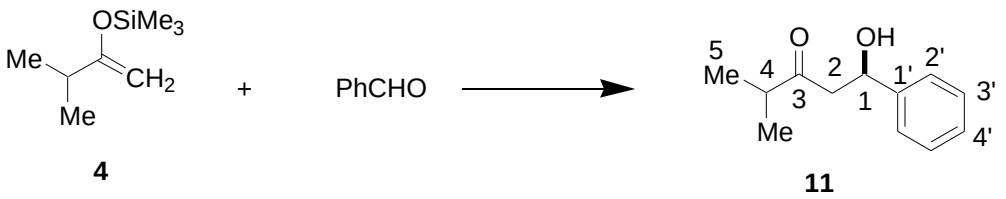
Data for **11**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.38-7.26 (m, 5 H, H(aryl)), 5.15 (dt, *J* = 8.3, 3.2, 1 H, HC(1)), 3.51 (d, *J* = 3.2, 1 H, OH), 2.89 (m, 2 H, HC(2)), 2.59 (sept, *J* = 6.8, 1 H, H_2C(4)), 1.10 (d, *J* = 6.8, 6 H, 2 x H_3C(5))

SFC: (*R*)-**11** t_R 2.62 min (99.0%); (*S*)-**11** t_R 2.90 min (1.0%) (AD column, 125 bar, 3.0 mL/min, 7.0% MeOH)

Reaction of 4 and Benzaldehyde with 0.05 equiv of *i*-Pr_2NEt (11) [JRH-II-47]



4 **11**

Diisopropylethylamine (9 μL, 0.025 mmol, 0.05 equiv) was added via syringe to a flame-dried, 5-mL, 2-neck flask under N_2 containing a solution of 42 mg (0.05 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** in CH_2Cl_2 (0.5 mL). Into this reaction mixture was added 102 μL (1.0 mmol) of benzaldehyde in one portion. To this resulting mixture 172 μL (1.5 mmol, 1.5 equiv) of $SiCl_4$ and the reaction mixture was cooled to –78 °C (bath temperature) over 15 min. Then, 237 μL (190 mg, 1.2 mmol, 1.2 equiv) of **4** was added dropwise over 5 min. The resulting mixture was stirred at –78 °C for 3 h whereupon 2.5 mL of chilled CH_2Cl_2 was added before the cold reaction mixture was poured into a rapidly stirring solution of 1/1 sat. aq. $NaHCO_3$/ sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 188 mg (96%) of **11** as a clear, colorless oil.[4]

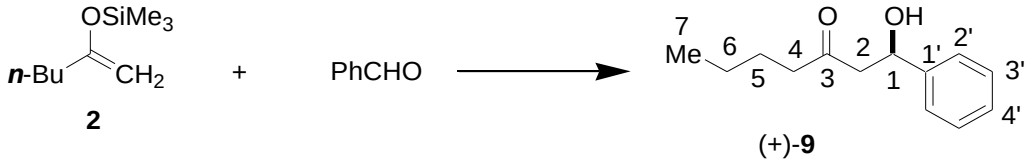
Data for **11**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.38-7.26 (m, 5 H, H(aryl)), 5.15 (dd, *J* = 8.6, 3.9, 1 H, HC(1)), 3.46 (br s, 1 H, OH), 2.88 (m, 2 H, HC(2)), 2.59 (sept, *J* = 7.0, 1 H, H_2C(4)), 1.10 (d, *J* = 6.8, 6 H, 2 x H_3C(5))

SFC: (*R*)-**11** t_R 2.54 min (98.5%); (*S*)-**11** t_R 2.804 min (1.5%) (AD column, 125 bar, 3.0 mL/min, 7.0% MeOH)

Reaction of 2 and Benzaldehyde with 1 mol % of (*R,R*)-7 (9) [JRH-II-66]



Diisopropylethylamine (18 μL, 0.1 mmol, 0.1 equiv) was added via syringe to a flame-dried, 5-mL, 2-neck flask under N_2 containing a solution of 8.4 mg (0.01 mmol, 0.01 equiv) of bisphosphoramide (*R,R*)-**7** in CH_2Cl_2 (2 mL). Into this reaction mixture was added 102 μL (1.0 mmol, 1.0 equiv) of benzaldehyde in one portion. To the resulting mixture was added 172 μL (1.5 mmol, 1.5 equiv) of $SiCl_4$ in one portion and the reaction mixture was cooled to –72 °C over 15 min. Then, 206 mg (1.2 mmol, 1.2 equiv) of **2** was added dropwise neat over 5 min. The resulting mixture was allowed to stir at –72 °C for 3 h whereupon 2.5 mL of chilled CH_2Cl_2 was added before the cold reaction mixture was poured into a rapidly stirring solution of 1/1 sat. aq. $NaHCO_3$/ sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 198 mg (96%) of (+)-**9** as a clear, colorless oil.[4]

Data for (+)-**13**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.36-7.25 (m, 5 H, H(aryl)), 5.15 (dd, J = 9.0, 3.3, 1 H, HC(1)), 3.43 (br s, 1 H, OH), 2.84 (ABX, J_{AB} = 17.4, J_{AX} = 9.6, 1 H, H_aC(2)), 2.78 (ABX, J_{AB} = 17.4, J_{BX} = 2.8, 1 H, H_bC(2)), 2.42 (t, J = 7.3, 2 H, H_2C(4)), 1.56 (quint, J = 7.5, 2 H, H_2C(5)), 1.30 (sext, J = 7.4, 2 H, H_2C(6)), 0.90 (t, J = 7.3, 3 H, H_3C(7))

^{13}C NMR: (126 MHz, $CHCl_3$)

211.36 (C(3)), 142.87 (C(1')), 128.30 (C(3')), 127.39 (C(4')), 125.47 (C(2')), 69.73 (C(1)), 50.91 (C(2)), 43.23 (C(4)), 25.41 (C(5)), 22.06 (C(6)), 13.67 (C(7))

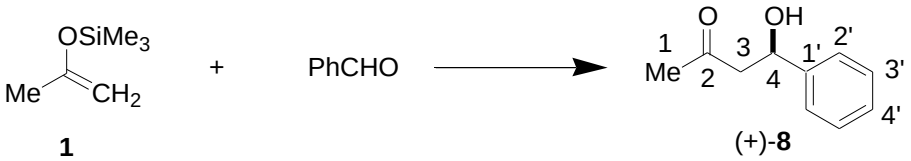
Opt. Rot.: $[\alpha]_D^{24}$ +30.28 (c = 2.20, EtOH)

$[\alpha]_D^{24}$ +71.99 (c = 1.10, $CHCl_3$)

SFC: (*R*)-**9** t_R 4.21 min (99.5%); (*S*)-**9** t_R 4.65 min (0.5%) (AD column, 125 bar, 2.5 mL/min, 5.0% MeOH)

Survey of Silyl Enol Ethers with Benzaldehyde.

(+)-(*R*)-4-Hydroxy-4-phenyl-2-butanone (8) [JRH-II-62]



1 (+)-**8**

Diisopropylethylamine (18 μL, 0.1 mmol, 0.1 equiv) was added via syringe to a flame-dried, 5-mL, 2-neck flask under N_2 containing a solution of 42 mg (0.05 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** in CH_2Cl_2 (2 mL). To this solution was added 102 μL (1.0 mmol) of benzaldehyde in one portion. To the resulting solution was added 172 μL (1.5 mmol, 1.5 equiv) of $SiCl_4$ in one portion and the reaction mixture was cooled to –72 °C over 15 min. Then, 198 μL (156 mg, 1.2 mmol, 1.2 equiv) of **1** was added dropwise over 5 min. The resulting mixture was stirred at –72 °C for 3 h, whereupon 2.5 mL of chilled CH_2Cl_2 was added before the cold reaction mixture was poured into a rapidly stirring solution of 1/1 sat. aq. $NaHCO_3$/ sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 1/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 159 mg (97%) of (+)-**8** as a clear, colorless oil.[4]

Data for (+)-**8**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.37-7.26 (m, 5 H, H(aryl)), 5.16 (dt, J = 9.3, 3.2, 1 H, HC(4)), 3.7 (d, J = 2.9, 1 H, OH), 2.89 (ABX, J_{AB} = 17.8, J_{AX} = 9.6, 1 H H_aC(3)), 2.83 (ABX, J_{AB} = 17.8, J_{BX} = 2.9, 1 H, H_bC(3)), 2.20 (s, 3 H H_3C(1))

^{13}C NMR: (126 MHz)

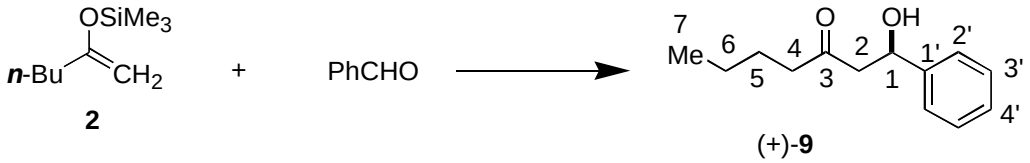
208.94 (C(2)), 142.77 (C(1')), 128.38 (C(3')), 127.50 (C(4')), 125.51 (C(2')), 69.66 (C(4)), 51.86 (C(3)), 30.58 (C(1))

Opt. Rot.: $[\alpha]_D^{24}$ +37.16 (c = 2.10, EtOH)

$[\alpha]_D^{24}$ +74.22 (c = 1.10, $CHCl_3$)

SFC: (*R*)-**8** t_R 3.13 min (98.0%); (*S*)-**8** t_R 3.48 min (2.0%) (AS column, 125 bar, 2.5 mL/min, 5.0% MeOH)

(+)-(*R*)-1-Hydroxy-1-phenyl-3-heptanone (9) [JRH-II-60]



Diisopropylethylamine (18 μL, 0.1 mmol, 0.1 equiv) was added via syringe to a flame-dried, 5-mL, 2-neck flask under N_2 containing a solution of 42 mg (0.05 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** in CH_2Cl_2 (2 mL). To this solution was added 102 μL (1.0 mmol) of benzaldehyde in one portion. To the resulting solution was added 172 μL (1.5 mmol, 1.5 equiv) of $SiCl_4$ in one portion and the reaction mixture was cooled to –72 °C over 15 min. Then, 206 mg (1.2 mmol, 1.2 equiv) of **2** was added dropwise neat over 5 min. The resulting mixture was stirred at –72 °C for 3 h whereupon 2.5 mL of chilled CH_2Cl_2 was added before the cold reaction mixture was poured into a rapidly stirring solution of 1/1 sat. aq. $NaHCO_3$/ sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was

washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 203 mg (99%) of (+)-**9** as a clear, colorless oil.[4]

Data for (+)-**9**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.37-7.26 (m, 5 H, H(aryl)), 5.16 (dd, J = 8.8, 3.4, 1 H, HC(1)), 3.43 (br s, 1 H, OH), 2.87 (ABX, J_{AB} = 17.3, J_{AX} = 9.7, 1 H, $H_aC(2)$), 2.80 (ABX, J_{AB} = 17.3, J_{BX} = 2.8, 1 H, $H_bC(2)$), 2.43 (t, J = 7.3, 2 H, $H_2C(4)$), 1.57 (quint, J = 7.3, 2 H, $H_2C(5)$), 1.30 (sext, J = 7.3, 2 H, $H_2C(6)$), 0.90 (t, J = 7.3, 3 H, $H_3C(7)$)

^{13}C NMR: (126 MHz, $CHCl_3$)

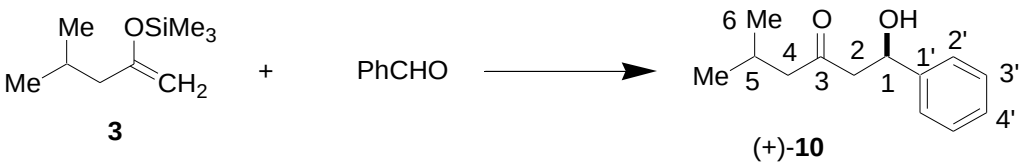
211.38 (C(3)), 142.91 (C(1')), 128.32 (C(3')), 127.41 (C(4')), 125.50 (C(2')), 69.75 (C(1)), 50.91 (C(2)), 43.22 (C(4)), 25.40 (C(5)), 22.03 (C(6)), 13.63 (C(7))

Opt. Rot.: $[\alpha]_D^{24}$ +27.07 (c = 1.10, EtOH)

$[\alpha]_D^{24}$ +69.09 (c = 1.40, $CHCl_3$)

SFC: (*R*)-**9** t_R 4.21 min (99.5%); (*S*)-**9** t_R 4.65 min (0.5%) (AD column, 125 bar, 2.5 mL/min, 5.0% MeOH)

(+)-(*R*)-1-Hydroxy-5-methyl-1-phenyl-3-hexanone (10) [JRH-II-65]



Diisopropylethylamine (18 μL, 0.1 mmol, 0.1 equiv) was added via syringe to a flame-dried, 5-mL, 2-neck flask under N_2 containing a solution of 42 mg (0.05 mmol, 0.05 equiv) of bisphosphoramide (*R,R*)-**7** in CH_2Cl_2 (2 mL). To this solution was added 102 μL (1.0 mmol) of benzaldehyde in one portion. To the resulting solution was added 172 μL (1.5 mmol, 1.5 equiv) of $SiCl_4$ in one portion and the reaction mixture was cooled to –72 °C over 15 min. Then, 206 mg (1.2 mmol, 1.2 equiv) of **3** was added dropwise neat over 5 min. The resulting mixture was stirred at –72 °C for 3 h whereupon 2.5 mL of chilled CH_2Cl_2 was added before the cold reaction mixture was poured into a rapidly stirring solution of 1/1 sat. aq. $NaHCO_3$/ sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 202 mg (98%) of (+)-**10** as a clear, colorless oil.[4]

Data for (+)-**10**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.39-7.28 (m, 5 H, H(aryl)), 5.18 (dd, J = 9.0, 3.4, 1 H, HC(1)), 3.35 (br s, 1 H, OH), 2.85 (ABX, J_{AB} = 17.4, J_{AX}=9.6, 1 H, H_aC(2)), 2.80 (ABX, J_{AB} = 17.4, J_{BX} = 2.8, 1 H, H_bC(2)), 2.30 (d, J = 7.1, 2 H, H_2C(4)), 2.17 (septet, J = 6.7, 1 H, H_2C(5)), 0.94 (d, J = 6.7, 6 H, 2 x H_3C(6))

^{13}C NMR: (126 MHz, $CHCl_3$)

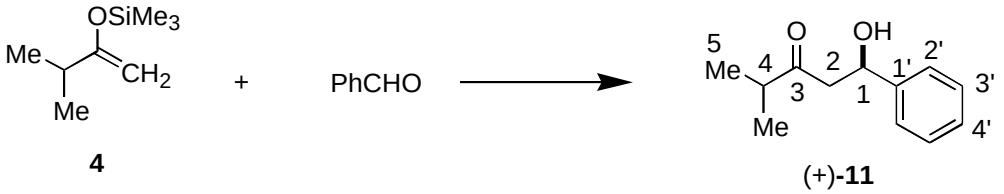
211.05 (C(3)), 142.91 (C(1')), 128.34 (C(3')), 127.43 (C(4')), 125.52 (C(2')), 69.71 (C(1)), 52.45 (C(2)), 51.40 (C(4)), 24.23 (C(5)), 22.34 (C(6))

Opt. Rot.: $[\alpha]_D^{24}$ +30.84 (c = 2.40, EtOH)

$[\alpha]_D^{24}$ +58.30 (c = 1.50, $CHCl_3$)

SFC: (*R*)-**10** t_R 2.76 min (99.0%); (*S*)-**10** t_R 3.09 min (1.0%) (AD column, 125 bar, 2.5 mL/min, 7.0 % MeOH)

(+)-(*R*)-1-Hydroxy-4-methyl-1-phenyl-3-pentanone (**11**) [JRH-II-64]



4 (+)-**11**

Diisopropylethylamine (18 μL, 0.1 mmol, 0.1 equiv) was added via syringe to a flame-dried, 5-mL, 2-neck flask under N_2 containing a solution of 42 mg (0.05 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** in CH_2Cl_2 (2 mL). To this solution was added 102 μL (1.0 mmol) of benzaldehyde in one portion. To the resulting solution was added 172 μL (1.5 mmol, 1.5 equiv) of $SiCl_4$ and the reaction mixture was cooled to –72 °C over 15 min. Then, 237 μL (190 mg, 1.2 mmol, 1.2 equiv) of **4** was added dropwise over 5 min. The resulting mixture was stirred at –72 °C for 3 h whereupon 2.5 mL of chilled CH_2Cl_2 was added before the cold reaction mixture was poured into a rapidly stirring solution of 1/1 sat. aq. $NaHCO_3$/ sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (pentane/Et_2O 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 182 mg (95%) of (+)-**11** as a clear, colorless oil.[4]

Data for (+)-**11**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.34-7.25 (m, 5 H, H(aryl)), 5.11 (dd, J = 9.2, 3.2, 1 H, HC(1)), 3.51 (br s, 1 H, OH), 2.88 (ABX, J_{AB} = 15.0, J_{AX}= 9.1, 1 H, H_aC(2)), 2.85 (ABX, J_{AB} = 15.0, J_{BX} = 2.9, 1 H, H_bC(2)), 2.59 (sept, J = 7.0, 1 H, H_2C(4)), 1.10 (d, J = 6.8, 6 H, 2 x H_3C(5))

^{13}C NMR: (126 MHz, $CHCl_3$)

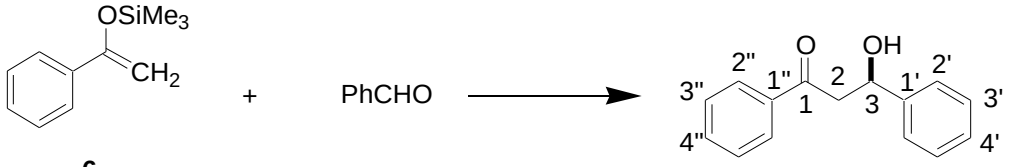
215.02 (C(3)), 142.97 (C(1')), 128.35 (C(3')), 127.44 (C(4')), 125.53 (C(2')), 69.82 (C(1)), 48.68 (C(2)), 41.37 (C(4)), 17.70 (C(5))

Opt. Rot.: $[\alpha]_D^{24}$ +29.19 (c = 2.00, EtOH)

$[\alpha]_D^{24}$ +70.59 (c = 1.60, $CHCl_3$)

SFC: (*R*)-**11** t_R 2.57 min (99.5%); (*S*)-**11** t_R 2.88 min (0.5%) (AD column, 125 bar, 2.5 mL/min, 7.0% MeOH)

(+)-(*R*)-3-hydroxy-1,3-diphenyl-1-propanone (12) [JRH-II-67]



6 (+)-**12**

Diisopropylamine (18 μL, 0.1 mmol, 0.1 equiv) was added via syringe to a flame-dried, 5-mL, 2-neck flask under N_2 containing a solution of 42 mg (0.05 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** in CH_2Cl_2 (2 mL). To this solution was added 102 μL (1.0 mmol) of benzaldehyde in one portion. To the resulting solution was added 172 μL (1.5 mmol, 1.5 equiv) of $SiCl_4$ in one portion and the reaction mixture was cooled to –72 °C over 15 min. Then, 248 μL (231 mg, 1.2 mmol, 1.2 equiv) of **6** was added dropwise over 5 min. The resulting mixture was stirred at –72 °C for 3 h whereupon 2.5 mL of chilled CH_2Cl_2 was added before the cold

reaction mixture was poured into a rapidly stirring solution of 1/1 sat. aq. $NaHCO_3$/ sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 8 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 221 mg (98%) of (+)-**12** as a white solid.[4]

Data for (+)-**12**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.96 (d, *J* = 7.5, 2 H, 2 x HC(2")), 7.58 (t, *J* = 7.3, 1 H, HC(4")), 7.47-7.43 (m, 4 H, 2 x HC(3"')) + 2 x HC(2')), 7.39 (t, *J* = 7.3, 2 H, 2 x HC(3')), 7.31 (t, *J* = 7.5, 1 H, HC(4')), 5.35 (dd, *J* = 8.7, 3.7, 1 H, HC(1)), 3.79 (br s, 1 H, OH), 3.39 (ABX, J_{AB} = 17.6, J_{AX}= 9.3, 1 H, H_aC(2)), 3.35 (ABX, J_{AB} = 17.6, J_{BX} = 2.9, 1 H, H_bC(2))

^{13}C NMR: (126 MHz, $CHCl_3$)

199.92 (C(3)), 142.96 (C(1')), 136.43 (C(1")), 133.45 (C(4')), 128.53 (C(2')), 128.39 (C(3')), 128.03 (C(2")), 127.48 (C(4')), 125.64 (C(3")), 69.82 (C(1)), 47.25 (C(2))

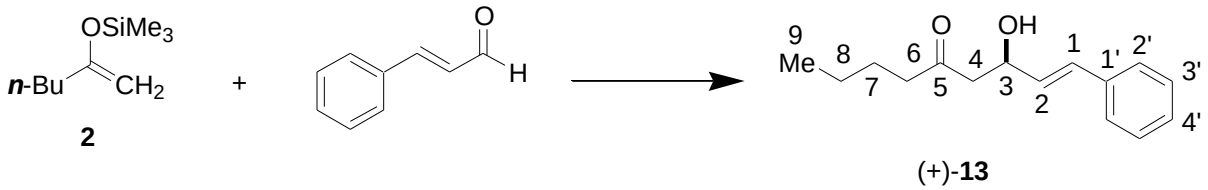
Opt. Rot.: $[\alpha]_D^{24}$ +31.85 (c = 1.80, EtOH)

$[\alpha]_D^{24}$ +68.85 (c = 1.10, $CHCl_3$)

SFC: (*R*)-**12** t_R 5.21 min (99.5%); (*S*)-**12** t_R 5.83 min (0.5%) (Welko column, 125 bar, 3.0 mL/min, 7.0% MeOH)

Survey of Aldehydes with Silyl Enol Ether 2.

(+)-(*R*)-3-Hydroxy-1-phenyl-1-nonen-5-one (13) [JRH-II-97]



(+)-**13**

Diisopropylethylamine (18 μL, 0.1 mmol, 0.1 equiv) was added via syringe, to a flame-dried, 5-mL, Schlenk flask under N_2 containing a solution of 42 mg (0.05 mmol, 0.05 equiv) of bisphosphoramide (*R,R*)-**7** in CH_2Cl_2 (2 mL). To this solution was added 126 μL (1.0 mmol) of cinnamaldehyde in one portion. To the resulting solution was added 172 μL (1.5 mmol, 1.5 equiv) of $SiCl_4$ in one portion and the reaction mixture was cooled to –72 °C over 15 min. Then, 206 mg (1.2 mmol, 1.2 equiv) of **2** was added dropwise neat over 5 min. The resulting mixture was stirred at –72 °C for 4 h whereupon 3.0 mL of chilled CH_2Cl_2 was added before the cold reaction mixture was poured into a rapidly stirring solution of 1/1 sat. aq. $NaHCO_3$/ sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 4 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 226 mg (97.5%) of (+)-**13** as a clear, colorless oil.[4]

Data for (+)-**13**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.37 (dd, *J* = 8.1, 1.0, 2 H, 2 x HC(2')), 7.31 (dt, *J* = 7.5, 1.5, 2 H, 2 x HC(3')), 7.25 (tt, *J* = 7.3, 1.6, 1 H, HC(4')), 6.64 (dd, *J* = 15.9, 1.1, 1 H, HC(1)), 6.20 (dd, *J* = 15.9, 6.2, 1 H, HC(2)), 4.76 (m, 1 H, HC(3)), 3.18 (d, *J* = 3.6, 1 H, OH), 2.73 (m, 2H, H_2C(4)), 2.46 (t, *J* = 7.4, 2 H, H_2C(6)), 1.58 (quint, *J* = 7.5, 2 H, H_2C(7)), 1.33 (sext, *J* = 7.4, 2 H, H_2C(8)), 0.91 (t, *J* = 7.3, 3 H, H_3C(9))

^{13}C NMR: (126 MHz, $CHCl_3$)

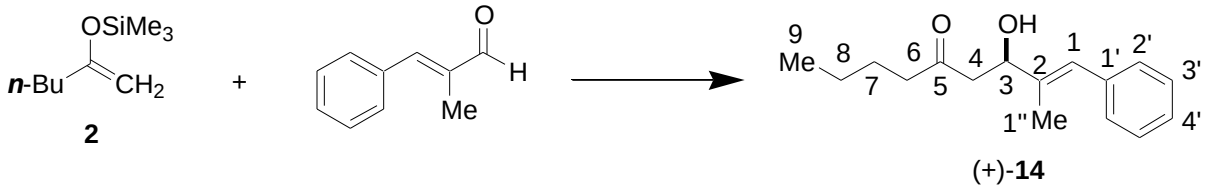
211.08 (C(5)), 136.38 (C(1')), 130.33 (C(1)), 129.91 (C(2)), 128.35 (C(3')), 127.45 (C(4')), 126.27 (C(2')), 68.24 (C(3)), 48.87 (C(4)), 43.21 (C(6)), 25.35 (C(7)), 21.99 (C(8)), 13.59 (C(9))

Opt. Rot.: $[\alpha]_D^{24}$ +1.37 (c = 1.80, EtOH)

$[\alpha]_D^{24}$ +23.70 (c = 1.30, $CHCl_3$)

SFC: (*R*)-**13** t_R 3.28 min (99.5%); (*S*)-**13** t_R 3.53 min (0.5%) (AD column, 125 bar, 2.5 mL/min, 15.0% MeOH)

(+)-(*R*)-3-Hydroxyl-2-methyl-1-phenyl-1-nonen-5-one (14) [JRH-II-92]



Diisopropylethylamine (18 μL, 0.1 mmol, 0.1 equiv) was added via syringe to a flame-dried, 5-mL, Schlenk flask under N_2 containing a solution of 84 mg (0.05 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** in CH_2Cl_2 (2 mL). To this solution was added 140 μL (1.0 mmol) of (*E*)-2-methylcinnamaldehyde in one portion. To the resulting solution was added 172 μL (1.5 mmol, 1.5 equiv) of $SiCl_4$ in one portion and the reaction mixture was cooled to –60 °C over 15 min. Then, 206 mg (1.2 mmol, 1.2 equiv) of **2** was added dropwise neat over 5 min. The resulting mixture was allowed to stir at –60 °C for 24 h whereupon 3.0 mL of chilled CH_2Cl_2 was added before the cold reaction mixture was poured into a rapidly stirring solution of 1/1 sat. aq. $NaHCO_3$/ sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 4 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1). The product-containing

fractions were combined and the solvent was removed *in vacuo* to yield 132 mg (54%) of **14** as a clear, colorless oil.[4]

Data for (+)-**14**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.33 (t, J = 7.5, 2 H, 2 x HC(2')), 7.27 (d, J = 7.3, 2 H, 2 x HC(3')), 7.21 (t, J = 7.3, 1 H, HC(4')), 6.57 (s, 1 H, HC(1)), 4.63 (dd, *J* = 7.3, 4.5, 1 H, HC(3)), 3.12 (s, 1 H, OH), 2.73 (m, 2 H, H_2C(4)), 2.48 (t, *J* = 7.4, 2 H, H_2C(6)), 1.88 (s, 3 H, H_3C (1")), 1.59 (quint, *J* = 7.4, 2 H, H_2C(7)), 1.33 (sext, *J* = 7.4, 2 H, H_2C(8)), 0.92 (t, *J* = 7.4, 3 H, H_3C(9))

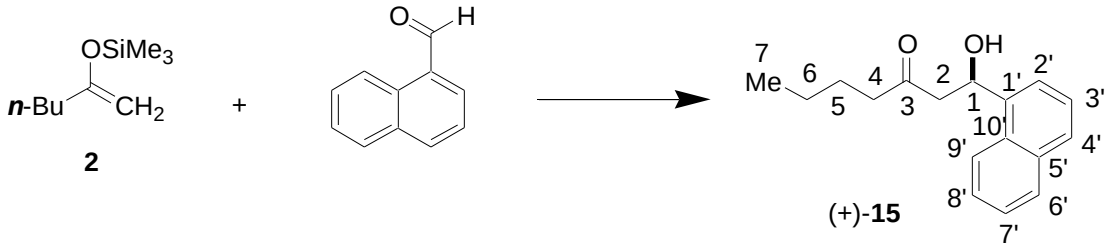
^{13}C NMR: (126 MHz, $CHCl_3$)

211.96 (C(5)), 138.36.37 (C(2)), 137.40 (C(1')), 128.97 (C(3')), 128.11 (C(2')), 126.52 (C(4')), 125.68 (C(1)), 73.09 (C(3)), 47.66 (C(4)), 43.52 (C(6)), 25.64 (C(7)), 22.25 (C(8)), 13.97 (H_3C (1")), 13.79 (C(9))

Opt. Rot.: $[\alpha]_D^{24}$ +1.15 (c = 1.00, $CHCl_3$)

SFC: (*R*)-**14** t_R 2.91 min (78.0%); (*S*)-**14** t_R 3.42 min (22.0%) (AD column, 125 bar, 2.5 mL/min, 15.0 % MeOH)

(+)-(*R*)-1-Hydroxy-1-(1-napthyl)-3-heptanone (15) [JRH-II-87]



Diisopropylethylamine (18 μL, 0.1 mmol, 0.1 equiv) was added via syringe to a flame-dried, 5-mL, schlenk flask under N_2 containing a solution of 42 mg (0.05 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** in CH_2Cl_2 (2 mL). To this solution was added 136 μL (1.0 mmol) of 1-naphthaldehyde in one portion. To the resulting solution was added 172 μL (1.5 mmol, 1.5

equiv) of $SiCl_4$ in one portion and the reaction mixture was cooled to –72 °C over 15 min. Then, 206 mg (1.2 mmol, 1.2 equiv) of **2** was added dropwise neat over 5 min. The resulting mixture was stirred at –72 °C for 10 h whereupon 3.0 mL of chilled CH_2Cl_2 was added before the cold reaction mixture was poured into a rapidly stirring solution of 1/1 sat. aq. $NaHCO_3$/ sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 4 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1). The product-containing fractions were combined and the solvent was removed *in vacuo* to yield 242 mg (95%) of (+)-**15** as a clear, colorless oil.[7b]

Data for (+)-**15**:

^{1}H NMR: (500 MHz, $CHCl_3$)

8.00 (d, J = 8.3, 1 H, HC(2')), 7.88 (d, J = 7.8, 1 H, HC(6')), 7.79 (d, J = 8.3, 1 H, HC(4')), 7.70 (d, J = 7.1, 1 H, HC(9')), 7.54-7.48 (m, 3 H, HC(3'), HC(7'), HC(8')), 5.96 (dt, J = 8.8, 3.1, 1 H, HC(1)), 3.48 (d, J = 3.21 H, OH), 2.99 (ABX, J_{AB} = 17.8, J_{AX} = 9.2, 1 H, $H_aC(2)$), 2.95 (ABX, J_{AB} = 17.8, J_{BX} = 3.0, 1 H, $H_bC(2)$), 2.46 (t, J = 7.3, 2 H, $H_2C(4)$), 1.60 (quint, J = 7.6, 2 H, $H_2C(5)$), 1.33 (sext, J = 7.3, 2 H, $H_2C(6)$), 0.91 (t, J = 7.3, 3 H, $H_3C(7)$)

^{13}C NMR: (126 MHz, $CHCl_3$)

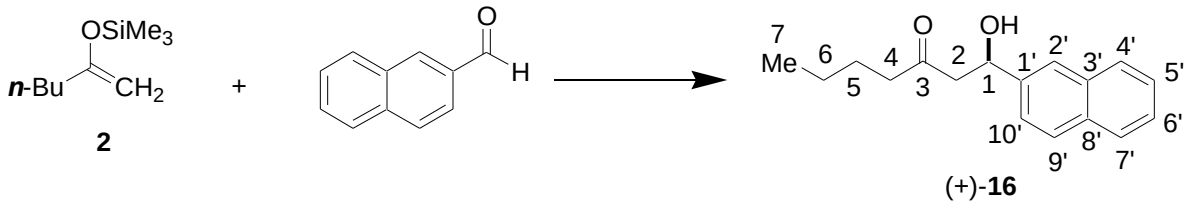
211.82 (C(3)), 138.37 (C(1')), 133.75 (C(5')), 129.86 (C(10')), 129.01 (C(6')), 128.03 (C(4')), 126.71 (C(6')), 125.54 (C(7')), 125.52 (C(3')), 122.96 (C(9')), 122.73 (C(2')), 66.76 (C(1)), 50.29 (C(2)), 43.39 (C(4)), 25.63 (C(5)), 22.21 (C(6)), 13.76 (C(7))

Opt. Rot.: $[\alpha]_D^{24}$ +44.47 (c = 1.30, EtOH)

$[\alpha]_D^{24}$ +79.94 (c = 1.40, $CHCl_3$)

SFC: (*R*)-**15** t_R 4.41 min (96.0%); (*S*)-**15** t_R 4.86 min (4.0%) (AD column, 125 bar, 2.5 mL/min, 15.0% MeOH)

(+)-(*R*)-1-Hydroxy-1-(2-napthyl)-3-heptanone (16) [JRH-II-95]



Diisopropylethylamine (18 μL, 0.1 mmol, 0.1 equiv) was added via syringe to a flame-dried, 5-mL, Schlenk flask under N_2 containing a solution of 42 mg (0.05 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** in CH_2Cl_2 (2 mL). To this solution was added 156 mg (1.0 mmol) of 2-naphthaldehyde in one portion. To the resulting solution was added 172 μL (1.5 mmol, 1.5 equiv) of $SiCl_4$ in one portion and the reaction mixture was cooled to –72 °C over 15 min. Then, 206 mg (1.2 mmol, 1.2 equiv) of **2** was added dropwise neat over 5 min. The resulting mixture was stirred at –72 °C for 4 h whereupon 3.0 mL of chilled CH_2Cl_2 was added before the cold reaction mixture was poured into a rapidly stirring solution of 1/1 sat. aq. $NaHCO_3$/ sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 4 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1) to give a solid, which was recrystallized from hexanes to give 235 mg (92%) of (+)-**16** as white needles.

Data for (+)-**16**:

mp: 55-56 °C (hexanes)

^{1}H NMR: (500 MHz, $CHCl_3$)

7.83 (m, 4 H, H(aryl)), 4.57 (m, 3 H, H(aryl)), 5.33 (dt, *J* = 8.3, 3.5, 1 H, HC(1)), 3.49 (m, 1 H, OH), 2.91 (m, 2 H, $H_2C(2)$), 2.46 (t, *J* = 7.4, 2 H, $H_2C(4)$), 1.58 (quint, *J* = 7.6, 2 H, $H_2C(5)$), 1.32 (sext, *J* = 7.5, 2 H, H2C(6)), 0.90 (t, *J* = 7.4, 3 H, $H_3C(7)$)

^{13}C NMR: (126 MHz, $CHCl_3$)

211.66 (C(3)), 140.22 (C(1')), 133.27 (C(3')), 132.90 (C(8')), 128.28 (C(7')), 127.95 (C(4')), 127.64 (C(10')), 126.16 (C(9')), 125.86 (C(2')), 124.30 (C(5')), 123.72 (C(6')), 70.00 (C(1)), 50.89 (C(2)), 43.39 (C(4)), 25.57 (C(5)), 22.17 (C(6)), 13.74 (C(7))

IR: ($CHCl_3$)

3602 (m), 3504 (m), 3155 (m), 3060 (m), 2960 (m), 2933 (m), 2875 (m), 1793 (m), 1703 (s), 1603 (m), 1468 (m), 1383 (m), 1327 (m), 1269 (m), 1124 (m), 1093 (m)

MS: (EI, 70 eV)

257 (11), 256 (M+, 48), 157 (44), 156 (100), 155 (51), 154 (10), 153 (19), 129 (40), 128 (47), 127 (48), 126 (12)

Opt. Rot.: $[\alpha]_D^{24}$ +31.76 (c = 1.00, EtOH)

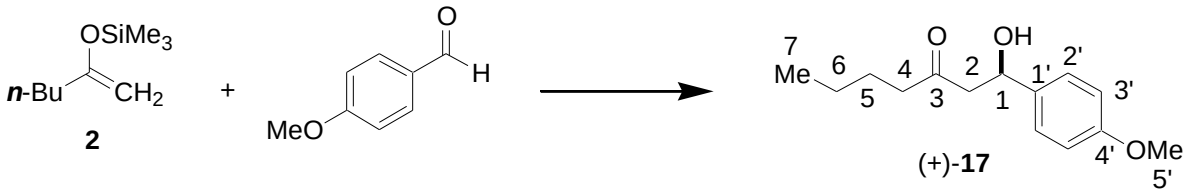
TLC: R_f 0.24 (hexane/EtOAc, 3/1) [silica gel]

SFC: (*R*)-**16** t_R 7.86 min (99.5%); (*S*)-**16** t_R 8.54 min (0.5%) (AD column, 125 bar, 3.0 mL/min, 8.0% MeOH)

Analysis: $C_{17}H_{20}O_2$ (256.34)

Calcd:	C, 79.65;	H, 7.86%
Found:	C, 79.56;	H, 7.86%

(+)-(*R*)-1-Hydroxy-1-(4-methoxyphenyl)-3-heptanone (17) [JRH-III-16]



Diisopropylethylamine (18 μL, 0.1 mmol, 0.1 equiv) was added via syringe to a flame-dried, 5-mL, Schlenk flask under N_2 containing a solution of 42 mg (0.05 mmol, 0.05 equiv) of bis-phosphoramide (*R*,*R*)-**7** in CH_2Cl_2 (2 mL). To this solution was added 122 μL (1.0 mmol) of 4-trifluoromethylbenzaldehyde in one portion. To the resulting solution was added 172 μL (1.5 mmol, 1.5 equiv) of $SiCl_4$ in one portion and the reaction mixture was cooled to –72 °C over 15 min. Then, 206 mg (1.2 mmol, 1.2 equiv) of **2** was added dropwise neat over 5 min. The resulting mixture was stirred at –72 °C for 4 h whereupon 3.0 mL of chilled CH_2Cl_2 was added before the cold reaction mixture was poured into a rapidly stirring solution of 1/1 sat. aq. $NaHCO_3$/ sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 1 h before being filtered through Celite. The phases were then separated and the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1) to give 230 mg (97.8%) of (+)-**17** as a clear, colorless oil.

Data for (+)-**17**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.29-7.27 (m, 2 H, HC(2')), 6.90-6.87 (m, 2 H, HC(3')), 5.11 (dd, J = 9.0, 3.2, 1 H, HC(1)), 3.80 (s, 3 H, H_3C(5')), 3.28 (br s, 1 H, OH), 2.84 (($\underline{A}$BX, J_{AB} = 17.3, J_{AX} = 11.4, 1 H, H_aC(2)), 2.77 (A$\underline{B}$X, J_{AB} = 17.3, J_{BX} = 1.3, 1 H, H_bC(2)), 2.43 (t, J = 7.3, 2 H, H_2C(4)), 1.56 (quint, J = 7.3, 2 H, H_2C(5)), 1.31 (sext, J = 7.5, 2 H, H_2C(6)), 0.90 (t, J = 7.3, 3 H, H_3C(7))

^{13}C NMR: (126 MHz, $CHCl_3$)

211.80 (C(3)), 159.12 (C(4')), 135.04 (C(1')), 126.92 (C(2')), 113.90 (C(3')), 69.59 (C(1)), 55.28 (C(5')), 50.95 (C(2)), 43.41 (C(4)), 25.61 (C(5)), 22.22 (C(6)), 13.78 (C(7))

IR: (neat)

3458 (s), 2999 (m), 2958 (s), 2933 (s), 2873 (s), 2837 (m), 2060 (w), 1890 (w), 1709 (s), 1612 (s), 1587 (m), 1514 (s), 1464 (s), 1406 (s), 1381 (s), 1302 (s), 1176 (s), 1128 (m), 1078 (m), 1036 (s), 833 (s)

MS: (CI, CH_4)

236 (M+, 15), 220 (17), 219 (100), 137 (52), 136 (6), 135 (10), 85 (25)

Opt. Rot.: $[\alpha]_D^{24}$ +27.47 (c = 1.20, EtOH)

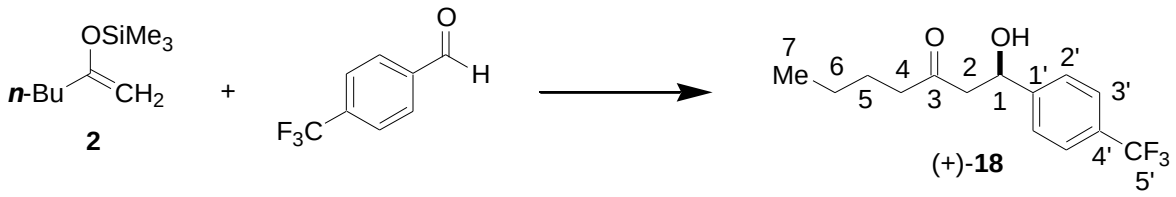
TLC: R_f 0.22 (hexane/EtOAc, 2/1) [silica gel]

SFC: (*R*)-**17** t_R 4.21 min (99.5 %); (*S*)-**17** t_R 4.83 min (0.5 %) (AS column, 125 bar, 3.0 mL/min, 4.0 % MeOH)

Analysis: $C_{14}H_{20}O_3$ (236.31)

Calcd:	C, 71.16;	H, 8.53%
Found:	C, 70.98;	H, 8.53%

(+)-(*R*)-1-Hydroxy-1-(4-trifluoromethylphenyl)-3-heptanone (18) [JRH-III-07]



Diisopropylethylamine (18 μL, 0.1 mmol, 0.1 equiv) was added via syringe to a flame-dried, 5-mL, Schlenk flask under N_2 containing a solution of 42 mg (0.05 mmol, 0.05 equiv) of bisphosphoramide (*R,R*)-**7** in CH_2Cl_2 (2 mL). To this solution was added 137 μL (1.0 mmol) of 4-trifluoromethylbenzaldehyde in one portion. To the resulting solution was added 172 μL (1.5

mmol, 1.5 equiv) of $SiCl_4$ in one portion and the reaction mixture was cooled to –72 °C over 15 min. Then, 206 mg (1.2 mmol, 1.2 equiv) of **2** was added dropwise neat over 5 min. The resulting mixture was stirred at –72 °C for 4 h whereupon 3.0 mL of chilled CH_2Cl_2 was added before the cold reaction mixture was poured into a rapidly stirring solution of 1/1 sat. aq. $NaHCO_3$/ sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 4 h after which the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1) to give an oil which was distilled (bulb-to-bulb) to give 264 mg (96%) of (+)-**18** as a clear, colorless oil.

Data for (+)-**18**:

bp: 210 ^oC (0.2 mmHg, ABT)

^{1}H NMR: (500 MHz, $CHCl_3$)

7.61 (d, *J* = 8.3, 2 H, HC(2')), 7.48 (d, J = 8.1, 2 H, HC(3')), 5.21 (t, *J* = 6.2, 1 H, HC(1)), 3.57 (br s, 1 H, OH), 2.81 (d, *J* = 6.1, 2 H, H_2C(2)), 2.44 (t, J = 7.4, 2 H, H_2C(4)), 1.57 (quint, *J* = 7.3, 2 H, H_2C(5)), 1.31 (sext, *J* = 7.4, 2 H, H_2C(6)), 0.90 (t, *J* = 7.3, 3 H, H_3C(7))

^{13}C NMR: (126 MHz, $CHCl_3$)

211.46 (C(3)), 146.78 (C(1')), 129.67 (q, J_{CF} = 32, C(4')), 125.91 (C(2')), 125.46 (q, J_{CF} = 4, C(3')), 124.10 (q, J = 272, C(5')), 69.30 (C(1)), 50.70 (C(2)), 43.36 (C(4)), 25.58 (C(5)), 22.19 (C(6)), 13.74 (C(7))

^{19}F NMR: (376 MHz, $CHCl_3$ w/C_6F_6)

-62.716

IR: (neat)

3444 (m), 2962 (m), 2935 (m), 2875 (m), 1711 (s), 1620 (m), 1468 (m), 1412 (m), 1327 (s), 1165 (s), 1126 (s), 1068 (s), 1018 (m), 839 (m)

MS: (CI, CH_4)

274 (M+, 6), 256 (6), 257 (9), 255 (20), 217 (7), 175 (7), 101 (9), 85 (100), 59 (6)

Opt. Rot.: $[\alpha]_D^{24}$ +29.07 (c = 1.20, EtOH)

TLC: R_f 0.26 (hexane/EtOAc, 3/1) [silica gel]

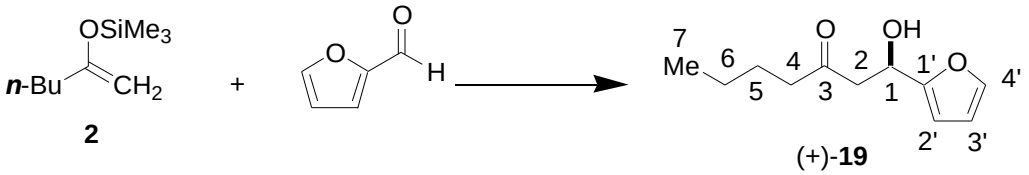
SFC: (*R*)-**9** t_R 7.76 min (>99.5%); (*S*)-**9** t_R 8.70 min (<0.5%) (Welko column, 125 bar, 2.5 mL/min, 1.0% MeOH)

Analysis: $C_{14}H_{17}F_3O_2$ (274.28)

Calcd: C, 61.31; H, 6.25%

Found: C, 61.41; H, 6.43%

(+)-(*R*)-1-Hydroxy-1-fural-3-heptanone (19) [JRH-III-17]



Diisopropylethylamine (18 μL, 0.1 mmol, 0.1 equiv) was added via syringe to a flame-dried, 5-mL, Schlenk flask under N_2 containing a solution of 42 mg (0.05 mmol, 0.05 equiv) of bis-phosphoramide (*R*,*R*)-**7** in CH_2Cl_2 (2 mL). To this solution was added 82 μL (1.0 mmol) of 2-furaldehyde in one portion. To the resulting solution was added 172 μL (1.5 mmol, 1.5 equiv) of $SiCl_4$ in one portion and the reaction mixture was cooled to –72 °C over 15 min. Then, 206 mg (1.2 mmol, 1.2 equiv) of **2** was added dropwise neat over 5 min. The resulting mixture was stirred at –72 °C for 6 h whereupon 3.0 mL of chilled CH_2Cl_2 was added before the cold reaction mixture was poured into a rapidly stirring solution of 1/1 sat. aq. $NaHCO_3$/ sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 1 h before being filtered through Celite. The phases were then separated and the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/Et_2O, 4/1) to give 173 mg (88%) of (+)-**19** as a clear, colorless oil

Data for (+)-**19**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.36 (m, 1 H, HC(4')), 6.33 (m, 1 H, HC(3')), 6.26 (m, 1 H, HC(2')), 5.17 (dd, J = 9.0, 3.2, 1 H, HC(1)), 3.32 (br s, 1 H, OH), 3.03 ((ABX, J_{AB} = 17.6, J_{AX} = 9.9, 1 H, $H_aC(2)$), 2.90 (ABX, J_{AB} = 17.6, J_{BX} = 2.1, 1 H, $H_bC(2)$), 2.43 (t, J = 7.3, 2 H, $H_2C(4)$), 1.58 (quint, J = 7.3, 2 H, $H_2C(5)$), 1.32 (sext, J = 7.3, 2 H, $H_2C(6)$), 0.91 (t, J = 7.3, 3 H, $H_3C(7)$)

^{13}C NMR: (126 MHz, $CHCl_3$)

211.04 (C(3)), 155.03 (C(1')), 142.05 (C(4')), 110.24 (C(3')), 106.20 (C(2')), 63.83 (C(1)), 47.04 (C(2)), 43.28 (C(4)), 25.57 (C(5)), 22.17 (C(6)), 13.74 (C(7))

IR: (neat)

3431 (s), 3149 (m), 3120 (m), 2958 (s), 2933 (s), 2873 (s), 1711 (s), 1600 (m), 1504 (m), 1465 (m), 1408 (s), 1379 (s), 1269 (m), 1217 (m), 1147 (s), 1070 (s), 1012 (s)

MS: (CI, CH_4)

196 (M+, 18), 180 (13), 179 (100), 139 (10), 97 (9), 85 (59)

Opt. Rot.: $[\alpha]_D^{24}$ +36.27 (c = 1.00, EtOH)

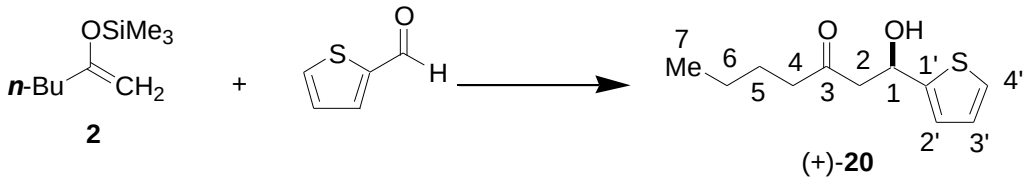
TLC: R_f0.29 (hexane/EtOAc, 2/1) [silica gel]

SFC: (*R*)-**19** t_R 3.85 min (95.0%); (*S*)-**19** t_R 4.20 min (5.0%) (OD column, 125 bar, 3.0 mL/min, 2.5% MeOH)

Analysis: $C_{11}H_{16}O_3$ (196.24)

Calcd:	C, 67.32;	H, 8.22%
Found:	C, 67.17;	H, 8.28%

(+)-(*R*)-1-Hydroxy-1-thiophene-3-heptanone (20) [JRH-III-17]



Diisopropylethylamine (18 μL, 0.1 mmol, 0.1 equiv) was added via syringe to a flame-dried, 5-mL, Schlenk flask under N_2 containing a solution of 42 mg (0.05 mmol, 0.05 equiv) of bisphosphoramide (*R*,*R*)-**7** in CH_2Cl_2 (2 mL). To this solution was added 94 μL (1.0 mmol) of 2-thiophenecarboxaldehyde in one portion. To the resulting solution was added 172 μL (1.5 mmol, 1.5 equiv) of $SiCl_4$ in one portion and the reaction mixture was cooled to –72 °C over 15 min. Then, 206 mg (1.2 mmol, 1.2 equiv) of **2** was added dropwise neat over 5 min. The resulting mixture was stirred at –72 °C for 6 h whereupon 3.0 mL of chilled CH_2Cl_2 was added before the cold reaction mixture was poured into a rapidly stirring solution of 1/1 sat. aq. $NaHCO_3$/ sat. aq. KF (25 mL) at 0° C. This biphasic mixture was stirred vigorously for 1 h before being filtered through Celite. The phases were then separated and the aqueous layer was washed with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (Silica gel, pentane/Et_2O, 4/1) to give 167 mg (79%) of (+)-**20** as a clear, colorless oil.

Data for (+)-**20**:

^{1}H NMR: (500 MHz, $CHCl_3$)

7.25 (m, 1 H, HC(4')), 6.97 (m, 2 H, HC(3'), HC(2')), 5.41 (dt, J = 8.5, 3.7, 1 H, HC(1)), 3.32 (d, J = 3.7, 1 H, OH), 2.98 ((ABX, J_{AB} = 17.3, J_{AX} = 9.2, 1 H, H_aC(2)), 2.93 (ABX, J_{AB} = 17.3, J_{BX} = 3.1, 1 H, H_bC(2)), 2.46 (t, J = 7.3, 2 H, H_2C(4)), 1.58 (quint, J = 7.4, 2 H, H_2C(5)), 1.32 (sext, J = 7.4, 2 H, H_2C(6)), 0.91 (t, J = 7.3, 3 H, H_3C(7))

^{13}C NMR: (126 MHz, $CHCl_3$)

211.07 (C(3)), 146.61 (C(1')), 126.60 (C(3')), 124.59 (C(4')), 123.42 (C(2')), 66.15 (C(1)), 50.70 (C(2)), 43.29 (C(4)), 25.48 (C(5)), 22.13 (C(6)), 13.72 (C(7))

IR: (neat)

3440 (m), 3107 (m), 3072 (w), 2958 (s), 2933 (s), 2872 (m), 2360 (w), 2341 (w) 1709 (s), 1464 (m), 1441 (m), 1404 (m), 1381 (s), 1309 (m), 1269 (m), 1227 (m), 1128 (m), 1078 (m), 1038 (s), 852 (m), 833 (m), 700 (s)

MS: (EI, 70 eV)

212 (M+, 70), 155 (26), 127 (28), 113 (100), 112 (34), 111 (28), 110 (14), 109 (19), 85 (51), 58 (46), 57 (34)

Opt. Rot.: $[\alpha]_D^{24}$ +15.96 (c = 1.00, EtOH)

TLC: R_f0.36 (hexane/EtOAc, 2/1) [silica gel]

SFC: (*R*)-**20** t_R 6.32 min (90.0 %); (*S*)-**20** t_R 6.78 min (10.0 %) (OD column, 125 bar, 3.5 mL/min, 3.0 % MeOH)

Analysis: $C_{11}H_{16}O_2S$ (212.31)

Calcd:	C, 62.23;	H, 7.60%
Found:	C, 62.37;	H, 7.56%

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