

**Highly Stereoselective Synthesis of a Chiral Methyl Group by a Facially
Controlled Sigmatropic [1,5]-Hydrogen Shift**

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Supporting Information

General

The following general procedures were used in all reactions unless noted otherwise. Reaction vessels were dried by repeated heating under vacuum (heat gun) followed by purging with dry argon. Oxygen- and moisture sensitive reactions were carried out under a positive pressure of dry argon from a manifold or balloon. Sensitive liquids and solutions were transferred by double tipped needle or syringe through rubber septa.

All commercially available reagents were purchased in the best quality available and used without further purification with the following exceptions: THF, benzene, D₆-benzene and Et₂O were distilled from potassium benzophenone ketyl under argon immediately before

use. Hexanes and EtOAc were purified by fractional distillation. Methylene chloride were distilled from CaH_2 under argon.

Thin layer chromatography (TLC) was carried out on silica gel 60 plates with a 254 nm fluorescent indicator from Merck. Plates were developed in a covered chamber and visualized by ultraviolet light, acidic anisaldehyde, permanganate or ceric sulphate stain. Analytical high performance liquid chromatography (HPLC) was performed with a Macherey-Nagel 5 μm Nucleosil column (250x20). The separations were monitored with UV- and RI-detectors. Preparative column chromatography and flash chromatographyⁱ was performed with silica gel 60 from Merck (230 - 400 mesh). Preparative HPLC was performed with a Waters Prep PAK 500 system.

Melting points were determined on a Kofler apparatus or a Büchi SMP 510 apparatus and are uncorrected. Elemental analyses were performed with a Perkin-Elmer 240 and a Heraeus CHN-Rapid elemental analyzer. NMR spectra were measured on a Bruker AC 250 (^1H at 250 MHz, ^{13}C at 63 MHz), AM 270, WH 270 (^1H at 270 MHz, ^{13}C at 68 MHz), AM 400, AMX 400 (^1H at 400 MHz, ^{13}C at 100 MHz), DRX 600 (^1H at 600 MHz, ^{13}C at 150 MHz) magnetic resonance spectrometer. Proton NMR spectra are reported as chemical shifts in parts-per-million (ppm) downfield from tetramethylsilane (0 ppm). The following abbreviations are used to describe spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, m = multiplet, mc = centered multiplet, b = broad, dd = doublet of doublets, dt = doublet of triplets, dq = doublet of quartets, ddd = doublet of doublet of doublet, other combinations derive from those listed. ^{13}C -NMR spectra are reported as chemical shifts in ppm based on the middle peak of chloroform-d (77.0 ppm) and were

recorded with complete heterodecoupling. Mass spectra were obtained under electron impact (EI). The following instruments were used: Varian MAT 711, Micro Mass, Fisions Instruments, Trio 200. Infrared spectra were recorded on a Perkin-Elmer 1600 FT and a Nicolet FTIR 55XC spectrometer.

The steps which was carried out in the radio lab was checked before by working with non radioactive compounds.

For example tritiodesilylation reaction was checked on a non-deuterated derivative of (*S*)-**13**, by using ^2H -TFA. The stereoselection for the double bound in 1- position was 96 % de, as detected by ^1H -NMR.

Experimental Procedures

Synthesis of 2- $[\text{}^2\text{H}_1]$ -Isobutylbromide:

A solution of (28.2 ml, 215.4 mmol, 1.2 eq) diisopropylamine in 100 ml of abs. hexane was cooled to 0 °C and 86.2 ml (215.4 mmol, 1.2 eq) of BuLi (2.5 M in hexane) is added. The solution is stirred for 10 min and then evaporated to dryness under reduced pressure. The remaining solid was dissolved in 600 ml abs. THF and the resulting solution was cooled to – 78 ° C. (24 ml, 179.6 mmol, 1 eq) ethylisobutyrate in 100 ml abs. THF was added dropwise. After 1 h, (86.2 ml, 215.4 mmol, 1.2 eq) of BuLi 2.5 M in hexane was added and the reaction mixture stirred for 0.5 h. (12 ml, 538.7 mmol, 3 eq) D₂O in 100 abs. THF was added and the cold bath was removed. When the suspension had reached room temperature

300 ml tech. ether and 100 ml of 6 N HCl is added carefully and the mixture is poured into a separating funnel. The layers were separated after vigorous shaking. The organic layer was washed with 3 N HCl (50 ml), sat. aq. NaHCO₃ solution (50 ml) and brine and afterwards dried with MgSO₄. The product was isolated by fractional distillation under atmospheric pressure. (16 g, 76 %) 2-[²H₁]-Ethylisobutyrate (bp = 113 °C) was obtained containing >98 % ²H as detected by ¹H-NMR.

2-[²H]- isobutylalcohol was prepared by reduction of (16.8 g, 143.7 mmol, 1 eq) 2-[²H]-ethylisobutyrate with (4.1 g, 107.8 mmol, 0.75 eq) LAH in 200 ml abs. Ether. After heating under reflux for 2 h and work up was the 2-[²H₁]- isobutylalcohol purified by fractional distillation (bp = 101 °C).

7.8 g (72 %) was obtained containing >98 % ²H as detected by ¹H-NMR.

(7.8 g, 103.0 mmol, 1 eq) 2-[²H₁]- isobutylalcohol was mixed with 50 ml abs. DMF and (29.8 g, 113.3 mmol, 1.1 eq) Ph₃P and heated to 55 °C. (5.8 ml, 113.3 mmol, 1.1 eq) bromine was added slowly until the solution remained slightly orange. The isobutylbromide was distilled at 8 mbar into a cooled flask (- 78 °C). The crude product was poured into ice water and the organic layer separated and dried over CaCl₂. Fractional distillation (bp = 92 °C) yielded 8.8 g (65 %) 2-[²H₁] isobutylbromid containing >98 % ²H as detected by ¹H-NMR.

Synthesis of the Dienes (Z)-7a-d:

Standard Procedure

To a suspension of (1 eq) (2-Phenyl-2-propenyl)-triphenylphosphoniumbromid **5** in abs. THF (2.5 ml per mmol) at -40°C was slowly added, BuLi (1eq). After warming to 0°C (1 eq) of aldehyde (*rac*)-**6a-d** in abs. THF (2 ml per g aldehyde) was added and stirred for 30 min. Pentane (same volume then THF) was added to the reaction mixture. The mixture was filtered through silicagel (1 cm). The solvent was removed carefully in vacuum (bath temperature = 40°C max. 250 mbar). Column chromatography on silicagel with pentane gave diastereomeric mixture of the dienes (*E*)/(*Z*)-**7a-d**, which was separated by HPLC.

(*Z*)-5-Methyl-2-phenyl-1,3-heptadiene (*Z*)-**7a**:

According to the standard procedure the phosphonium salt **5** (5.0 g, 10.9 mmol, 1 eq) was suspended in 35 ml abs. THF. The suspension was cooled to -40°C and (6.8 ml, 10.9 mmol, 1 eq) BuLi was added slowly. After warming to 0°C , (1.03 g, 12 mmol, 1.1 eq) 2-methylbutanal in 5 ml abs. THF was added. After standard work up and purification by column chromatography 2.0 g (89 % yield) of a mixture (*E*)/(*Z*)-**7a** (1 : 3) was obtained.

Anal. HPLC: 100% i- hexane, MN-Nucleosil 50-10, flow 2 ml/min, R_t (*Z*)-**7a** = 3.0 min, R_t (*E*)-**7a** = 3.5 min.

Semi-Prep. HPLC: i-hexane, Nucleosil, 250 x 20 mm, flow 6ml/min, R_t (Z)-**7a** = 2.7 min,
 R_t (E)-**7a** = 3.5 min.

(Z)-**7a**:

$^1\text{H-NMR}$ (250 MHz, CDCl_3): δ = 7.50- 7.20 (m, 5H, Ph), 6.10 (dt, 1H, J = 1.5, 11.5 Hz ,
H-2), 5.50 (t, 1H, J = 1.5 Hz, H-1'), 5.45 (dd, 1H, J = 10.0, 11.5 Hz, H-3), 5.14 (t, 1H, J =
1.5 Hz, H-1), 2.46 (m, 1H, H-5), 1.29 (m, 2H, H-6 und H-6'), 0.95 (d, 3H, J = 7 Hz, CH_3),
0.83 (t, 3H, J = 7.5 Hz, $-\text{CH}_3$, H-7) ppm.

$^{13}\text{C-NMR}$ (63 MHz, CDCl_3): δ = 140.8, 128.9, 128.9, 128.0, 127.2, 114.3, 30.5, 21.2, 12.1
ppm.

MS (EI, 70 eV, 300°C): m/z = 186 (M), 174, 128, 115, 102, 91, 77, 63, 57.

IR (KBr-disc) : ν = 3416, 3082, 3058, 3026, 2998, 2960, 2926, 2873, 2300, 1945, 1878,
1796, 1754, 1610, 1456, 1445, 1413, 1376, 1313, 1291, 1262, 1154, 1100, 1090, 1071,
1027, 970, 938, 897, 843, 774, 702, 476, 463 cm^{-1} .

Anal. Calcd. for $\text{C}_{14}\text{H}_{18}$ (186.27): C: 90.26 H: 9.74. Found C: 90.51 H: 9.78

(Z)-5,6,-Dimethyl-2-phenyl-1,3-heptadiene (Z)-**7b**:

According to the standard procedure the phosphonium salt **5** (7.0 g, 12.8 mmol) was suspended in 60 ml abs. THF. The suspension was cooled to -40°C and (8.0 ml, 12.8 mmol) BuLi was added slowly. After warming to 0°C , (1.29 g, 12.8 mmol) 2,3-Dimethylbutanal (*rac*)-**6b** in 5 ml abs. THF was added. After standard work up and purification by column chromatography 1.84 g (72 % yield) of a mixture (*E*)/(*Z*)-**7b** (1 : 1) was obtained.

Anal. HPLC: 100% hexane, Supersphere Si 60, 244x4 mm, flow 2.0 ml/min R_t (*Z*)-**7b** = 2.0 min, R_t (*E*)-**7b** = 2.4 min.

Semi-prep. HPLC: 100% hexane, Supersphere, 241x16 mm, flow 20 ml/min, R_t (*Z*)-**7b** = 2.2 min, R_t (*E*)-**7b** = 2.8 min.

(*Z*)-**7b**:

^1H -NMR (250 MHz, C_6D_6): δ = 7.47 - 7.42 (m, 2H), 7.20 - 7.05 (m, 3H), 6.15 (d, J = 11.6 Hz, 1H), 5.51 - 5.42 (m, 2H), 5.17 (dd, J = 1.7, 3.6 Hz, 1H), 2.44 (dq, J = 11.6, 6.8 Hz, 1H), 1.36 (oct, J = 6.8 Hz, 1H), 0.91 (d, J = 6.8 Hz, 1H), 0.85 (d, J = 6.8 Hz, 3H), 0.83 (d, J = 6.8 Hz, 3H) ppm.

^{13}C -NMR (63 MHz, C_6D_6): δ = 139.3, 128.7, 128.0, 127.1, 114.4, 38.8, 34.0, 22.7, 20.4, 20.3, 18.7 ppm.

MS (EI, 70 eV, 40°C): m/z = 201 (M+1), 200 (M.), 185, 157 (100.0%), 143, 142, 141, 129, 115, 105, 91, 77, 51.

IR (Si-plate): ν = 3854, 3822, 3802, 3752, 3712, 3676, 3630, 3568, 3454, 3424, 3385, 3358, 3300, 3060, 3027, 3002, 2958, 2870, 2362, 2341, 1610, 1574, 1492, 1458, 1384, 1369, 1292, 1106, 896, 817, 774, 739, 703, 611, 566, 514 cm^{-1} .

Anal. Calcd. for $\text{C}_{15}\text{H}_{20}$ (200.32): C: 89.94 H: 10.06. Found. C: 89.91 H: 9.95

(Z)-5-Cyclohexyl-2-phenyl-1,3-hexadiene (Z)-7c:

According to the standard procedure the phosphonium salt **5** (7.0 g, 12.8 mmol) was suspended in 60 ml abs. THF. The suspension was cooled to -40°C and (6.2 ml, 2.5 M in hexane, 12.8 mmol, 1eq) BuLi was added slowly. After warming to 0°C , (1.79 g, 12.8 mmol) 2-cyclohexyl-butanal (*rac*)-**6c** in 5 ml abs. THF was added. After standard work up and purification by column chromatography 2.58 g (84 % yield) of a mixture (*E*)/(*Z*)-**7c** (2.1 : 1) was obtained.

Anal. HPLC: 100% hexane, Hibar-Merck Supersphere Si 60,250x4 mm, flow 2.0 ml/min
 R_t (*Z*)-**7c** = 3.2 min R_t (*E*)-**7c** = 3.6 min.

Semi-prep. HPLC: 100% hexane, Supersphere, 241x16 mm, flow 20 ml/min, R_t (*E*)-**7c** = 3.8 min, R_t (*E*)-**7c** = 4.0 min.

(*Z*)-**7c**:

$^1\text{H-NMR}$ (400 MHz, C_6D_6): δ = 7.47 – 7.33 (m, 2H), 7.18 – 7.06 (m, 3H), 6.15 (d, J = 11.3 Hz, 1H), 5.49 (d, J = 2.0 Hz, 1H), 5.47 (t, J = 11.3 Hz, 1H), 5.19 (m, 1H), 2.46 (m, 1H), 1.79 – 1.53 (m, 5H), 1.23 – 0.78 (m, 4H), 1.23 – 0.98 (m, 2 H), 0.93 (d, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C-NMR}$ (63 MHz, CDCl_3): δ = 145.5, 141.5, 139.7, 128.7, 128.5, 128.0, 127.1, 114.4, 43.9, 38.0, 31.2, 31.0, 27.2, 27.1, 27.1, 18.7 ppm.

MS (EI, 70 eV, 30°C): m/z = 240 (M), 226, 183, 157 (100%), 135, 130, 122.

IR (Si-plate): ν = 3082, 3058, 3026, 2998, 2925, 2851, 2664, 2362, 1944, 1802, 1610, 1574, 1492, 1448, 1412, 1370, 1291, 1264, 1103, 1028, 992, 944, 897, 776, 704, 611, 514 cm^{-1} .

Anal: Calcd. for $\text{C}_{18}\text{H}_{24}$ (240.38): C: 89.94 H: 10.06. Found. C: 89.71 H: 10.20.

(*Z*)-5,6,6-Trimethyl-2-phenyl-1,3-heptadiene (*Z*)-**7d**:

According to the standard procedure the phosphonium salt (21.46 g, 56 mmol, 1.1 eq) was suspended in 150 ml abs. THF. The suspension was cooled to -40°C and (35 ml, 56 mmol, 1.1 eq) BuLi was added slowly. After warming to 0°C , (5.82 g, 51 mmol, 1 eq) 2,3,3-trimethyl-butanal (*rac*)-**6d** in 5 ml abs. THF was added. After standard work up and purification by column chromatography 8.1 g (74 % yield) of a mixture (*E*)/(*Z*)-**7d** (1.3 : 1) was obtained.

Anal. HPLC: 100% hexane, Supersphere Si 60, 244x4 mm, flow 2.0 ml/min, R_t (*Z*)-**7d** = 1.9 min, R_t (*E*)-**7d** = 2.2 min.

Semi-prep. HPLC: 100% hexane, Supersphere, 241x16 mm, flow 20 ml/min, R_t (*Z*)-**7d** = 2.1 min, R_t (*E*)-**7d** = 2.4 min.

(*Z*)-**7d**:

^1H -NMR (250 MHz, CDCl_3): δ = 7.40 - 7.16 (m, 5H, Ph), 6.13 (d, 1H, J = 12.5 Hz), 5.56 (d, 1H, J = 1.5 Hz, H-1'), 5.16 (d, 1H, J = 1.5 Hz, H-1), 2.42 (m, 1H, H-4), 0.96 (d, 3H, J = 7.5 Hz, $-\text{CH}_3$), 0.85 (s, 9H, t-Bu) ppm.

^{13}C -NMR (63 MHz, CDCl_3): δ = 144.5, 140.8, 137.6, 128.0, 127.9, 127.3, 126.4, 113.8, 41.3, 32.8, 27.3, 15.9 ppm.

MS (EI, 70 eV, 120°C): m/z = 214 (M), 199, 171, 157, 143, 128, 115, 105, 91, 84, 57.

IR(KBr-disc): ν = 3851, 3448, 3026, 2999, 2928, 2834, 2361, 2342, 1718, 1654, 1606, 1570, 1496, 1464, 1430, 1364, 1303, 1273, 1251, 1234, 1160, 1143, 1082, 1041, 952, 914, 876, 846, 813, 731, 695 cm^{-1} .

Anal. Calcd. for $\text{C}_{16}\text{H}_{22}$ (214.34): C: 89.66 H: 10.34. Found C: 89.39 H: 10.32

Thermolysis:

The dienes (*Z*)-**7a-d** were azeotropically dried with 2 ml portions of abs. benzene. The flask was flushed with argon and abs. C_6D_6 was added to give a 0.2 molar solution. An aliquot (0.6 ml) of this solution 0.6 ml was placed into a dry, argon flushed nmr tube, using dioxane as an internal standard. Any remaining oxygen was removed using three freeze and thaw cycles. Finally, the solution was frozen and the tube was sealed under reduced pressure. The tube was placed in a thermostatically controlled bath and ^1H -NMR spectra recorded at appropriate intervals by chilling with liquid nitrogen. After completion of the rearrangement, the solvent was removed under reduced pressure and the crude product was purified by column chromatography eluting with pentane (100 mbar). Column

chromatography with silicagel and pentane as eluent furnished the clean dienes (*E*)/(*Z*)-**8a-c** and (*E*)-**8d**. The isomers (*E*)/(*Z*)-**8a-c** could not be separated by HPLC and were characterized by ¹H-NMR, combustion analysis and ROESY or NOESY-experiments.

(*E,Z*)-5-Methyl-2-phenyl-2,4-heptadiene (*E*)-**8a** and (*E,Z*)-5-Methyl-2-phenyl-2,4-heptadiene (*Z*)-**8a**:

¹H-NMR (400 MHz, C₆D₆): δ = 7.41 – 7.05 (m, 10H, Ar-H), 6.81 (m, 2H, H-5_Z + H-5_Z), 6.30 (d, J = 10.5 Hz, 1H, H-4_E), 6.25 (d, J = 11.5 Hz, 1H, H-4_E), 2.15 (q, J = 7.6 Hz, 2H, H-6_Z), 2.08 – 2.01 (m, 8H, H-1_E + H-1_Z + H-6_E), 1.75 (s, 3H, Allyl-H, H-5_Z), 1.70 (s, 3H, Allyl-H, H-5_E), (t, J = 7.5 Hz, 3H, CH₂-Me, H-7_E), 0.94 (t, J = 7.6 Hz, 3H, CH₂-Me, H-7_Z) ppm.

Anal. Calcd. for C₁₄H₁₈ (186.29): C: 90.26 H: 9.74. Found C: 90.55 H: 9.54.

(*E,E*)-5,6,-Dimethyl-2-phenyl-2,4-heptadiene (*E*)-**8b** and (*E,Z*)-5,6,-Dimethyl-2-phenyl-2,4-heptadiene (*Z*)-**8b**:

¹H-NMR (400 MHz, C₆D₆): δ = 7.46 – 7.40 (m, 4H, m- ArH), 7.24 – 7.06 (m, 6 H, o,p - ArH), 6.91 (d, J = 11.4 Hz, 1H, H-3_Z), 6.82 (dd, J = 11.2, 1.4 Hz, H-3_E), 6.34 (m, 1H, H-4_E), 6.22 (m, 1H, H-4_Z), 3.08 (h, J = 6.9 Hz, 1H, H-6_Z), 2.29 (h, J = 6.8 Hz, 1H, H-6_E), 2.07 (s,

3H, H-1_E), 2.05 (s, 3H, H-1_Z), 1.70 (s, 3H, H-6_Z), 1.67 (s, 3H, H-6_E), 1.03 (d, J = 6.8 Hz, CH₃-6_E), 0.95 (d, J = 6.9 Hz, 6H, CH₃-6_Z) ppm.

Anal. Calcd. for C₁₅H₂₀ (200.32): C: 89.94 H: 10.06 .Found C: 90.15 H: 10.18

(E,E)-5-Cyclohexyl-2-phenyl-2,4-hexadiene (E)-8c and (E,Z)-5-Cyclohexyl-2-phenyl-2,4-hexadiene (Z)-8c :

¹H-NMR (400 MHz, C₆D₆): δ = 7.48 – 7.43 (m, 4H, m-ArH), 7.23 – 7.05 (m, 6H, o,p-ArH), 6.99 (d, J = 12.0 Hz, 1H, H-3_Z), 6.73 (d, J = 11.0 Hz, 1H, H-3_E), 6.27 (m, 1H, H-4_Z), 2.81 (m, 1H, H-6_E), 2.47 (m, 1H, H-6_Z), 2.09 (m, 3H, H-1_E), 2.07 (m, 3H, H-1_Z), 1.79 – 1.53 (m, 16H, H-6_E, H-6_Z, c-Hexyl-H), 1.43 – 0.98 (m, 10H, c-Hexyl-H) ppm.

Anal.: Calcd. for C₁₈H₂₄ (240.38) :C: 89.94 H: 10.06. Found C: 90.12 H: 10.12.

(E,E)-5,6,6-Trimethyl-2-phenyl-2,4-heptadiene (E)-8d:

¹H-NMR (250 MHz, CDCl₃): δ = 7.40 – 7.14 (m, 5H, ArH), 6.60 (d, 1H, J = 15 Hz, H-3), 6.22 (d, 1H, J = 15 Hz, H-4), 2.11 (s, 3H, CH₃, H-1), 1.82 (s, 3H, CH₃, H-5), 1.05 (s, 9H, t-Bu) ppm.

^{13}C -NMR (63 MHz, CDCl_3): δ = 147.7, 144.1, 134.3, 128.1, 126.5, 125.6, 124.0, 117.8, 36.9, 28.9, 15.9, 13.4 ppm.

MS (EI, 80 eV, 30°C): m/z = 214 (M), 171, 157, 145, 142, 141, 131, 129, 83.

IR (KBr- disc): ν = 3396, 3385, 3363, 3346, 3300, 3287, 3266, 3147, 3124, 3058, 3027, 2995, 2932, 2870, 2833, 2732, 2348, 2281, 2068, 1996, 1945, 1872, 1836, 1795, 1774, 1732, 1719, 1709, 1686, 1670, 1664, 1654, 1452, 1444, 1430, 1382, 1359, 1320, 1303, 1274, 1251, 1234, 1159, 1143, 1127, 1106, 1081, 1042, 951, 912, 868, 843, 812, 776, 757, 731, 695 cm^{-1} .

Anal. Calcd. for $\text{C}_{16}\text{H}_{22}$ (214.34): C: 89.66 H: 10.34. Found C: 89.86 H: 10.34.

Synthesis of (S)-1

3,3- Dimethyl- [(4*R*,3*S*)- 5-methyl- 2-oxo-4-phenyl-oxazolidin-3-yl]-butan-1-one (9):

A stirred, cooled (-78 °C) solution of (2.0 g, 11.3 mmol, 1 eq) methyl-phenyl-oxazolidinone in 50 ml abs. THF was metalated with (7.1 ml, 1.6 N in hexane, 11.3 mmol, 1 eq) BuLi. Then (1.71 ml, 12.3 mmol, 1.1 eq) tert. Butylacetyl chloride in 5 ml THF was

added and the mixture warmed to room temperature and stirred for an additional 0.5 h. The reaction was quenched with sat. aq. ammonium chloride (10 ml). The resultant two-phase mixture was separated and the organic layer was washed with water and brine. The aqueous layer was extracted with dichloromethane (3x20 ml). The combined organic layers were dried with MgSO_4 and after filtration concentrated under reduced pressure to give a pale yellow solid. Recrystallisation from hexane gave 2.42 g (80%), of white crystals.

mp = 92°C

$[\alpha]_D^{20} = 128^\circ$, c (CHCl_3) = 0.7

$^1\text{H-NMR}$ (250 MHz, CDCl_3): δ = 7.46 – 7.28 (m, 5H, Ar-H), 5.63 (d, 1H, J = 7.3 Hz, Bn-H), 4.80 (dq, 1H, J = 6.6, 7.3 Hz), 3.03 (d, J = 14.5 Hz, H-2), 2.83 (d, 1H, J = 14.5 Hz, H-2'), 1.09 (s, 9H, t-Bu), 0.90 (d, 3H, J = 6.6 Hz, $-\text{CH}_3$) ppm.

$^{13}\text{C-NMR}$ (63 MHz, CDCl_3): δ = 171.6, 133.3, 128.6, 125.5, 78.5, 54.7, 46.0, 31.4, 29.4, 14.4 ppm.

MS (EI, 80 eV, 120°C): m/z = 276 ($M+1$), 260, 232, 220, 219, 178, 176, 175, 160, 142, 135, 134, 119, 108, 100, 91, 84, 83, 70 (100%).

IR (KBr-disc): ν = 3851, 3534, 3367, 3072, 3047, 2992, 2956, 2938, 2908, 2868, 1776, 1692, 1654, 1586, 1496, 1457, 1434, 1371, 1351, 1339, 1306, 1259, 1221, 1201, 1169,

1133, 1118, 1093, 1068, 1049, 1029, 1004, 979, 927, 906, 858, 822, 792, 766, 739, 705, 646, 631, 607, 518, 458 cm^{-1} .

Anal. Calcd. for $\text{C}_{16}\text{H}_{23}\text{NO}_3$: (275.34): C 69.80 H: 7.69 N: 15.25. Found C: 68.98 H: 7.50 N: 15.42

(S)-2,3,3-Trimethyl-[(4R,3S)-5-methyl-2-oxo-4-phenyl-oxazolidin-3-yl]-butan-1-one:

To a cold ($-78\text{ }^{\circ}\text{C}$) solution of (39.05 g, 141.8 mmol, 1 eq) of the oxazolidinone **9** in 400 ml abs. THF was added dropwise a solution of (41.61 g, 226.9 mmol, 1.6 eq) Na-HMDS in 150 ml abs. THF. The reaction mixture was stirred for 1.5 h at $-78\text{ }^{\circ}\text{C}$ and then (35.3 ml, 567.3 mmol, 4 eq) Methyl iodide was added over a period of 1 h. After a further 0.5 h the mixture was allowed to warm to rt and was quenched with sat. aq. ammonium chloride solution (100 ml). The layers were separated and the aqueous phase three times extracted with ether (30 ml). The combined organic extracts were washed with (20 ml) 1M H_2SO_4 , sat. aq. NaHCO_3 solution and brine and dried with MgSO_4 . The crude product was concentrated under reduced pressure, filtered through silicagel and purified by column chromatography, eluting with hexane - ethylacetate (5: 1). The title compound (19.3g, 77%) was obtained as a white solid.

mp = 99°C

$[\alpha]_{\text{D}}^{20} = 64.8^{\circ}$, c (CHCl₃) = 1

¹H-NMR (250 MHz, CDCl₃): δ = 7.33 (m, 5H), 5.51 (s, 1H), 4.86 (dd, J = 3.1, 3.8 Hz, 1H), 4.30 (dq, J = 3.1, 6.9 Hz, 1H), 3.45 (d, J = 3.8 Hz, 1H), 1.95 (q, J = 7.1 Hz, 1H), 1.10 (d, J = 7.1 Hz, 3H), 1.01 (d, J = 6.9 Hz, 3H), 0.98 (s, 9H) ppm.

¹³C-NMR (63 MHz, CDCl₃): δ = 140.6, 128.0, 127.4, 126.3, 51.4, 50.7, 32.6, 27.6, 14.7, 12.9 ppm.

MS (EI, 70 eV, 160°C): m/z = 264 (M+1), 246, 157, 134, 100, 85 (100.0%), 79.

IR (KBr - disc): ν = 2877, 2850, 2727, 2689, 2639, 2486, 2463, 2386, 2340, 2320, 2304, 2254, 2228, 2142, 2078, 2044, 1965, 1932, 1872, 1806, 1793, 1697, 1689, 1636, 1609, 1589, 1517, 1487, 1460, 1447, 1354, 1328, 1261, 1227, 1092, 1077, 1152, 1122, 1092, 1077, 1047, 1019, 1005, 992, 968, 937, 925, 896, 862, 839, 794, 766, 711 cm⁻¹.

(S)-2,3,3-Trimethylbutan-1-ol:

Benzylthiol (15.9 ml, 135.6 mmol, 5 eq) was added to abs. THF (180 ml) in a dry argon-

flushed, 1-l, 3-necked flask equipped with a dropping funnel. The solution was cooled to 0 °C and BuLi (67.8 ml, 1.6N in hexane, 108.5 mmol, 4 eq) was added dropwise. The resulting mixture was stirred for 15 min and then the methylated derivative of compound **9** (7.9 g, 27.1 mmol, 1eq) in abs. THF (100 ml) was added. The solution was stirred for 3.5 h, during which time it was allowed to warm to rt. The reaction mixture was re-cooled to 0 °C and LAH (81.9 ml, 1.0 M in THF, 81.4 mmol, 3 eq) was added slowly. After TLC analysis confirmed complete reduction of the thioester, the reaction was quenched by addition of ether (100 ml) and sat. aq. ammonium chloride (10 ml) and the mixture stirred for 1 h. The resulting suspension was filtered and the solvent removed by distillation. The crude product was purified by column chromatography eluting with pentane/ether 5 : 1 then pentane/ether 3 : 1. The solvent was removed by distillation under atmosphere pressure. The reaction yielded 2.9 g (91%) (*S*)-2,3,3-Trimethylbutanol. An ee of 97% ee was detected by chiral GC analysis (50 m, 0.25 mm Chiral FS-Hydrodex-βPM, He 20 psi, Inj. 0.5 µl hexane, 250 °C FID 250°, 110° isotherm).

$$[\alpha]_D^{20} = -29.73^\circ, c(\text{CHCl}_3) = 0.47$$

¹H-NMR (250 MHz, CDCl₃): δ = 3.78 (dd, 1H, J = 10.0, 3.8 Hz), 3.28 (dd, 1H, 2J = 10.0, 8.8 Hz), 1.4 (m, 2H, H-2, C-OH), 0.95 (d, 3H, J = 7.5 Hz, -CH₃), 0.88 (s, 9H, t-Bu) ppm.

(R)-2,3,3-Trimethylbutanal (R)-6d:

(3.46 g, 16.1 mmol, 1.3 eq) PCC was suspended in 30 ml abs. dichloromethane and (S)-2,3,3-trimethylbutanol the 1.44 g (12.38 mmol, 1 eq) in 10 ml abs. dichloromethane was added. The suspension was stirred for 2.5 – 3 h at room temperature. The reaction course was checked by TLC (consumption of starting material). Then 40 ml ether was added and stirred for 15 min. The reaction mixture was filtered through florisil. The PCC residue was washed with ether (30 ml) three times. The solvent was removed under reduced pressure (> 300 mbar) and the crude aldehyde (R)-6d 1.2 g (9.9 mmol) was used without further purification.

¹H-NMR (250 MHz, CDCl₃): δ = 9.82 (s, 1H), 2.65 (m, 1H, H-2), 1.2 (d, 3H, J = 7.5 Hz, CH₃), 1.0 (s, 9H, t-Bu) ppm.

(S)-[Z]-3,4,4- Trimethyl-1-iod-1-pentene (S)-10:

To a suspension of (7.88 g, 14.9 mmol, 1.2 eq) iodomethyltriphenylphosphonium iodide in 300 abs THF at 0° C was slowly added (2.50 g, 13.7 mmol, 1.1 eq) NaHMDS in 150 ml

abs. THF. After stirring for 5 min, the solution was cooled to -78°C and the crude aldehyde (1.2 g) was added in abs. THF (10 ml). The cold bath was removed and stirring was continued for 30 min. Pentane (150 ml) was added to the reaction mixture and the mixture was filtered through silica gel. The solvent was removed carefully under reduced pressure. Column chromatography eluting with pentane gave the title compound 2.1 g (72 % yields over two steps). An ee of 97% ee was detected by chiral GC analysis (50 m, 0.25 mm Chiral FS-Hydrodex- β PM, He 20 psi, Inj. 0.5 μl hexane, 250 $^{\circ}\text{C}$ FID 250 $^{\circ}$, 110 $^{\circ}$ isotherm).

$$[\alpha]_{\text{D}}^{20} = -10.04^{\circ}, c(\text{CHCl}_3) = 1.24$$

^1H -NMR (250 MHz, CDCl_3): δ = 6.07 (d, J = 7.4 Hz, 1H), 5.93 (dd, J = 9.6 Hz, J = 7.4 Hz, 1H), 2.24 (dq, J = 9.5, 6.9 Hz, 1H), 0.80 (d, J = 6.9 Hz, 3H), 0.79 (s, 9H) ppm.

^{13}C -NMR (68 MHz, CDCl_3): δ = 144.2, 81.2, 58.9, 33.0, 27.5, 14.3 ppm.

MS (EI, 70 eV, 40 $^{\circ}\text{C}$): m/z = 194 (M-44), 180 (M-58), 103 (M-135), 57 (M-181).

IR (NaCl-plate): ν = 2960, 2869, 1732, 1609, 1365, 1271, 1097, 1031 cm^{-1} .

Anal: Calcd. for $\text{C}_8\text{H}_{15}\text{I}$ (238.11): C: 40.35 H: 6.35. Found. C: 40.12 H: 6.36

(S)-(Z, Z)-[1-²H₁]-5,6,6-Trimethyl-2-phenyl-1-trimethylsilyl-1,3-heptadiene (S)-13:

(31 ml, 31 mmol, 3 eq) 2-[²H₁]-Isobutylmagnesiumbromid (1M in ether) was treated with (409 mg, 1.64 mmol, 0.16 eq) dichlorotitanocene at 0 °C for 90 min. (3.58 g, 20.55 mmol, 2.4 eq) Trimethylsilylphenylacetylene **11** was added dropwise and the mixture was stirred at room temperature for 4 h. The reaction mixture is cooled to 0 °C and (31 ml, 1 M in ether, 31 mmol, 3 eq) ethereal ZnCl₂ solution was added and transmetallated for 30 min, during which time the reaction mixture was allowed to warm to rt. A mixture of (2.0 g, 8.41 mmol, 1 eq) vinylhalide (S)-**10** and (355 mg, 0.31 mmol, 0.03 eq) Tetrakis(triphenylphosphine) palladium was added in abs. ether (10 ml) and stirred for 2 h. The reaction was quenched with ether (30 ml) and sat. aq. ammonium chloride solution (5 ml). The solids were removed by filtration through silica and celite. The organic layer was dried over MgSO₄. The solvent was removed carefully under reduced pressure. Column chromatography eluting with pentane gave the title compound (S)-**13** 1.61 g (67%). An ee of 96.4 % ee was detected by chiral GC analysis (50 m, 0.25 mm Chiral FS-Hydrodex-BPM, He 20 psi, Inj. 0.5 µl hexane, 250 °C FID 250°, 110° isotherm).

$$[\alpha]_{\text{D}}^{20} = -131.98^{\circ}, c(\text{CHCl}_3) = 1.16$$

¹H-NMR (250 MHz, CDCl₃): δ = 7.34 – 7.24 (m, 2H), 7.20 – 7.16 (m, 3H), 6.10 (d, J = 12.0 Hz, 1H), 5.36 (t, J = 12.0 Hz, 1H), 1.96, (m, 1H), 0.76 (m, 12H), -0.18 (s, 9H) ppm.

^{13}C -NMR (63 MHz, CDCl_3): δ = 155.1, 143.2, 136.4, 132.8, 132.6, 128.6, 127.6, 127.0, 40.4, 32.7, 27.2, 15.6, 0.4, 0.0 ppm.

MS (EI, 70 eV, 200 °C): m/z = 287 (M), 272, 184, 156.

IR (KBr-plate): ν = 3791, 3148, 3099, 3058, 3024, 3000, 2959, 2899, 2870, 2715, 2403, 2348, 2287, 1945, 1880, 1806, 1758, 1709, 1619, 1601, 1585, 1550, 1490, 1475, 1458, 1442, 1405, 1394, 1364, 1300, 1256, 1247, 1219, 1192, 1156, 1121, 1072, 1052, 1022, 993, 915, 835, 780 cm^{-1} .

Anal: Calcd. for $\text{C}_{19}\text{H}_{29}\text{SiD}$ (287.33): C: 79.53 H: 10.85. Found. C: 79.56. H: 10.58

Synthesis of (S)-14:

Azeotropically dried (S)-13 (benzene, 3 x 0.5 ml)(737 mg, 2.56 mmol, 1 eq) was dissolved in abs. pentane (5 ml). The solution was cooled to 5 °C and ^3H -TFA (473 μl , 6.14 mmol, 2.4 eq) [prepared from ^3HHO (100 μl , 5.56 mmol) and TFAA (784 μl , 5.56 mmol)]. TLC showed completion after 20 min and the reaction was quenched with sat. aq. NaHCO_3 solution. The layers were separated and the aqueous layer extracted with pentane (2 ml). The combined organic extracts were washed with brine and dried with MgSO_4 . The solvent

was removed by distillation at atmospheric pressure and the product purified by column chromatography, eluting with pentane. After removal of the solvent by distillation, the title compound (*S*)-**14** 520 mg (94%) was isolated (6.5 mCi).

Thermolysis of (*S*)-**14**:

The crude diene (*S*)-**14** was dissolved in an Ace pressure tube (purchased from Aldrich) in 6 ml abs. benzene. The pressure tube was sealed and heated to 200.0° in a thermostatically controlled bath over 4 h 10'. The tube was cooled to rt and opened. The reaction mixture was poured into a round bottom flask. The solvents were removed by distillation at atmospheric pressure and the product purified by column chromatography, eluting with pentane. After removal of the solvent by distillation, the title compound (*S*)-**15** 494 mg (95%) was isolated (4.7 mCi).

Degradation of (*S*)-**15**:

Alkene (*S*)-**15** was dissolved in CH₂Cl₂/MeOH (20 : 1) and the solution was cooled to – 78 °C. Oxygen was bubbled through it for 2 min, after which time ozone was passed through until the reaction mixture adopted a blue color. The solution was then purged with oxygen for 2 min (disappearance of blue color) and (2.10 g, 8 mmol) Ph₃P was added. The cooling

bath was removed and the reaction mixture was allowed to reach room temperature and stirred for additional 1 h. The solvents was removed by distillation at atmospheric pressure and the product purified by column chromatography, eluting with pentane/ ether (5 : 1). After removal of the solvent by distillation crude (*S*)-[^3H , $^2\text{H}_1$]-Acetophenon was used directly.

(882.7 μl , 6.25 mmol) TFAA was added dropwise to a stirred mixture of (2.35 g, 25 mmol) UHP, (3.1 g, 21.9 mmol) Na_2HPO_4 and the (*S*)-[^3H , $^2\text{H}_1$]-Acetophenon in 45 ml abs. CH_2Cl_2 . The mixture was heated for 2 h under reflux. The reaction mixture was cooled to room temperature and the layers separated. The remaining solid was washed with dichloromethane. The combined organic layers were washed with sat. aq. NaHCO_3 solution and brine and dried over MgSO_4 . The solvent were removed by distillation at atmospheric pressure and the crude product was added to 15 ml 1N NaOH and stirred at room temperature for 30 min and then brought to $\text{pH} = 8.4$ with 1 N H_2SO_4 . The solution was steam distilled to give 300 ml of distillate. After addition of 2 N H_2SO_4 (3 ml) the acetic acid was distilled steam to give 200 ml of distillate. The distillate was titrated with 0.1 N KOH (7.4 ml) to a $\text{pH} = 7.6$ detected by a pH-elektrode. Thus the yield of the *S*-Acetate (*S*)-**16** was therefore 0.84 mmol (36%) over the last three steps from (*S*)-**13**. The specific activity was measured to 2.05 mCi/mol. To store the sample the water was removed by distillation under reduced pressure.