A Synthesis of (+)-Manoalide via a Copper(I)-Mediated 1,2-Metallate Rearrangement

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SUPPLEMENTARY INFORMATION

Preparation and spectroscopic data for **1**, **4**, **5**, **7**, **10**, (*R*)-**13**, (*S,R*)-**14**, (*S,S*)-**14**, **26**, **27**, **28** and **33** together with experimental procedures for the asymmetric propargylation of 5-triethylsilyl-3-furaldehyde (**12**).

Compound	Page	$[\alpha]_D$	IR	^1H NMR	^{13}C NMR	LRMS	HRMS	Anal
1	S13	√	√	√	√	√	√	—
4	S4	N/A	√	√	√	—	—	√
5	S9	√	√	√	√	√	√	√
7 (prep only)	S2	—	—	—	—	—	—	—
10 (prep only)	S3	—	—	—	—	—	—	—
(<i>R</i>)- 13	S6	√	√	√	√	√	√	—
(<i>S,R</i>)- 14	S5	√	√	√	√	√	√	—
(<i>S,S</i>)- 14	S5	√	√	√	√	√	√	—
26	S10	√	√	√	√	√	√	—
27	S12	√	√	√	√	√	√	—
28	S13	√	√	√	√	√	—	—
33	S14	—	√	√	√	√	√	—

General Experimental Procedures. All reactions requiring anhydrous conditions were conducted in flame-dried apparatus under an atmosphere of dry oxygen-free nitrogen, or high purity argon where stated. Anhydrous solvents and reagents were prepared by distillation from the usual drying agent prior to use: THF from sodium and benzophenone; pyridine, diisopropylamine, triethylamine and dichloromethane from calcium hydride. Diethyl ether was distilled from sodium. The titer of commercial organolithium reagents (Aldrich) was determined by titration against 1,3-diphenylacetone-*p*-toluenesulfonylhydrazone according to the method of Lipton et al. [M. F. Lipton, C. M. Sorensen, A. C. Sadler, and R. H. Shapiro, *J. Organometal. Chem.*, 1981, **186**, 155]. All reactions were magnetically stirred unless otherwise stated. Organic extracts were evaporated on a Büchi rotary evaporator using a diaphragm pump. All reactions were monitored by TLC on silica gel pre-coated on aluminium foil sheets, layer thickness 0.25 mm. Compounds were visualised with UV (254 nm) followed by 2M H₂SO₄ in methanol and 0.2 M vanillin in ethanol or by 5% w/w phosphomolybdic acid in ethanol.

¹H and ¹³C NMR spectra were recorded in Fourier Transform mode at the field strength specified. All spectra were obtained in CDCl₃ solution in 5 mm diameter tubes, and the chemical shift in p.p.m. is quoted relative to the residual signals of chloroform (δ_{H} 7.27, δ_{C} 77.2) as the internal standard unless otherwise specified. Multiplicities in the ¹H NMR spectra are described as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and br = broad. Coupling constants (*J*) are reported in Hz. ¹³C NMR spectra refer to the number of protons attached to carbon as revealed by the Distortionless Enhancement by Phase Transfer (DEPT) spectral editing technique, with secondary pulses at 90° and 135°. Signal assignments were based on COSY, HMQC and HMBC correlations. Ion mass/charge (*m/z*) ratios are reported as values in atomic mass units followed, in parenthesis, by the peak intensity relative to the base peak (100%). Signal patterns generated by compounds containing tin atoms are quoted as the signals derived from the ¹²⁰Sn isotope. Mass spectra were recorded on samples judged to be $\geq 95\%$ pure by ¹H and ¹³C NMR spectroscopy.

Dihydro- β -ionone (7).

Procedure: Laube, T.; Schröder, J.; Stehle, R.; Seifert, K. *Tetrahedron* **2002**, *58*, 4299-4309.

A mixture of β -ionone **6** (1.92 g, 10.0 mmol), triethylsilane (1.74 g, 15.0 mmol) and tris(triphenylphosphane)rhodium(I) chloride (9.3 mg, 0.01 mmol) was stirred under nitrogen for 5 h at 80–85 °C in the absence of solvent. The reaction was cooled to 0 °C whereupon MeCN (50 mL) was added followed by 48% aqueous HF (0.4 mL, 11.0 mmol). The ice bath was removed and the reaction mixture was stirred vigorously at ambient temperature for 30 min. K₂CO₃ (2 g) was added and the mixture stirred for a further 30 min. The solids were removed by filtration through a plug of silica gel (2 cm)

and the solvent evaporated. The residue was purified by column chromatography on silica gel (50 g, gradient elution with hexanes–ether 50:1 to 10:1) to give dihydro- β -ionone **7** (1.75 g, 9.0 mmol, 90%) as a colourless oil: bp 47–49 °C/0.01 mmHg. Compound **7** gave ^1H and ^{13}C NMR spectra identical to those reported previously.

2-But-3-ynyl-1,3,3-trimethylcyclohexene (**8**).

Procedure: Negishi, E.; King, A. O.; Klima, W. L. *J. Org. Chem.* **1980**, 45, 2526.

Alkyne **8** was prepared in 73% yield (110 mmol scale) by the method of Negishi.

(*E*)-4-Methyl-6-(2,6,6-trimethyl-cyclohex-1-enyl)-hex-3-en-1-ol (**10**).

Procedure: Wipf, P.; Lim, S. *Angew. Chem. Int. Ed.* **1993**, 32, 1068-1071.

To a yellow solution of AlMe_3 (2 M in heptanes, 133 mL, 266 mmol) and Cp_2ZrCl_2 (2.6 g, 8.9 mmol) in CH_2Cl_2 (150 mL) at -23°C was slowly added water (2.4 mL, 133 mmol) with vigorous stirring. After 10 min, a solution of alkyne **8** (15.6 g, 88.5 mmol) in CH_2Cl_2 (50 mL) was added. The reaction mixture was stirred for another 45 min at -23°C whereupon a solution of oxirane (13 mL, 266 mmol) in CH_2Cl_2 (25 mL) was added. The mixture was allowed to warm to rt for 12 h, then a 5% aqueous solution of HCl was added to pH 2. The organic layer was separated and the aqueous layer extracted with Et_2O (3×200 mL). The combined organic layers were dried (MgSO_4), filtered and evaporated. The residue was purified by column chromatography on silica gel (200 g, gradient elution with hexanes – ether 10:1 to 4:1) to give alcohol **10** (12.85 g, 54.3 mmol, 62%) as colourless oil. The ^1H and ^{13}C NMR spectra of **10** were identical to those previously reported: Bury, P.; Hareau-Vittini, G.; Kocienski, P.; Dhanak, D. *Tetrahedron* **1994**, 50, 8793-8808.

2-[(*E*)-6-Iodo-3-methyl-hex-3-enyl]-1,3,3-trimethyl-cyclohexene (**4**).

To a solution of alcohol **10** (4.30 g, 18.2 mmol), triphenylphosphine (5.76 g, 22.0 mmol) and imidazole (2.04 g, 30.0 mmol) in CH_2Cl_2 (50 mL) at 0°C was added dropwise a solution of iodine (5.59 g, 22.0 mmol) in CH_2Cl_2 (50 mL). The cooling bath

was removed and mixture stirred at ambient temperature for 2 h. The reaction mixture was poured into a saturated solution of $\text{Na}_2\text{S}_2\text{O}_3$ (20 mL) and shaken. The organic layer was separated and the aqueous layer was extracted with Et_2O (3×50 mL). The combined organic layers were dried (MgSO_4), filtered and evaporated. The residue was purified by column chromatography on silica gel (100 g, hexanes) to give iodoalkane **4** (5.74 g, 16.8 mmol, 92%) as colourless oil. Iodoalkane **4** can be stored as a solution in Et_2O (30 mL) at -27 °C for a month without decomposition. IR (film): 2926 s, 2864 s, 2828 s, 1662 m, 1474 s, 1455 s, 1381 m, 1339 m, 1245 m, 1165 s cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ_{H} 5.16 (1H, br t, $J = 7.0$ Hz, $\text{C4H}'$), 3.16 (2H, t, $J = 7.5$ Hz, $\text{C6}'\text{H}_2$), 2.62 (2H, q, $J = 7.5$, $\text{C5}'\text{H}_2$), 2.02–2.14 (4H, m, $\text{C1}'\text{H}_2$ and $\text{C2}'\text{H}_2$), 1.94 (2H, br t, $J = 6.2$ Hz, C4H_2), 1.69 (3H, s, $\text{C3}'\text{Me}$), 1.64 (3H, s, C3Me), 1.64–1.57 (2H, m, C5H_2), 1.47–1.43 (2H, m, C6H_2), 1.03 (6H, s, C1Me_2); ^{13}C NMR (75 MHz, CDCl_3): δ_{C} 139.6 (C), 137.3 (C), 127.5 (C), 122.7 (CH), 40.6 (CH_2), 40.2 (CH_2), 35.4 (C), 33.1 (CH_2), 32.8 (CH_2), 29.0 (2CH_3), 28.1 (CH_2), 20.3 (CH_3), 20.0 (CH_2), 16.8 (CH_3), 6.6 (CH_2); Anal. Calcd for $\text{C}_{16}\text{H}_{27}\text{I}$: C, 55.5 ; H, 7.86; I, 36.65 %. Found: C, 55.8; H, 7.8; I, 36.5%.

5-(Triethylsilyl)-3-furaldehyde (**12**)

Aldehyde **12** was prepared from commercial (Aldrich) 3-furaldehyde on a 4 mmol scale by the procedure of Lee and co-workers: Lee, G. C. M.; Holmes, J. M.; Harcourt, D. A.; Garst, M. E. *J. Org. Chem.* **1992**, 57, 3126-3131.

(*RS*)-1-(5-Triethylsilylfuran-3-yl)-but-3-yn-1-ol (*rac*-**13**).

To a mixture of Mg (2.6 g, 108 mmol) and HgCl_2 (50 mg) in Et_2O (150 mL) was added at rt a solution of propargyl bromide (80% in toluene, 0.3 mL, 3.8 mmol). After the reaction started, the solution was cooled to -20 °C and the remainder of the bromide (80% in toluene, 9.5 mL, 88 mmol) was added dropwise over 40 min. At the end of addition the cooling bath was removed and the reaction mixture was stirred for 30 min at ambient temperature and then cooled to -40 °C whereupon a solution of aldehyde **5** (5.25 g, 25 mmol) in Et_2O (20 mL) was added dropwise. The mixture was allowed to warm slowly up to rt over 3 h. A saturated solution of NH_4Cl was added. After separation of the organic layer, the aqueous layer was extracted with Et_2O (3×50 mL), dried (MgSO_4), filtered and evaporated. The residue was purified by column chromatography on silica gel (100 g, hexanes-ether 5:1) to give the racemic alcohol **13**.

(5.68 g, 22.7 mmol, 91%) as a colourless oil. For spectroscopic data see the preparation of (*R*)-13 below.

(*R*)-1-(5-Triethylsilyl-furan-3-yl)-but-3-yn-1-ol [(*R*)-13].

A. By chromatographic resolution of the *O*-acetyl-mandelate esters

To a magnetically stirred solution of racemic alcohol **rac-13** (2.0 g, 8.0 mmol) in CH_2Cl_2 (10 mL) at $-10\text{ }^\circ\text{C}$ were added (*S*)-*O*-acetyl mandelic acid (1.71 g, 8.8 mmol), DCC (1.81 g, 8.8 mmol) and a catalytic amount of DMAP. After 3 h at -10 to $0\text{ }^\circ\text{C}$, the mixture was filtered and the white precipitate washed with CH_2Cl_2 . The filtrate was evaporated and the residue purified by column chromatography on silica gel (hexanes–ether 9:1) to give first mandelate (*S,R*)-**14** (1.39 g, 3.26 mmol, 41%, >96% ee) followed by a mixture of (*S,S*)-**14** and (*S,R*)-**14** (1.06 g, 2.48 mmol, 31%) and finally mandelate (*S,S*)-**14** (0.75 g, 1.76 mmol, 22%, >96% ee).

(*S*)-Acetoxypheylacetic acid (*R*)-1-[5-(triethylsilyl)furan-3-yl]but-3-ynyl ester [(*S,R*)-**14**]: $[\alpha]_{\text{D}} = +74.8$ (*c* 1, CHCl_3); IR (film): 3296 m, 2956 s, 2914 s, 2876 s, 1754 s, 1458 m, 1372 m, 1232 s, 1206 s, 1058 s, 738 s, 726 s cm^{-1} ; ^1H NMR (360 MHz, CDCl_3): δ_{H} 7.68 (1H, s, C2'H), 7.46–7.52 (2H, m, PhH), 7.35–7.40 (3H, m, PhH), 6.60 (1H, s, C4'H), 5.95 (1H, s, CHOAc), 5.95 (1H, apparent t, $J = 6.4$ Hz, C1H), 2.64 (2H, apparent dd, $J = 6.3, 2.5$ Hz, C2H₂), 2.21 (3H, s, Ac), 1.77 (1H, t, $J = 2.7$ Hz, C4H), 0.98 (9H, t, $J = 7.8$ Hz), 0.75 (6H, q, $J = 7.8$ Hz); ^{13}C NMR (90 MHz, CDCl_3): δ_{C} 170.3 (C), 168.2 (C), 159.6 (C), 144.6 (CH), 133.7 (C), 129.2 (C), 128.7 (2CH), 127.8 (2CH), 122.9 (C), 119.5 (CH), 78.9 (C), 74.7 (CH), 70.7 (CH), 68.1 (CH), 25.0 (CH₂), 20.8 (CH₃), 7.33 (3CH₃), 3.2 (3CH₂); LRMS (EI mode): $m/z = 426$ ($\text{M}^{+\bullet}$, 15), 301 (89), 263 (62), 250 (100), 233 (64), 221 (21), 177 (17), 149 (87), 145 (68), 115 (47), 107 (54), 87 (44); HRMS (EI mode): Found $\text{M}^{+\bullet}$, 426.1860. $\text{C}_{24}\text{H}_{30}\text{O}_5\text{Si}$ requires M , 426.1863.

(*S*)-Acetoxypheylacetic acid (*S*)-1-[5-(triethylsilyl)furan-3-yl]but-3-ynyl ester [(*S,S*)-**14**]: $[\alpha]_{\text{D}} = +40.5$ (*c* 0.62, CHCl_3); IR (film): 3296 m, 2956 s, 2914 s, 2876 s, 1754 s, 1748 s, 1456 m, 1372 s, 1232 s, 1206 s, 1176 s, 1080 s, 1060 s, 1004 m, 962 m, 908 m, 738 s, 726 s, 698 s cm^{-1} ; ^1H NMR (360 MHz, CDCl_3): δ_{H} 7.44 (3H, m, PhH, C2'H), 7.36 (3H, m, PhH), 6.31 (1H, s, C4'H), 5.98 (1H, s, CHOAc), 5.94 (1H, t, $J = 6.5$ Hz, C1H), 2.78 (1H, ddd, $J = 9.2, 6.5, 2.6$ Hz, C2H_AH_B), 2.72 (1H, ddd, $J = 9.2, 6.5, 2.6$ Hz, C2H_AH_B), 2.20 (3H, s, Ac), 2.02 (1H, t, $J = 2.6$ Hz, C4H), 0.96 (9H, t, $J = 7.9$ Hz), 0.75 (6H, q, $J = 7.9$ Hz); ^{13}C NMR (90 MHz, CDCl_3): δ_{C} 170.3 (C), 167.9 (C), 159.3 (C), 144.3 (CH), 133.6 (C), 129.3 (CH), 128.8 (2CH), 127.8 (2CH), 122.8 (C), 119.2 (CH), 79.1 (C), 74.5 (CH), 71.0 (CH), 68.2 (CH), 25.3 (CH₂), 20.8 (CH₃), 7.3 (3CH₃), 3.2

(3CH₂); LRMS (EI mode): m/z = 426 (M⁺•, 17), 301 (82), 263 (58), 250 (100), 233 (61), 221 (21), 149 (90), 145 (79), 118 (41), 115 (26), 107 (56), 103 (39), 87 (46); HRMS (EI mode): Found M⁺•, 426.1864. C₂₄H₃₀O₅Si requires M, 426.1863.

Hydrolysis of ester (*S,R*)-14 to give (*R*)-13.

To a magnetically stirred solution of ester (*S,R*)-14 (1.1 g, 2.58 mmol) in MeOH (30 mL) at rt was added a 50 % aqueous solution of NaOH (5 mL). After 1.5 h, water (20 mL) was added and MeOH was partially removed *in vacuo*. The residue was overlaid with Et₂O (30 mL) and the pH adjusted to 5-7 with HCl (1 M). The layers were separated and the aqueous layer extracted with Et₂O (2 × 20 mL). The combined organic layers were washed with brine (20 mL), dried (MgSO₄), filtered and evaporated. The residue was purified by column chromatography on silica gel (hexanes-ether 1:1) alcohol to give (*R*)-13 (599 mg, 2.39 mmol, 93%) as a colourless oil after kugelrohr distillation: bp 85 °C (bath)/0.05 mmHg; [α]_D = +20.8 (*c* 1.0, CHCl₃). IR (film): 3400-3100 br s, 3311 s, 2955 s, 2896 s, 1592 m, 1461 s, 1415 s, 1078 s, 1050 s, 1019 s, 973 m, 907 m, 854 m, 827 m, 725 s cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ_{H} 7.57 (1H, s, C2'H), 6.59 (1H, s, C4'H), 4.77 (1H, br t, J = 5.9 Hz, C1H), 2.61–2.54 (2H, m, C2H), 2.33 (1H, br s, OH), 2.01 (1H, t, J = 2.6 Hz, C4H), 0.9 (9H, t, J = 7.8 Hz, Me), 0.72–0.63 (6H, m, SiCH); ¹³C NMR (75 MHz, CDCl₃): δ_{C} 160.0 (C), 143.9 (CH), 127.5 (C), 119.6 (CH), 81.1 (CH), 71.5 (C), 65.8 (CH), 28.8 (CH₂), 7.7 (3CH₃), 3.6 (3CH₂); LRMS (EI mode): m/z = 250 (M⁺•, 18), 221 (25), 211 (67), 181 (100), 175 (22), 153 (82), 125 (41), 118 (27), 115 (30), 87 (30); HRMS (EI mode): Found M⁺•, 250.1386. C₁₄H₂₂O₂Si requires M, 250.1389.

B. By Sharpless kinetic resolution.

To a mixture of crushed 4Å molecular sieves (5 g) and Ti(O-*i*Pr)₄ (6.7 mL, 22.5 mmol) in CH₂Cl₂ (100 mL) at –20 °C was added (*R,R*)-(+)-diisopropyl tartrate (5.8 mL, 27.7 mmol). The mixture was vigorously stirred for 30 min at –20 °C and then cooled to –30 °C. A solution of racemic alcohol *rac*-13 (5.63 g, 22.5 mmol) in CH₂Cl₂ (20 mL) was added and the mixture was stirred for 30 min whilst maintaining the temperature between –30 and –20 °C. The mixture was cooled again to –30 °C and a solution of *tert*-butyl hydroperoxide in CH₂Cl₂ (4.2 M, 4.2 mL, 17.6 mmol) was added. After stirring for 24 h at –21 °C, Me₂S (2 mL) was added and the mixture was stirred for 30 min. To this mixture was added sequentially 10% aqueous tartaric acid (5 mL), Et₂O (100 mL) and NaF (30 g). The resulting mixture was vigorously stirred for 2 h at ambient temperature. The white precipitate was filtered through Celite and washed with Et₂O (200 mL). The filtrate was evaporated and the residue was purified by column chromatography on silica gel (100 g, hexanes-ether 5:1) to give (*R*)-13 (2.31 g, 9.22

mmol, 41%) as a colourless oil after kugelrohr distillation: $[\alpha]_D +19.3$ (c 3.4, CHCl_3). The ee (>95%) was determined by integration of the characteristic singlets at 6.31 (*S*) and 6.60 (*R*) of the protons at C4' on the furan ring in the ^1H NMR spectra of the *O*-acetyl mandelate esters prepared as described above.

Enantioselective propargylation of 5-triethylsilyl-3-furaldehyde (12).

A. Using dibenzyl (2*S*,3*S*)-tartrate (15) as chiral ligand.

Procedure: Ikeda, N.; Arai, I.; Yamamoto, H. *J. Am. Chem. Soc.* **1986**, *108*, 483-486.

A suspension of flame-dried molecular sieves (5Å, 1.5 g), allenylboric acid (276 mg, 3.29 mmol) and (D)-dibenzyl tartrate (825 mg, 2.50 mmol) in dry toluene (10 mL) was stirred at rt for 24 h. The resultant solution was added to the aldehyde **7** (280 mg, 1.33 mmol) at $-78\text{ }^{\circ}\text{C}$ with the aid of additional aliquots of toluene ($2 \times 4\text{ mL}$). The reaction mixture was kept at $-78\text{ }^{\circ}\text{C}$ for 3 d and then poured into a solution of NaHCO_3 (25 mL). The organic layer was separated and the aqueous layer extracted with Et_2O ($3 \times 10\text{ mL}$). The combined organic extracts were dried (MgSO_4), filtered and evaporated to a volume of 5 mL and hexanes (50 mL) added. The white precipitate was removed by filtration to give recovered dibenzyl tartrate (750 mg, 90%) and filtrate was evaporated. The residue was purified by column chromatography on silica gel (30 g, gradient elution with hexanes-ether 50:1 to 5:1) to give product **13** (235 mg, 0.94 mmol, 71%, R:S = 80:20) as a colourless oil. The er was determined by NMR spectroscopic analysis of the ester prepared from (*S*)-*O*-acetyl mandelic acid.

B. Using (*S*)-diphenyl(1-benzylpyrrolidin-2-yl)methanol (16) as chiral ligand.

Procedure: Watanabe, M.; Soai, K. *J. Chem. Soc., Perkin Trans. 1* **1994**, 4264-4268.

To a freshly distilled solution of a mixture of 1-iodo-1,2-propadiene and 3-iodo-1-propyne (2:1, 357 mg, 2.20 mmol, obtained by treatment of propargyl bromide with sodium iodide in refluxing acetone) in toluene (5 mL) was added a solution of Et_2Zn (1.1 M in toluene, 2 mL, 2.20 mmol) at $0\text{ }^{\circ}\text{C}$. After stirring at $0\text{ }^{\circ}\text{C}$ for 1 h, a solution of (*S*)-BDPPM (69 mg, 0.2 mmol) and the aldehyde **7** (210 mg, 1.00 mmol) in toluene (5 mL) was added, and stirring was continued at the same temperature for 4 h. To the reaction mixture was added a saturated solution of NH_4Cl (10 mL). The mixture was extracted with Et_2O ($3 \times 10\text{ mL}$), dried (MgSO_4), filtered and evaporated. The residue was purified by column chromatography on silica gel (20 g, hexanes-ether 5:1) to give the alcohol **13** (200 mg, 0.80 mmol, 80%, R:S = 30:70) as a colourless oil.

C. Using (1*R*,2*S*)-*N,N*-dibenzyl-norephedrine (17) as chiral ligand.

Procedure: Soai, K.; Yokoyama, S.; Hayasaka, T. *J. Org. Chem.* **1991**, *56*, 4264-4268.

The reaction was carried out as described in the preceding procedure using a mixture of 1-iodo-1,2-propadiene and 3-iodo-1-propyne (in ratio 2:1) (357 mg, 2.20 mmol), a solution of Et₂Zn (1.1M in toluene, 2mL, 2.20 mmol), ligand **17** (53 mg, 0.2 mmol) and the aldehyde **12** (210 mg, 1.00 mmol) to give the alcohol **13** (209 mg, 0.84 mmol, 84%, R:S = 55:45) as colourless oil.

D. Using (*R*)-BINOL as chiral ligand.

Procedure: Keck, G.E.; Krishnamurthy, D.; Chen, X. *Tetrahedron Lett.*, **1994**, *35*, 8323; Yu, C.-M.; Choi, H.-S.; Jung, W.-H.; Baek, K. *J. Chem. Soc., Chem. Commun.* **1997**, 763-764.

To a suspension of (*R*)-BINOL (72 mg, 0.25 mmol) and crushed molecular sieves (4Å, 1 g) in dry CH₂Cl₂ (2 mL) at rt was added a freshly prepared solution of Ti(O-*i*Pr)₄ (0.5 M in CH₂Cl₂, 0.5 mL, 0.25 mmol). After 3 h the reaction mixture was cooled to -30 °C and a solution of the aldehyde **12** (210 mg, 1.00 mmol) in CH₂Cl₂ (1 mL), allenyltributylstannane (706 mg, 2.00 mmol) and *i*Pr-SBEt₂ (288 mg, 2.00 mmol) were added. The reaction was placed in a freezer and kept at -20 °C for 10 days. Then a saturated aqueous solution of NaHCO₃ (5 mL) was added to the reaction mixture and product was extracted into Et₂O (3 × 10 mL). The combined organic layers were dried (MgSO₄), filtered and evaporated. The residue was purified by column chromatography on silica gel (20 g, gradient elution with hexanes-ether 50:1 to 5:1) to give the starting material **7** (85 mg, 40%) and **13** (131 mg, 0.52 mmol, 52% or 87% based on recovered starting material, R:S = 96:4) as a colourless oil.

E. Using (*S,S*)-(-)-*N,N'*-bis-(2,6-*p*-toluenesulfonyl)-1,2-diphenylethylenediamine (**18**) as chiral ligand.

Procedure: Corey, E. J.; Yu, C.-M.; Lee, D.-H. *J. Am. Chem. Soc.*, **1990**, *119*, 878-879
To a solution of bis(sulfonamide) **18** (522 mg, 1.00 mmol) in dry CH₂Cl₂ (10 mL) at 0 °C was added a solution of BBr₃ (1.0 M in CH₂Cl₂, 1 mL, 1.00 mmol) and the reaction mixture was stirred for 40 min at rt. After evaporation of the solvent and HBr, the pale brown, moisture sensitive solid was dissolved in CH₂Cl₂ (10 mL), cooled to 0 °C and 2-propynyl-1-triphenylstannane (353 mg, 1.00 mmol) was added. The resulting solution was stirred for 4 h at 0 °C and for 30 min at rt. The reaction mixture was then cooled to -78 °C and a solution of the aldehyde **12** (189 mg, 0.90 mmol) in CH₂Cl₂ (2 mL) was added. After stirring for 4 h at -78 °C, ethanolamine (0.5 mL) was added and the reaction was warmed up to rt and poured into water (15 mL) with vigorous agitation. The organic layer was separated and the aqueous layer was extracted with Et₂O (3 × 10 mL). The combined organic layers were dried (MgSO₄), filtered, evaporated to a volume of ca. 5 mL and a mixture of ether-hexanes (3:1, 25 mL) was added. The white precipitate was separated by filtration to give recovered bis(sulfonamide) **18** (442 mg, 85%). The filtrate was evaporated and the residue purified by column chromatography on silica gel (20 g, gradient elution with hexanes-ether 100:1 to 5:1) to give **13** (110 mg, 0.44 mmol, 49%, R:S = 91:9) as a colourless oil.

(-)-(2*R*)-5'-Triethylsilyl-5-tributylstannanyl-2,3-dihydro-[2,3']bifuranyl (**5**).

A magnetically stirred solution of $\text{Mo}(\text{CO})_6$ (330 mg, 1.25 mmol) in Et_2O (25 mL) and Et_3N (12.5 mL) in a Pyrex tube was irradiated by a Hg-lamp (250 W) for 45 min at 0 °C under a N_2 atmosphere to give a yellow solution of $\text{Et}_3\text{N}\cdot\text{Mo}(\text{CO})_5$. The light source was removed and a solution of alkynol (*R*)-**13** (1.25 g, 5.00 mmol) in Et_2O (15 mL) and a solution of Bu_3SnOTf (3.29 g, 7.50 mmol) in Et_2O (15 mL) were added sequentially. The mixture was stirred at rt for 48 h. The solvent was removed *in vacuo* and the residue was purified by column chromatography on silica gel (100 g) deactivated by 3% Et_2NH in hexanes. Elution with 1% Et_2NH in hexanes afforded the stannane **5** (1.76 g, 3.20 mmol, 64%) as a pale yellow oil: $[\alpha]_D = -12.0$ (*c* 1.0, CHCl_3); IR (film): 2955 s, 2873 s, 2854 s, 1584 m, 1464 s, 1075 m, 1057 m, 1019 m, 724 s cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ_{H} 7.50 (1H, s, C2'H), 6.54 (1H, s, C4'H), 5.35 (1H, dd, $J = 10.5$, 7.9 Hz, C2H), 4.96 (1H, t, $J = 2.4$ Hz, $J_{\text{Sn-H}} = 11.5$ Hz, C4H), 2.86 (1H, part A of ABXY app. ddd, $J = 15.1$, 7.9, 2.3 Hz, $J_{\text{Sn-H}} = 10.5$ Hz, C3H_AH_B), 2.48 (1H, part B of ABXY app. ddd, $J = 15.1$, 7.9, 2.3 Hz, $J_{\text{Sn-H}} = 10.0$ Hz, C3H_AH_B), 1.61–1.31 (6H, m), 1.25 (6H, sext, $J = 7.3$ Hz), 1.03–0.86 (15H, m), 0.81 (9H, t, $J = 7.3$ Hz), 0.71–0.62 (6H, m, SiCH_2); ^{13}C NMR (75 MHz, CDCl_3): δ_{C} 162.6 (C), 159.7 (C), 143.7 (CH), 128.2 (CH), 120.0 (CH), 111.2 (C), 76.2 (CH), 37.9 (CH_2), 29.4 (3 CH_2 , $J_{\text{Sn-C}} = 11.3$ Hz), 27.6 (3 CH_2), 14.1 (3 CH_3), 10.0 (3 CH_2), 7.7 (3 CH_3), 3.6 (3 CH_2); LRMS (EI mode): $m/z = 540$ ($\text{M}^{+\bullet}$, 5), 483 (73), 481 (54), 455 (56), 453 (41), 291 (59), 289 (48), 275 (63), 273 (50), 235 (59), 233 (60), 221 (44), 208 (56), 115 (37), 87 (100); HRMS (EI mode): Found $\text{M}^{+\bullet}$, 540.2424. $\text{C}_{26}\text{H}_{48}\text{O}_2\text{SiSn}$ requires M , 540.2446. Anal. Calcd for $\text{C}_{26}\text{H}_{48}\text{O}_2\text{SiSn}$: C, 57.89; H, 8.97 %. Found: C, 57.6; H, 9.1

(+)-(1*R*)-(3*Z*,7*E*)-4-Iodo-8-methyl-1-(5'-triethylsilylfuran-3'-yl)-10-(2'',6'',6''-trimethylcyclohex-1-enyl)deca-3,7-dien-1-ol (26).

To a solution *t*-BuLi (1.5 M in pentane, 3.0 mL, 4.50 mmol) was added dropwise at –78 °C a solution of iodoalkane **4** (921 mg, 2.66 mmol) in Et_2O (3 mL) over 10 min. The white suspension was stirred for 30 min at –78 °C and for 1 h at 0 °C to give a colourless solution of alkylolithium whereupon THF (0.5 mL) was added and the mixture stirred for 1 h at rt to destroy any excess *t*-BuLi. The resultant pale yellow solution was added dropwise to a suspension of 1-pentynylcopper (242 mg, 1.85 mmol) in Et_2O (5 mL) at –78 °C. After addition was complete, the mixture was allowed to warm up to 0

°C over 1 h and stirred for an additional 40 min at 0 °C to give an orange-brown solution to which was added Me₂S (2.5 mL) immediately before use in the next step.

In the meantime, a solution of the lithiated dihydrofuran **21** was prepared as follows. To a solution of stannane **5** (1.00 g, 1.85 mmol) in Et₂O (3.6 mL) and pentane (5.4 mL) at –60 °C was added dropwise a solution of *s*-BuLi (1.3M in cyclohexane/hexane = 92:8, 1.75 mL, 2.21 mmol). Stirring was continued for 20 min to give a yellow solution of the lithiated dihydrofuran **21**.

The lithiated dihydrofuran solution was cooled to –78 °C whereupon the solution of cuprate described above was added *via* cannula with the aid of two additional 1 mL aliquots of Et₂O. The reaction mixture was allowed to warm up to rt over 12 h. The resultant brown solution was cooled to –78 °C whereupon a solution of I₂ (762 mg, 3.00 mmol) in Et₂O (10 mL) was added dropwise. The mixture was stirred for 5 min and a saturated solution of Na₂S₂O₃ (10 mL) was added. The cooling bath was replaced and the reaction mixture was warmed to rt. Then the reaction mixture was poured into a mixture of saturated aqueous solutions of NH₃ and NH₄Cl (1:1, 50 mL) and stirred vigorously for 30 min. The layers were separated and the aqueous layer extracted with Et₂O (3 × 25 mL). The combined organic layers were dried (MgSO₄), filtered and evaporated. The residue was purified by column chromatography on silica gel (70 g, gradient elution with hexanes–ether 50:1 to 10:1) to give the iodoalkene **26** (728 mg, 1.22 mmol, 66% based on the stannane **5**) as a pale yellow oil: [α]_D = +2.78 (*c* 5.4, CHCl₃); IR (film): 3334 br s, 2956 s, 1459 s, 1238 m, 1074 s, 1019 s, 908 m, 826 m, 738 s cm^{–1}; ¹H NMR (300 MHz, CDCl₃): δ_H 7.51 (1H, s, C2'H), 6.58 (1H, s, C4'H), 5.51 (1H, t, *J* = 6.7 Hz, C3H), 5.02 (1H, br t, *J* = 6.9 Hz, C7H), 4.70 (1H, br t, *J* = 6.4 Hz, C1H), 2.55–2.49 (2H, m, C2H₂), 2.45 (2H, t, *J* = 7.3 Hz, C5H), 2.13 (2H, apparent q, *J* = 7.4, C6H), 2.02–1.88 (4H, m, C9H₂ and C10H₂), 1.83 (2H, br t, *J* = 6.3 Hz, C3''H₂) overlap with 1.78 (1H, br s, OH), 1.59 (3H, s, C8Me), 1.52 (3H, s, C2''Me) overlap 1.52–1.44 (2H, m, C4''H₂), 1.36–1.33 (2H, m, C5''H), 0.92 (6H, s, C6''Me₂) overlap 0.91 (9H, t, *J* = 7.8 Hz, SiCH₂Me), 0.72–0.63 (6H, m, SiCH₂); ¹³C NMR (75 MHz, CDCl₃): 160 (C), 143.7 (CH), 138 (C), 137.5 (C), 131.1 (CH), 128.5 (C), 127.4 (C), 121.9 (CH), 119.8 (CH), 112.3 (C), 66.4 (CH), 46.1 (CH₂), 45.3 (CH₂), 40.7 (CH₂), 40.2 (CH₂), 35.4 (C), 33.2 (2CH₃), 28.5 (CH₂), 28.3 (CH₂), 20.3 (CH₃), 20.0 (CH₂), 16.7 (CH₃), 7.8 (3CH₃), 3.6 (3CH₂); LRMS (EI mode): *m/z* = 212 (17), 211 (100), 137 (38), 95 (14); HRMS (EI mode): Found M⁺•, 596.2568. C₃₀H₄₉O₂SiI requires M, 596.2547.

1,2-Metallate rearrangement using CuCN.

To a solution *t*-BuLi (1.5 M in pentane, 1.6 mL, 2.40 mmol) at –78 °C was added a solution of iodoalkane **4** (484 mg, 1.44 mmol) in Et₂O (3 mL) over 10 min. The white suspension was stirred for 30 min at –78 °C and for 1 h at 0 °C to give a colourless solution of alkyllithium whereupon THF (0.24 mL) was added and the mixture stirred at rt for 1 h to destroy any excess *t*-BuLi. The resultant pale yellow solution was added dropwise to a suspension of CuCN (90 mg, 1.00 mmol) in Et₂O (5 mL) and Me₂S (2.5 mL) at –78 °C and the mixture was warmed up to –40 °C and stirred for 20 min to give an orange-red solution of the cyanocuprate.

In the meantime, a solution of the lithiated dihydrofuran **21** was prepared as follows. To solution of stannane **5** (540 mg, 1.00 mmol) in Et₂O (1.8 mL) and pentane (2.7 mL) at

–60 °C was added dropwise a solution of *s*-BuLi (1.3M in cyclohexane/hexane = 92:8, 0.92 mL, 1.20 mmol). Stirring was continued for 20 min to give a yellow solution of the lithiated dihydrofuran **21**.

The lithiated dihydrofuran solution was cooled to –78 °C whereupon the cyanocuprate solution was added *via* cannula with the aid of two additional 1 mL aliquots of Et₂O. The reaction mixture was allowed to warm up to rt over 12 h. The resultant yellow-green solution was cooled to –78 °C whereupon a solution of I₂ (215 mg, 0.85 mmol) in Et₂O (5 mL) was added dropwise. The mixture was stirred for 5 min and a saturated solution of Na₂S₂O₃ (10 mL) was added. The cooling bath was removed and the reaction mixture allowed to warm to rt. Then the reaction mixture was poured into a mixture of saturated aqueous solutions of NH₃ and NH₄Cl (1:1, 15 mL) and stirred vigorously for 30 min. The layers were separated and the aqueous layer was extracted with Et₂O (3 × 25 mL). The combined organic layers were dried (MgSO₄), filtered and evaporated. The residue was purified by column chromatography on silica gel (70 g, gradient elution with hexanes-ether 50:1 to 10:1) to give the iodoalkene **26** (346 mg, 0.58 mmol, 58 % based on stannane **5**) as a pale yellow oil.

(+)-(6*R*)-3-[(*E*)-4'-Methyl-6'-(2'',6'',6''-trimethylcyclohex-1''-enyl)hex-3'-enyl]-6-(5'''-triethylsilylfuran-3'''-yl)-5,6-dihdropyran-2-one (27).

A solution of iodoalkene **26** (130 mg, 0.22 mmol) and freshly prepared Pd(PPh₃)₄ (8 mg, 0.007 mmol) in a mixture of iPr₂NEt (0.15 mL), MeOH (1.5 mL) and THF (3 mL) was heated at 65–70 °C under a balloon of CO for 24 h. The solvents were evaporated *in vacuo* and the residue was purified by column chromatography on silica gel (20 g, gradient elution with hexanes–ether 50:1 to 10:1) to give lactone **27** (98 mg, 0.20 mmol, 91%) as a colourless oil: [α]_D = +43.9 (*c* 3.35, CHCl₃); IR (film): 2956 s, 2876 s, 1722 s, 1458 m, 1379 m, 1225 m, 1113 s, 1072 s, 1018 m, 820 m cm^{–1}; ¹H NMR (360 MHz, CDCl₃): δ_H 7.67 (1H, t, *J* = 0.7 Hz, C2'''H), 6.68 (1H, d, *J* = 0.7 Hz, C4'''H), 6.61 (1H, ddt, *J* = 6.0, 2.6, 1.2 Hz, C4H), 5.37 (1H, ddd, *J* = 11.5, 4.1, 0.7 Hz, C6H), 5.14 (1H, tq, *J* = 7.1, 1.2 Hz, C3'H), 2.69 (1H, br dddq, *J* = 18.1, 11.7, 2.4 Hz, C5_AH_B), 2.56 (1H, ddd, *J* = 18.1, 6.1, 4.1 Hz, C5_AH_B), 2.50–2.28 (2H, m, C1'H₂), 2.21 (2H, q, *J* = 7.2, C2'H₂), 2.07–1.26 (4H, m, C5'H₂ and C6'H₂), 1.90 (2H, br t, *J* = 6.3 Hz, C3''H₂), 1.64 (3H, d, *J* = 1.3 Hz, C4'Me), 1.61 (3H, s, C2''Me) overlap with 1.60–1.54 (2H, m, C4''H₂), 1.44–1.39 (2H, m, C5''H₂), 1.00 (6H, s, C6''Me₂), 0.99 (9H, br t, *J* = 8.0 Hz, SiCH₂Me), 0.76 (6H, br t, *J* = 8.0 Hz, SiCH₂); ¹³C NMR (90 MHz, CDCl₃): δ_C 165.3 (C), 160.1 (C), 144.2 (CH), 138.4 (C), 137.4 (CH), 137.2 (C), 132.8 (C), 127.1 (C), 123.9 (CH), 122.6 (CH), 119.5 (CH), 72.6 (CH), 40.4 (CH₂), 40.0 (CH₂), 35.1 (C), 32.9 (CH₂), 31.1 (CH₂), 30.8 (CH₂), 28.8 (2CH₃), 28.1 (CH₂), 26.6 (CH₂), 19.9 (CH₃), 19.7 (CH₂), 16.2 (CH₃), 7.4 (3CH₃), 3.3 (3CH₂); LRMS (EI mode): *m/z* = 496 (M⁺•, 13), 361

(36), 333 (49), 291 (68), 208 (33), 179 (30), 137 (80), 136 (100), 115 (35), 103 (31), 95 (29); HRMS (EI mode): Found $M^{+\bullet}$, 496.3355. $C_{31}H_{48}O_3Si$ requires M , 496.3373.

(+)-(2*RS*,6*R*)-3-[(*E*)-4'-Methyl-6'-(2'',6'',6'''-trimethylcyclohex-1''-enyl)hex-3'-enyl]-6-(5'''-triethylsilylfuran-3'''-yl)-5,6-dihydro-2*H*-pyran-2-ol (28).

To a solution of lactone **27** (90 mg, 0.18 mmol) in CH_2Cl_2 (15 mL) at $-78\text{ }^{\circ}C$ was added dropwise a solution of DIBAL-H (1.5 M in toluene, 0.14 mL, 0.21 mmol). After addition was complete, the mixture was stirred at $-78\text{ }^{\circ}C$ for a further 15 min whereupon MeOH (0.1 mL) was added followed by HCl (2 M, 0.1 mL). The cooling bath was removed and the mixture was allowed to warm up to rt with vigorous stirring. The mixture was filtered through a plug of silica gel, and the filtrate evaporated. The residue was purified by column chromatography on silica gel (20 g, hexanes – ether 10:1) to give the lactol **28** (80 mg, 0.16 mmol, 89%) as a colourless oil: $[\alpha]_D = +42.9$ (c 3.95, $CHCl_3$); IR (film): 3409 br s, 2956 s, 2876 s, 1459 s, 1381 m, 1360 m, 1261 m, 1074 s, 1020 s, 908 m, 822 m, 803 m, 737 s, 725 s, 708 $m\text{ cm}^{-1}$; 1H NMR (300 MHz, $CDCl_3$): δ_H 7.63 (1H, t, $J = 0.7$ Hz, C2'''H), 6.69 (1H, d, $J = 0.7$ Hz, C4'''H), 5.73 (1H, br d, $J = 5.0$ Hz, C4H), 5.35 (1H, d, $J = 4.4$ Hz, C2H), 5.17 (1H, br t, $J = 5.8$ Hz, C3'H), 5.00 (1H, dd, $J = 11.1, 3.5$ Hz, C6H), 3.00 (1H, br s, OH), 2.44–2.30 (1H, m, C5H), 2.25–2.10 (5H, m, C5H, C1'H₂ and C2'H₂), 2.10–1.97 (4H, A₂B₂ system appearing as a distorted d, $J = 3.3$ Hz, C5'H and C6'H), 1.91 (2H, br t, $J = 6.0$ Hz, C3''H₂), 1.67 (3H, d, $J = 1.3$ Hz, C4'Me), 1.61 (3H, s, C2''Me), 1.61–1.54 (2H, m, C4''H₂), 1.44–1.39 (2H, m, C5''H₂), 1.00 (6H, s, C6''Me₂), 0.99 (9H, br t, $J = 8.0$ Hz, SiCH₂Me), 0.76 (6H, br q, $J = 8.0$ Hz, SiCH₂); ^{13}C NMR (90 MHz, $CDCl_3$): δ_C 159.6 (C), 143.9 (CH), 137.3 (C), 137.0 (C), 136.8 (C), 127.1 (C), 126.2 (C), 123.2 (CH), 122.5 (CH), 119.8 (CH), 92.0 (CH), 61.8 (CH), 40.4 (CH₂), 40.0 (CH₂), 35.1 (O), 32.9 (CH₂), 32.8 (CH₂), 31.7 (CH₂), 28.8 (2CH₃), 28.1 (CH₂), 26.2 (CH₂), 20.0 (CH₃), 19.9 (CH₂), 16.2 (CH₃), 7.4 (3CH₃), 3.3 (3CH₂); LRMS (EI mode): $m/z = 498$ ($M^{+\bullet}$, 3), 337 (25), 275 (32), 211 (43), 137 (100), 95 (39), 81 (23).

(5*RS*,2'*R*,6'*RS*)-5-Hydroxy-4-{6'-hydroxy-5'-[(*E*)-4''-methyl-6''-(2''',6''',6'''-trimethylcyclohex-1'''-enyl)hex-3''-enyl]-3',6'-dihydro-2*H*-pyran-2'-yl}-5*H*-furan-2-one. (Manoalide)

Dry oxygen was bubbled through a solution of furan **28** (74 mg, 0.148 mmol) and Rose Bengal (2 mg) in MeOH (7 mL) at $-78\text{ }^{\circ}\text{C}$ with irradiation by a tungsten lamp (100 W). The reaction was followed by TLC ($R_f = 0.2$ for product and $R_f = 0.65$ for substrate, hexanes–EtOAc 2:1). After all the starting material was consumed (15 min) the solvent was evaporated *in vacuo*. The residue was purified by column chromatography on silica gel (15 g, gradient elution with hexanes–ether 4:1 to 1:1) to give (+)-(R)-manoalide (**1**) (37 mg, 0.089 mmol, 60%) as a viscous, colorless oil: $[\alpha]_D = +77.5$ (c 1.30, CHCl_3); Lit. $[\alpha]_D = +80$ (c 0.2, MeOH) [Kobayashi, M.; Okamoto, T.; Hayashi, K.; Yokoyama, N.; Sasaki, T.; Kitagawa, I. *Chem. Pharm. Bull.* **1994**, *42*, 265-270]. IR (film): 3360 br s, 2928 s, 2865 s, 1760 s, 1440 s, 1265 m, 1132 s, 909 m, 735 cm^{-1} ; ^1H NMR: δ_H (300 MHz, CDCl_3): 6.16 (1H, br s, C5H), 6.10 (1H, br s, C3H), 5.77 (1H, br d, $J = 4.3$ Hz, C4'H), 5.33 (1H, s, C6'H), 5.14 (1H, m, C3''H), 4.87 (1H, br d, $J = 11.1$, Hz, C2'H), 4.75–4.25 (1H, br s, OH), 2.38–2.10 (6H, m, C3'H₂, C2''H₂ and C1''H₂), 2.15 (1H, s, OH), 2.10–1.97 (4H, m, C5''H₂ and C6''H₂), 1.90 (2H, br t, $J = 6.2$ Hz, C3'''H₂), 1.64 (3H, s, C4''Me), 1.60 (3H, s, C2'''Me), 1.60–1.53 (2H, m, C4'''H₂), 1.43–1.39 (2H, m, C5'''H₂), 0.99 (6H, s, C6'''Me₂); ^{13}C NMR (90 MHz, CDCl_3): δ_C 172.0 (C), 169.0 (C, br), 137.4 (C), 137.2 (C), 137.0 (C), 127.1 (C), 122.9 (CH), 121.0 (CH), 117.2 (CH, br), 98.3 (CH), 91.5 (CH), 63.1 (CH, br), 40.4 (CH₂), 40.0 (CH₂), 35.1 (0), 32.9 (2CH₂), 32.7 (CH₂), 28.8 (2CH₃), 28.0 (CH₂), 26.1 (CH₂), 19.9 (CH₃), 19.7 (CH₂), 16.2 (CH₃); LRMS (EI mode): $m/z = 137$ (100), 136 (52), 121 (26), 95 (61), 81 (53), 67 (26), 55 (25), 41 (26); HRMS (EI mode): Found $M^{+\bullet}$, 416.2520. $\text{C}_{25}\text{H}_{36}\text{O}_5$ requires M , 416.2563.

(E)-Dodec-7-en-5-one (33).

To a solution of 2-butylfuran (**29**) (0.25 g, 0.28 mL, 2 mmol) in THF (0.29 g, 0.32 mL, 4 mmol), at $-78\text{ }^{\circ}\text{C}$, was added dropwise a solution of tert-butyllithium (1.5 mL, 2 mmol, 1.35 M solution in pentane). After the addition, the flask containing the yellow semi-solid mixture was placed in an ice bath, stirred at $0\text{--}3\text{ }^{\circ}\text{C}$ for 30 min and then diluted with 4 mL of anhydrous diethyl ether to give a yellow solution of 5-butyl-2-furyllithium (**30**).

A separate flask was charged with freshly recrystallised $\text{CuBr}\cdot\text{SMe}_2$ complex (ref.: K. Jarowicki, P. J. Kocienski, and L. Qun, *Org. Synth.*, **2002**, *79*, 11) (0.453 g, 2.2 mmol) and anhydrous diethyl ether (10 mL). The suspension was cooled to $-78\text{ }^{\circ}\text{C}$ and a

solution of *n*-BuLi (2.75 mL, 4.4 mmol, 1.6 M solution in hexanes) added dropwise. After the addition was complete, the reaction mixture was placed in an ice bath and stirred at 0–3 °C for 6 min to give a light brown solution of lithium dibutylcuprate. The previously prepared solution of 5-butyl-2-furyllithium was then transferred by cannula under nitrogen pressure to the stirred solution of lithium dibutylcuprate at –78 °C. After the transfer, the flask containing the 5-butyl-2-furyllithium was washed with 2 mL of anhydrous diethyl ether. The reaction mixture was left in a cooling bath and allowed to warm up to rt overnight, then quenched with a saturated aqueous solution of ammonium chloride (20 mL) and extracted with diethyl ether (2 × 20 mL). The combined organic extracts were dried over sodium sulfate, filtered and concentrated. The residue was purified by column chromatography on silica gel eluting with hexanes–diethyl ether to give (*E*)-dodec-7-en-5-one (**33**) as a colourless oil (0.25 g, 68%): IR (film): 1717 cm^{–1}; ¹H NMR (500 MHz, CDCl₃) δ_H 5.58–5.48 (2H, m), 3.09 (2H, d, *J* = 5.2 Hz), 2.43 (2H, t, *J* = 7.5 Hz), 2.04 (2H, q, *J* = 6.6 Hz), 1.55 (2H, quintet, *J* = 7.6 Hz), 1.40–1.26 (6H, m), 0.91 (3H, t, *J* = 6.7 Hz), 0.89 (3H, t, *J* = 6.0 Hz); ¹³C NMR (75 MHz, CDCl₃) δ_C 209.9 (C), 135.2 (CH), 122.0 (CH), 46.9 (CH₂), 41.9 (CH₂), 32.4 (CH₂), 31.5 (CH₂), 25.9 (CH₂), 22.4 (CH₂), 22.3 (CH₂), 14.0 (CH₃), 13.9 (CH₃); LRMS (EI mode): *m/z* = 182 (M⁺•, 2), 86 (31), 85 (100), 84 (6), 83 (8), 81 (10), 67 (13), 58 (21), 57 (100), 56 (12), 55 (81), 54 (25), 53 (18), 41 (86), 42 (14), 43 (28), 39 (41); HRMS (ES mode): Found (M+1)⁺•, 183.1744. C₁₂H₂₃O requires M+1, 183.1749.

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 PROCNO 1

F2 - Acquisition Parameters

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1D NMR plot parameters

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 F2P -0.500 ppm
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 HZCM 82.53575 Hz/cm

4

Current Data Parameters
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 PROCNO 1

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F2 - Processing parameters
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1D NMR plot parameters
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 CY 0.00 cm
 FIP 12.500 ppm
 F1 6252.65 Hz
 F2P -1.500 ppm
 F2 -750.16 Hz
 PPMCM 0.51849 ppm/cm
 HZCM 259.36301 Hz/cm

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