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Brief Syntheses of (+)-Blastmycinone and Related γ-Lactones from an Asymmetrically Dihydroxylated Carboxylic Ester

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Abstract

A method for synthesizing optically active *trans,trans*-configurated α,β,γ-substituted γ-lactones is presented. Asymmetric hydroxylation of ester **8** with AD mix α (AD mix β) and subsequent dehydration provided butenolide *S*-**6** (*R*-**6**). Conjugate addition of $Li_2(Me_2PhSi)_2Cu(CN)$ to *S*-**6** followed by alkylation of the resulting enolate led to the stereopure silyllactones **9-11**. They furnished the title compounds after oxidative removal of the Me_2PhSi group. © 1998 Elsevier Science Ltd. All rights reserved.

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To the wealth of known syntheses of γ-lactones [1] we recently added a straightforward access to enantiopure or enantio-enriched γ-substituted γ-lactones [2]. Its key-step is an asymmetric Sharpless dihydroxylation [3] of an β,γ-unsaturated ester which one had almost never performed before [4]. In the investigation presented here we utilized this dihydroxylation strategy for preparing the optically active γ-lactones **1-5** (Scheme 1) from a common progenitor. Lactones **1-4** constitute hydrolysis products of the antimycins A_3 or A_1 [5]. The latters are secondary metabolites from *Streptomyces* and act as fungicides, insecticides, and ichthyotoxins. Lactone **5** was isolated from a related bacterial source [6]; so far there is no hint that it is a hydrolysis product, too. Despite their relatively simple structures lactones **1-5** have spurred the creativity of synthetic chemists a lot. The first syntheses of (+)-blastmycinone (**1**)

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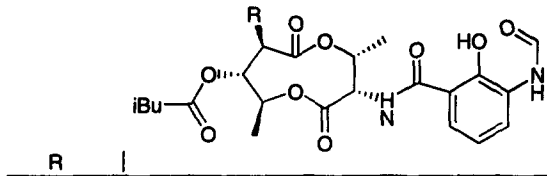
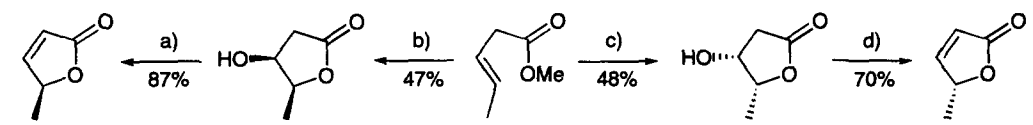
and (-)-blastmycinolactol (**3**) are 25 years old [7], those of (+)-antimycinone (**2**), (-)-NFX-2 (**4**), and (-)-NFX-4 (**5**) more recent [8-10], and the presently over 20 different approaches to these compounds [11] continue to be supplemented year by year [12].



R			
Bu	antimycin A_3	(+)-blastmycinone (**1**)	(-)-blastmycinolactol (**3**)
Hex	antimycin A_1	(+)-antimycinone (**2**)	(-)-NFX-2 (**4**)
$(CH_2)_4iPr$			(-)-NFX-4 (**5**)

Scheme 1.

Our syntheses of lactones **1-5** proceed via the butenolide *S*-**6** as the key intermediate (Scheme 2). Such a design was hitherto realized only once – albeit with entirely different reactions: in a 15-step synthesis of (-)-blastmycinolactol from L-tartaric acid [13]. The key butenolide *S*-**6** was obtained by dehydrating hydroxylactone *S,S*-**7** (78% *ee*) with mesyl chloride and triethylamine. The resulting *S*-**6** had a slightly diminished *ee* value of 75%. This is probably due to some racemization via the enolate which is stabilized because it is an O˙-substituted furan. Hydroxylactone *S,S*-**7** was obtained from the commercially available *trans*-configurated unsaturated ester **8** and AD mix α [14] in 47% yield, improving the 40% reported originally [2].

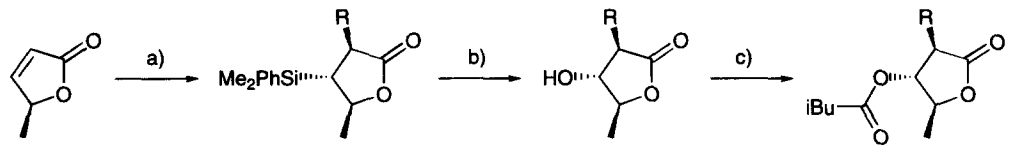


S-**6** (75% *ee*) *S,S*-**7** (78% *ee*) **8** *R,R*-**7** (80% *ee*) *R*-**6** (75% *ee*)

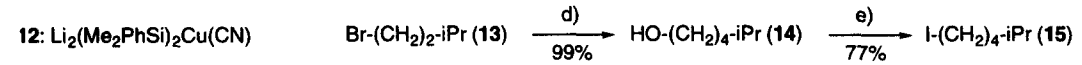
Scheme 2. a) NEt_3 (3.1 equiv.), methanesulfonyl chloride (1.8 equiv.), CH_2Cl_2, 0°C, 1 h.– b) AD mix α (1.40 g per mmol **8**), *t*BuOH/H_2O (1:1), 0°C, 10 d (ref. 2: 40% yield).– c) Same as (b) but with AD mix β, 2 d.– d) NEt_3 (2.6 equiv.), methanesulfonyl chloride (1.6 equiv.), CH_2Cl_2, 0°C, 11 h.

Next, we added $Li_2(Me_2PhSi)_2Cu(CN)$ [15] to the chiral unsaturated γ-lactone *S*-**6** 1,4- and *trans*-selectively (Scheme 3) [16]. This outcome was expected because of analogously proceeding additions of the same cuprate to chiral unsaturated δ-lactones [17]. When the initially obtained enolate is quenched with water a disubstituted lactone is obtained whose

trans-configuration was firmly established [17]. However, when this enolate was combined with excess – otherwise, the yields dropped considerably – butyl iodide, hexyl iodide, or iodide **15** selective mono-alkylations occurred. They affected the less hindered face of the enolate, i. e. the face opposite to the Me_2PhSi substituent rendering the γ-lactones **9-11** exclusively as the shown *trans,trans*-isomers. The undesired silyl groups were finally oxidized to OH groups by treatment with peracetic acid and KBr [18]. The target lactones **3-5** resulted in ca. 60% yield [19]. Einhorn esterifications of lactones **3** and **4** with isovaleroyl chloride provided the remaining target lactones **1** and **2**.



R		Yield		Yield		Yield
Bu	**9**	51%	**3**	60%	**1**	76%
Hex	**10**	66%	**4**	60%	**2**	92%
$(CH_2)_4iPr$	**11**	51%	**5**	63%		



Scheme 3. a) Li (10 equiv.), $PhMe_2SiCl$ (2.2 equiv.), THF, 0°C, 21-24 h; transferred to CuCN (1.1 equiv.), THF, -10 → 0°C, 20-40 min; → -78°C; addition of *S*-**6**, 2 h; addition of HexI or BuI or **15** (5-6.5 equiv.), -78 → -40°C, 11-12 h.– b) AcOOH (32% in AcOH, 30-50 equiv.), KBr (1.2-2.0 equiv.), NaOAc (6-12 equiv.), AcOH, 0°C → room temp., 20-29 h.– c) Isovaleroyl chloride (3.0-3.5 equiv.), pyridine, room temp., 22-25 h.– d) **13** (1.7 equiv.), Mg (1.5 equiv.), THF, reflux, 40 min; →0°C, CuI (0.2 equiv.), 5 min; → -40 - -30°C, 10 h.– e) PPh_3 (1.3 equiv.), imidazole (1.4 equiv.), I_2 (3.0 equiv.), Et_2O/CH_3CN (2:1), 0°C, 30 min.

Our syntheses of lactones **1-5** encompass only 4-5 steps from an inexpensive commercially available starting material and stay thereby below the step requirement of almost all previous syntheses (cf. the literature cited in ref. 7-13). More importantly, the strategy exemplified in Schemes 2 and 3 should be extendable to synthesizing optically active *trans,trans*-configurated α,β,γ-trisubstituted γ-lactones *in general*. Provided that the C=C bond of the starting β,γ-unsaturated ester contains a C_2H_5 or – better – a still larger alkyl group (instead of the CH_3 group of the ester **8** used here) the enantiomeric excesses of these lactones should be 90% - >95% (instead of the 75% found here) [2].

EXPERIMENTAL

General methods. All reactions were performed in oven-dried (80°C) glassware under N_2. THF was freshly distilled from K, CH_2Cl_2 from CaH_2. Products were purified by flash chromatography on Merck silica gel 60 (eluents given in brackets). Yields refer to analytically pure samples.– ^1H [$CHCl_3$ (7.26 ppm) as internal standard in $CDCl_3$] and APT ^{13}C-NMR [$CDCl_3$ (77.00 ppm) as internal standard in $CDCl_3$; assignments in accord with signal phases]: Varian VXR 200 and Bruker AMX 300; integrals in accord with assignments; coupling constants in Hz. The assignments of ^1H- and ^{13}C-NMR resonances refer to the IUPAC nomenclature; primed numbers belong to side-chain. Combustion analyses: F. Hambloch, Institute of Organic Chemistry, University of Göttingen. IR spectra: Perkin-Elmer 1600 Series FTIR; film or KBr. Optical rotations: Perkin-Elmer polarimeter 241 at 589 nm; rotational values are the average of 5 measurements of α in a given solution of the respective sample. Chiral capillary gas chromatography: 20% heptakis-(2,6-di-*O*-methyl-3-*O*-pentyl-ß-cyclodextrin in 80% OV1701, 25 m, 70 kPa H_2; 110°C isothermal. Melting points (uncorrected): Dr. Tottoli apparatus (Fa. Büchi).

(+)-Blastmycinone (**1**) was prepared as described for **2** from a solution of (-)-blastmycinolactol (**3**; 85.8 mg, 0.498 mmol) in pyridine (10 ml) and isovaleroyl chloride (300 ml, 297 mg, 2.46 mmol, 4.9 equiv.) as a colorless liquid (97.2 mg, 76%); $[\alpha]_D^{25}$ = +7.3 (*c* = 1.75 in $CHCl_3$) {ref. [12a] $[\alpha]_D^{25}$ = +11.3 (*c* = 1.18 in $CHCl_3$)}; ^1H NMR, ^{13}C NMR, and IR data in accordance with published data [12a]; Anal calcd. for $C_{14}H_{24}O_4$ (256.3), C 65.60, H 9.44; found C 65.35, H 9.69.

(+)-Antimycinone (2). At 0°C isovaleroyl chloride (70.0 ml, 69.2 mg, 0.574 mmol, 3.5 equiv.) was added dropwise to a solution of (-)-NFX-2 (**4**; 33.0 mg, 0.165 mmol) in pyridine (3 ml). After stirring for 25 h at room temp. the solution was added to ice water (10 ml). After extraction with EtOAc (4 × 15 ml) the combined organic extracts were washed with aqueous HCl (2 M, 20 ml), satd. aqueous solutions of Na_2CO_3 (15 ml) and NaCl (20 ml). Drying with $MgSO_4$, evaporation of the solvent and flash chromatography on silica gel (eluent: petroleum ether / *tert*-butylmethyl ether 5:1) yielded the title compound (43.3 mg, 92%) as a colorless liquid; $[\alpha]_D^{25}$ = +7.8 (*c* = 1.75 in $CHCl_3$) {ref. [12a] $[\alpha]_D^{25}$ = +10.8 (*c* = 0.50 in $CHCl_3$)}; ^1H NMR, ^{13}C NMR, and IR data in accordance with published data [12a]; Anal calcd for $C_{16}H_{28}O_4$ (284.4), C 67.57, H 9.92; found C 67.71, H 10.14.

(-)-Blastmycinolactol (3). Same procedure as for **5**. Treatment of dimethyl(phenyl)silane **9** (300 mg, 1.03 mmol) with peracetic acid (26% in acetic acid, 12.5 ml, 47.8 mmol, 47 equiv.), KBr (204 mg, 2.05 mmol, 2.0 equiv.) and anhydrous NaOAc (1.03 g, 12.4 mmol, 12 equiv.) at room temp. for 20 h gave the title compound (114 mg, 60%) as white crystals; mp 43-44°C (ref. [12a] mp 49-51°C); $[\alpha]_D^{25}$ = -17.1 (*c* = 1.47 in $CHCl_3$) {ref. [12a] $[\alpha]_D^{25}$ = -19.4 (*c* = 1.01 in $CDCl_3$)}; ^{1}H NMR, ^{13}C NMR, and IR data in accordance with published data [12a]; Anal calcd for $C_{11}H_{20}O_3$ (172.1), C 62.97, H 9.36; found C 62.54, H 9.10.

(4*S*,5*R*)-3-Hexyl-4,5-dihydro-4-hydroxy-5-methyl-2(3*H*)-furanone [(-)-NFX-2] (4) was prepared as described for **5** from silane **10** (210 mg, 0.659 mmol), peracetic acid (26% in acetic acid, 8.5 ml, 32 mmol, 50 equiv.), KBr (122 mg, 0.920 mmol, 1.5 equiv.), and anhydrous NaOAc (691 mg, 8.32 mmol, 12 equiv.) as white crystals (81 mg, 60%); mp 56-57°C (ref. [12a] mp 56-58°C); $[\alpha]_D^{25}$ = -13.2 (*c* = 2.08 in $CHCl_3$) {ref. [12a] $[\alpha]_D^{25}$ = -15.1 (*c* = 1.20 in MeOH)}; ^{1}H NMR, ^{13}C NMR, and IR data in accordance with published data [12a]; Anal calcd for $C_{11}H_{20}O_3$ (200.1), C 65.97, H 10.07; found C 65.69, H 9.88.

(4*S*,5*R*)-4,5-Dihydro-4-hydroxy-5-methyl-3-(5-methylhexyl)-2(3*H*)-furanone [(-)-NFX-4[(5). At 0°C KBr (40 mg, 0.34 mmol, 1.2 equiv.) and anhydrous NaOAc (70 mg, 0.84 mmol, 3.1 equiv.) were added to a solution of silane **11** (91 mg, 0.27 mmol) in peracetic acid (16% in acetic acid, 1.4 ml, 3.3 mmol, 12 equiv.). More anhydrous NaOAc (209 mg, 2.5 mmol, 2.5 equiv.) and peracetic acid (32% in acetic acid, 1.00 ml, 4.76 mmol, 17 equiv.) were added and the solution was stirred 21 h at room temp.. After addition of ether (125 ml), powdered $Na_2S_2O_3$ (2.5 g) and NaI (ca. 0.3 g) the mixture was stirred vigorously for 1.5 h and then filtered through Celite. The organic layer was washed with satd. aqueous solutions of $NaHCO_3$ (2 × 40 ml, 1 × 20 ml) and NaCl (50 ml) and dried with $MgSO_4$. Evaporation of the solvent and flash chromatography on silica gel (eluent: petroleum ether / *tert*-butylmethyl ether 1:1) yielded the title compound (37 mg, 63%) as white crystals; mp 51-53°C (ref. [12a] mp 61-63°C); $[\alpha]_D^{25}$ = -11.4 (*c* = 0.97) {ref. [12a] $[\alpha]_D^{25}$ = -11.2 (*c* = 1.62 in MeOH)}; ^{1}H NMR, ^{13}C NMR, and IR data in accordance with published data [12a]; Anal calcd for $C_{12}H_{22}O_3$ (214.3), C 67.26, H 10.35; found C 67.36, H 10.55.

(5*S*)-5-Methyl-2(5*H*)-furanone (*S*-6). *S*-**6** was prepared according to the procedure reported in ref. [17] (1.43 g, 87%). Chiral gas chromatography (R_T = 179 s for *S*-**6** and R_T = 176 s for *R*-

6) revealed *ee* = 75%; $[\alpha]_D^{25}$ = +88.8 (*c* = 0.88 in $CHCl_3$) {ref. 13 for *R*-**6** $[\alpha]_D^{20}$ = +95.9 (*c* = 0.7 in $CHCl_3$)}; ^{1}H NMR, ^{13}C NMR, and IR data in accordance with published data [13, 17].

(5*R*)-5-Methyl-2(5*H*)-furanone (*R*-6). *R*-**6** was prepared as described for *S*-**6** from a solution of *R,R*-**7** (634 mg, 5.80 mmol, 80% *ee*) in CH_2Cl_2 (20 ml), NEt_3 (2.10 ml, 1.52 g, 15.1 mmol, 2.6 equiv.), and methanesulfonyl chloride (0.72 ml, 1.1 g, 9.2 mmol, 1.6 equiv.) as a colorless liquid (400 mg, 70%). Chiral gas chromatography (R_T = 176 s for *R*-**6** and R_T = 179 s for *S*-**6**) revealed *ee* = 75%; $[\alpha]_D^{25}$ = -89.8 (*c* = 0.78 in $CHCl_3$); ^{1}H NMR and IR data identical with those of *S*-**6**.

(4*S*,5*S*)-4,5-Dihydro-4-hydroxy-5-methyl-2(3*H*)-furanone (*S,S*-7). *S,S*-**7** was prepared according to the procedure reported in ref. [17] (1.38 g, 47%). Chiral gas chromatography (R_T = 45.1 min for *S,S*-**7** and R_T = 44.0 min *R,R*-**7**) revealed *ee* = 78%; $[\alpha]_D^{25}$ = -60.0 (*c* = 1.57 in $CHCl_3$) {ref. 13 $[\alpha]_D^{20}$ = -73.7 (*c* = 1.60 in EtOH)}; ^{1}H NMR, ^{13}C NMR, and IR data in accordance with published data [13, 17]; Anal calcd for $C_5H_8O_3$ (116.1), C 51.72, H 6.94; found C 51.44, H 7.08.

(4*R*,5*R*)-4,5-Dihydro-4-hydroxy-5-methyl-2(3*H*)-furanone (*R,R*-7). *R,R*-**7** was prepared as described for *S,S*-**7** from ester **8** (0.50 ml, 0.47 g, 4.1 mmol) in *t*BuOH / H_2O (1:1, 40 ml) and AD mix β (5.70 g) as a colorless liquid (228 mg, 48%). Chiral gas chromatography (R_T = 44.3 min for *R,R*-**7** and R_T = 45.1 min *S,S*-**7**) revealed *ee* = 80%. $[\alpha]_D^{25}$ = +59.3 (*c* = 1.43 in $CHCl_3$); ^{1}H NMR and IR data identical with those of *S,S*-**7**.

(3*S*,4*R*,5*S*)-3-Butyl-4-(dimethylphenylsilyl)-4,5-dihydro-5-methyl-2(3*H*)-furanone (9) was prepared similarly as described for **10** from a suspension of CuCN (135 mg, 1.51 mmol, 1.1 equiv.), $Me_2PhSiLi$ [from $Me_2PhSiCl$ (0.750 ml, 770 mg, 4.51 mmol, 2.2 equiv.) and Li (140 mg, 20.2 mmol, 9.8 equiv.)] in THF (25 ml), butenolide *S*-**6** (201 mg, 2.05 mmol, 1.0 equiv.), and butyl iodide (1.20 ml, 1.94 g, 10.5 mmol, 5.1 equiv.) as a single diastereomer (303 mg, 51%); $[\alpha]_D^{25}$ = -9.48 (*c* = 3.13 in $CHCl_3$); ^{1}H NMR: δ = 0.40 (s, $SiMe_2$), 0.83 (t, $J_{4',3'}$ = 7.2, 4′-H_3), 1.13-1.63 (m, 1′-H_2, 2′-H_2, 3′-H_2), superimposed by 1.25 (d, $J_{5\text{-}Me,5}$ = 5.9, 5-CH_3) and 1.37 (dd, $J_{4,3}$ = 11.8, $J_{4,5}$ = 10.0, 4-H), 2.50 (ddd, $J_{3,4}$ = 11.9, $J_{3,1'\text{-}H(1)}$ = 6.4, $J_{3,1'\text{-}H(2)}$ = 4.2, 3-H), 4.36 (dq, $J_{5,4}$ = 9.8, $J_{5,5\text{-}Me}$ = 6.0, 5-H), 7.34-7.42 (m, 3 Ar-H), 7.46-7.51 (m, 2 Ar-H); ^{13}C-NMR (75 MHz): δ = -4.22 and -4.15 ($SiMe_2$), 13.83 (C-4′), 22.21, 22.67, 28.00 and 29.97 (5-CH_3, C-1′

C-2′, C-3′), 35.53 (C-4), 43.33 (C-3), 77.36 (C-5), 128.20 and 133.72 (*ortho*-C, *meta*-C), 129.84 (*para*-C), 135.67 (*ipso*-C), 179.44 (C-2); IR (film): 3050, 2955, 2930, 2860, 1765, 1445, 1430, 1385, 1350, 1250, 1185, 1105, 1065, 1050, 940, 840, 830, 735, 700, 655 cm^{-1}; Anal calcd for $C_{17}H_{26}SiO_2$ (290.5), C 70.29, H 9.02; found C 70.11, H 9.31.

(3*S*,4*R*,5*S*)-4-(Dimethylphenylsilyl)-3-hexyl-4,5-dihydro-5-methyl-2(3*H*)-furanone (10). At 0°C $Me_2PhSiCl$ (0.380 ml, 390 mg, 2.28 mmol, 2.2 equiv.) was added dropwise to a suspension of Li (70.0 mg, 10.1 mmol, 9.7 equiv.) in THF (3.5 ml). After stirring for 24 h at 0°C the mixture was cooled to -10°C and added dropwise to a stirred suspension of CuCN (102 mg, 1.14 mmol, 1.1 equiv.) in THF (4 ml). The resulting solution was warmed to 0°C, stirred for 20 min, and recooled to -78°C. Butenolide *S*-**6** (102 mg, 1.04 mmol, 1.0 equiv.) was added after 20 min, hexyl iodide (1.0 ml, 1.4 g, 6.6 mmol, 6.3 equiv.) after 2 h more. Stirring was continued at -40°C for 12 h. The reaction was quenched by adding a satd. aqueous solution of $NaHCO_3$ (10 ml). Extraction with petroleum ether / *tert*-butylmethyl ether (1:1, 3 × 20 ml), drying of the combined organic extracts with $MgSO_4$, evaporation of the solvent and flash chromatography on silica gel (eluent: petroleum ether / *tert*-butylmethyl ether 6:1) yielded the title compound (220 mg, 66%) as a single diastereomer; $[\alpha]_D^{25}$ = -10.9 (*c* = 3.04 in $CHCl_3$); ^1H NMR: δ = 0.40 (s, $SiMe_2$), 086 (t, $J_{6',5'}$ = 7.0 Hz, 6′-H_3), 1.10-1.62 (m, 1′-H_2, 2′-H_2, 3′-H_2, 4′-H_2, 5′-H_2), superimposed by 1.25 (d, $J_{5\text{-}Me,5}$ = 6.0 Hz, 5-CH_3) and 1.37 (dd, $J_{4,3}$ = 12.1 Hz, $J_{4,5}$ = 10.2 Hz, 4-H), 2.50 (ddd, $J_{3,4}$ = 11.9 Hz, $J_{3,1'\text{-}H(1)}$ = 6.2 Hz, $J_{3,1'\text{-}H(2)}$ = 4.2 Hz, 3-H), 4.36 (dq, $J_{5,4}$ = 9.8 Hz, $J_{5,5\text{-}Me}$ = 6.0 Hz, 5-H), 7.34-7.43 (m, 3 Ar-H), 7.46-7.51 (m, 2 Ar-H); ^{13}C NMR (75 MHz): δ = -4.33 and -4.22 ($SiMe_2$), 13.96 (C-6′), 22.16 (5-CH_3), 22.49, 25.76, 29.19, 30.24, and 31.49 (C-1′, C-2′, C-3′, C-4′, C-5′), 35.50 (C-4), 43.32 (C-3), 77.36 (C-5), 128.25 and 133.78 (*ortho*-C, *meta*-C), 129.90 (*para*-C), 135.75 (*ipso*-C), 179.53 (C-2); IR (film): 3070, 2955, 2930, 2855, 1765, 1455, 1430, 1380, 1355, 1250, 1185, 1115, 1050, 940, 840, 735, 700 cm^{-1}; Anal calcd for $C_{19}H_{30}SiO_2$ (318.5), C 71.64, H 9.49; found C 71.88, H 9.63.

(3*S*,4*R*,5*S*)-4-(Dimethylphenylsilyl)-4,5-dihydro-5-methyl-3-(5-methylhexyl)-2(3*H*)-furanone (11) was prepared similarly as described for **10** from a suspension of CuCN (28.4 mg, 0.317 mmol, 1.1 equiv.), $Me_2PhSiLi$ [prepared from $Me_2PhSiCl$ (105 ml, 107 mg, 0.631 mmol, 2.2 equiv.) and Li (21.3 mg, 3.07 mmol, 11 equiv.) at 0°C for 1 d] in THF (5 ml), butenolide *S*-**6** (28.1 mg, 0.286 mmol), and iodide **15** (420 mg, 1.85 mmol, 6.5 equiv.) as a single diastereomer (48.3 mg, 51%); $[\alpha]_D^{25}$ = -10.9 (*c* = 1.62 in $CHCl_3$). ^1H NMR: δ = 0.40 (s, $SiMe_2$), 0.84 (d, $J_{6',5'} = J_{5'\text{-}Me,5'}$ = 6.8, 5′-CH_3 and 6′-H_3), 1.05-1.60 (m, 1′-H_2, 2′-H_2, 3′-H_2, 4′-H_2,

5′-H_2), superimposed by 1.26 (d, $J_{5\text{-Me},5}$ = 6.0, 5-CH_3) and 1.37 (dd, $J_{4,3}$ = 11.9, $J_{4,5}$ = 10.0, 4-H), 2.50 (ddd, $J_{3,4}$ = 11.7, $J_{3,1'\text{-H(1)}}$ = 6.4, $J_{3,1'\text{-H(2)}}$ = 4.2, 3-H), 4.36 (dq, $J_{5,4}$ = 9.8, $J_{5,5\text{-Me}}$ = 6.0, 5-H), 7.34-7.42 (m, 3 Ar-H), 7.46-7.51 (m, 2 Ar-H); ^{13}C-NMR (75 MHz): δ = -4.26 and -4.09 ($SiMe_2$), 22.21 (5-CH_3), 22.58 (double intensity; 5′-CH_3, C-6′), 26.09, 27.33, 30.28 and 38.66 (C-1′, C-2′, C-3′, C-4′), 27.86 (C-5′), 35.53 (C-4), 43.35 (C-3), 77.36 (C-5), 128.20 and 133.72 (*ortho*-C, *meta*-C), 129.85 (*para*-C), 135.69 (*ipso*-C), 179.45 (C-2); IR (film): 3070, 2955, 2930, 2865, 1765, 1465, 1425, 1385, 1250, 1185, 1110, 1050, 940, 835, 815, 735, 700 cm^{-1}; Anal calcd for $C_{20}H_{32}SiO_2$ (332.6), C 72.23, H 9.70; found C 72.11, H 9.56.

5-Methyl-1-hexanol (14). At 5°C a solution of isobutyl bromide (32 ml of a 3.1 M solution in THF, 100 mmol, 1.7 equiv.) was added dropwise (50 min) to Mg (2.19 g, 90.2 mmol, 1.5 equiv.) in THF (170 ml). After refluxing the solution for 40 min it was cooled to 0°C, treated with CuI (1.89 g, 9.94 mmol, 11 mol-%) and cooled to -40°C. A solution of ethylene oxide (30 ml of a 2.0 M solution in THF, 60 mmol) was added dropwise. Stirring was continued at -30°C for 10 h. The reaction was quenched by adding a satd. aqueous solution of NH_4Cl (30 ml). Extraction with petroleum ether / *tert*-butylmethyl ether (1:1, 5 × 50 ml), drying of the combined organic extracts with $MgSO_4$, evaporation of the solvent, and distillation at 62°C / 0.1 torr yielded the title compound (6.92 g, 99%); ^{1}H NMR: δ = 0.86 (d, $J_{5\text{-Me},5} = J_{6,5}$ = 6.4, 5-CH_3, 6-H_3), 1.14-1.23 (m, 4-H_2), 1.28-1.40 (m, 3-H_2), 1.43 (br. s, OH), 1.54 (m_c, 2-H_2, 5-H), 3.63 (t, $J_{1,2}$ = 7.0, 1-H_2). ^{13}C-NMR (50 MHz): δ = 22.51 (double intensity; 5-CH_3, C-6), 23.50 (C-3), 27.90 (C-5), 32.94 (C-2), 38.72 (C-4), 62.80 (C-1); IR (film): 3330, 2955, 2930, 2870, 1465, 1385, 1365, 1055 cm^{-1}; Anal calcd for $C_7H_{16}OH$ (116.2), C 72.35, H 13.88; found C 72.50, H 14.00.

1-Iodo-5-methylhexane (15). At 0°C alcohol **14** (6.75 g, 58.1 mmol) was added dropwise to a solution of PPh_3 (20.1 g, 76.7 mmol, 1.3 equiv.) and imidazole (5.67 g, 83.3 mmol, 1.4 equiv.) in Et_2O / CH_3CN (2:1, 180 ml). After stirring the solution for 10 min it was treated with iode (22.1 g, 174 mmol, 3.0 equiv.), stirred for another 30 min, and then washed with a satd. aqueous solution of $Na_2S_2O_3$ (2 × 50 ml). Drying of the combined organic extracts with $MgSO_4$, evaporation of the solvent and distillation at 83°C / 19-23 torr yielded the title compound (10.1 g, 77%); ^{1}H NMR: δ = 088 (d, $J_{5\text{-Me},5} = J_{6,5}$ = 6.4, 5-CH_3, 6-H_3), 1.14-1.23 (m, 4-H_2), 1.39 (m_c, 3-H_2), 1.55 (qq, $J_{5,5\text{-Me}} = J_{5,6}$ = 6.7, 5-H), 1.81 (tt, $J_{2,1} = J_{2,3}$ = 7.3, 2-H_2), 3.20 (t, $J_{1,2}$ = 7.7, 1-H_2); ^{13}C-NMR (50 MHz): δ = 7.34 (C-1), 22.55 (double intensity; 5-CH_3, C-6), 27.80 (C-5), 28.31 (C-3), 33.75 (C-2), 37.75 (C-4); IR (film): 2955, 2930, 2870, 1465, 1425, 1385, 1220, 1175 cm^{-1}; Anal calcd for $C_7H_{15}I$ (226.1), C 37.19, H 6.69; found C 37.31, H 6.55.

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