VERSATILE ENANTIOSELECTIVE SYNTHESIS OF FOUR DIASTEREOMERS OF SERRICORNIN, A SEX PHEROMONE OF THE CIGARETTE BEETLE, USING THE SAMP/RAMP-HYDRAZONE METHOD

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Received February 2, 2000
Accepted March 16, 2000

Dedicated to Professor Otakar Červinka on the occasion of his 75th birthday in recognition of his outstanding contributions to the area of organic stereochemistry.

Serricornin is a female-produced sex pheromone of the cigarette beetle (*Lasioderma serricorne*), which is a pest of dried foodstuffs and tobacco. We report a versatile and short synthesis of all possible 6,7-*syn*-isomers of serricornin, including the natural isomer. Starting from the SAMP and RAMP derivatives of diethyl ketone we obtained four different enantiopure and diastereomerically pure serricornins. The main advantage of this method is that only a single kind of chiral starting material is needed for the construction of three stereogenic centers. During the synthesis further useful intermediates including (*R*)- and (*S*)-1-benzyloxy-2-methylpentan-3-one (**4**) and (2*S*,3*R*)- and (2*R*,3*S*)-1-iodo-3-(methoxymethoxy)-2-methylpentane (**9**) were obtained.

Key words: Asymmetric synthesis; Hydrazones; Natural products; Pheromones; Reductions; Total synthesis.

The title compound (4*S*,6*S*,7*S*)-7-hydroxy-4,6-dimethylnonan-3-one (**1**, serricornin) is the female-produced sex pheromone of the cigarette beetle (*Lasioderma serricorne*). This species is a pest of dried foodstuffs and tobacco. It was first isolated and characterized by Chuman[1] in 1979. Its absolute configuration was assigned by comparing different synthetic diastereomers and enantiomers of its acetate derivative with the acetate obtained from the natural serricornin[2]. The absolute configuration of the natural isomer was assigned to be 4*S*,6*S*,7*S*.

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The natural isomer of serricornin (**1**) exists as an equilibrium mixture of the cyclic hemiacetal **1b** and an open-chain form **1a** (**1b** : **1a** = 3 : 1, Scheme 1), whereas the (4*R*,6*S*,7*S*) isomer exists only in the open-chain form. This dif-

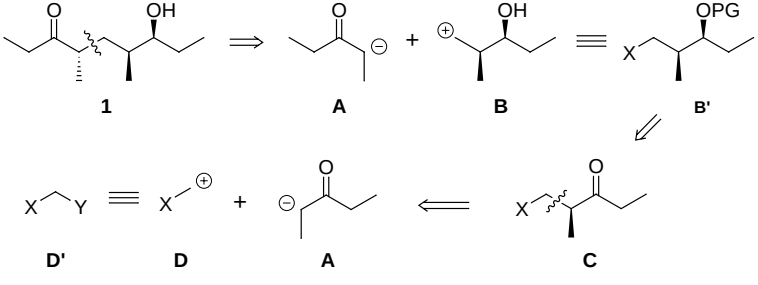
1a **1b**

SCHEME 1

ferent behaviour enables the separation of both isomers by simple column chromatography[3]. Since 1979 many synthetic and biological investigations have been made[4]. Even a large scale synthesis has been developed for the use of serricornin in commercial insect lures[4f,5]. Despite of all synthetic work carried out on serricornin, it is still a challenge for synthetic concepts and methods.

RESULTS AND DISCUSSION

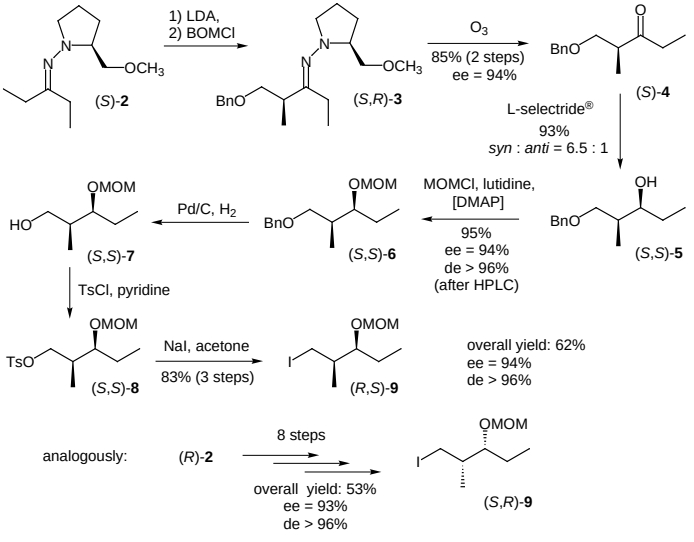
The retrosynthetic analysis depicted in Scheme 2 shows that it is possible to generate the three stereogenic centers of **1** based on a single chiral starting material. First a chiral equivalent of the diethyl ketone enolate **A** can be used to generate the stereogenic center of the substituted ketone **C** by an asymmetric α-alkylation. The carbonyl group of **C** can be reduced selectively to yield the *syn*-isomer of the intermediate **B′**. A second asymmetric α-alkylation of **A** with the halide **B′** generates the third stereogenic center in the target molecule. If both enantiomers of a chiral equivalent of **A** are available the combination of both synthetic pathways (Scheme 4) results in four diastereomers of serricornin (**1**).



SCHEME 2

The SAMP/RAMP-hydrazone methodology developed in this group[6] provides excellent conditions for this purpose. The natural diastereomer of serricornin can be obtained by using only (*S*)-1-amino-2-(methoxymethyl)-pyrrolidine (SAMP) as chiral auxiliary (*vide infra*).

The starting hydrazone (*S*)-2 can be obtained in quantitative yield from SAMP and diethyl ketone[7]. The reaction of the hydrazone (*S*)-**2** with lithium diisopropylamide and benzyloxymethyl chloride (BOMCl) provided the substituted hydrazone (*S*,*R*)-**3** in 94% de (Scheme 3). The configuration of the new stereogenic center was confirmed by NOE experiments and by the rotation value of the resulting ketone (*S*)-**4** (ref.[8]). This indicated that the reaction follows the mechanism for electrophilic substitution reactions of SAMP-hydrazones[9]. Ozonolytic cleavage of **3** provided the known ketone (*S*)-**4** in 94% ee and good yield. (*S*)-2-(Methoxymethyl)-1-nitrosopyrrolidine produced in the reaction with ozone can easily be separated from the product by column chromatography. The by-product can be recycled to SAMP by means of lithium aluminium hydride.



SCHEME 3

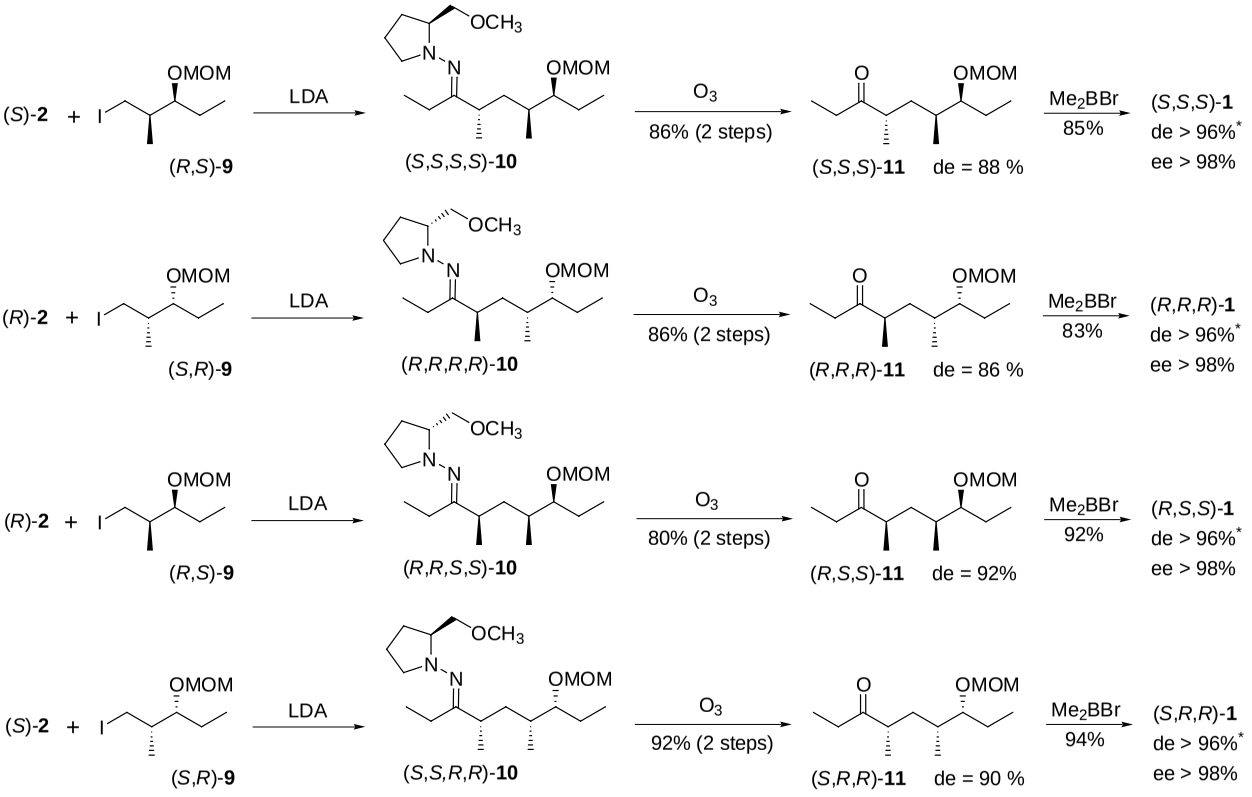
The second stereogenic center was generated by a *syn*-selective reduction of the carbonyl functionality of ketone **4**. Various known methods[10] were investigated using different solvent systems (Table I). The solvent given in the table corresponds to that in which the best selectivity was observed for the given reagent. Since the reaction with L-Selectride® in dichloromethane gave the best *syn/anti* ratio in our experiments and since the reagent is com-

mercially available, we have chosen this reagent for our synthesis. Although the *syn/anti* ratio was only 6.5 : 1, it was possible to separate the diastereomers of the methoxymethyl (MOM)-protected alcohol **6** by HPLC in the next step. Conversion of the diastereomeric mixture **5** to the MOM derivatives was achieved using methoxymethyl chloride and lutidine in the presence of a catalytic amount of 4-(dimethylamino)pyridine (DMAP) to obtain diastereomerically pure (*S*,*S*)-**6** in 94% ee after HPLC purification. The diastereomeric purity was determined by NMR analysis, while the enantiomeric excess was taken from the ketone **4** on the assumption that the reduction with L-Selectride® occurs without any racemization. The very low selectivities of the reduction (Table I, entries 3–9) can be explained by the absence of an unprotected hydroxy group for chelation and by a system with few steric demands.

A simple three-step sequence gave (*R*,*S*)-**9** from diether **6**. First the benzylic protective group was reduced with hydrogen and palladium on charcoal. The resulting alcohol **7** was then converted into the corresponding tosylate **8** by the reaction with tosyl chloride and pyridine. The crude product was subsequently refluxed with sodium iodide in acetone to provide the iodide (*R*,*S*)-**9** (ref.[11]) as intermediate for the synthesis of the (*S*,*S*,*S*) and (*R*,*S*,*S*) diastereomers of serricornin. The complete eight-step procedure was also accomplished starting from hydrazone (*R*)-**2** resulting in the enantiomeric iodide (*S*,*R*)-**9** (ee 93%) for the synthesis of the (*R*,*R*,*R*) and (*S*,*R*,*R*) diastereomers of serricornin.

TABLE I
Results of the diastereoselective reduction of ketone **4**

Entry	Reagent	Solvent	Temperature, °C	*syn/anti*-ratioi
1	L-Selectride®	CH_2Cl_2	–90	6.5:1
2	$LiBHBu_3$	CH_2Cl_2	–90	6.5:1
3	$Zn(BH_4)_2$	ether	–78	1.7:1
4	$NaBH_4$/AcOH	CH_2Cl_2	0	1.7:1
5	$LiAlH_4$	CH_2Cl_2	0	1.5>1
6	$NaBH_4/Bu_3B$	THF	–78	1.4:1
7	SmI_2/MeOH	THF	0	1.4:1
8	$NaBH_4$	EtOH	0	1.2:1
9	Catecholborane	THF	–20→0	1:1.3


(S)-2 + I
OMOM
(R,S)-9
LDA
OCH3
N
N
OMOM
(S,S,S,S)-10
O3
86% (2 steps)
O
OMOM
(S,S,S)-11 de = 88 %
Me2BBr
85%
(S,S,S)-1
de > 96%*
ee > 98%
(R)-2 + I
OMOM
(S,R)-9
LDA
OCH3
N
N
OMOM
(R,R,R,R)-10
O3
86% (2 steps)
O
OMOM
(R,R,R)-11 de = 86 %
Me2BBr
83%
(R,R,R)-1
de > 96%*
ee > 98%
(R)-2 + I
OMOM
(R,S)-9
LDA
OCH3
N
N
OMOM
(R,R,S,S)-10
O3
80% (2 steps)
O
OMOM
(R,S,S)-11 de = 92%
Me2BBr
92%
(R,S,S)-1
de > 96%*
ee > 98%
(S)-2 + I
OMOM
(S,R)-9
LDA
OCH3
N
N
OMOM
(S,S,R,R)-10
O3
92% (2 steps)
O
OMOM
(S,R,R)-11 de = 90 %
Me2BBr
94%
(S,R,R)-1
de > 96%*
ee > 98%
* after column chromatography

SCHEME 4

The hydrazones (*S*)-**2** and (*R*)-**2** were deprotonated with LDA and each subsequently treated with either of the iodides (*R*,*S*)-**9** and (*S*,*R*)-**9** (Scheme 4). The asymmetric α-alkylation was carried out for the four possible combinations, resulting in the four corresponding isomers of **10**. Ozonolytic cleavage yielded the corresponding MOM-protected serricornins **11** in good yields and with good diastereomeric excesses. The hydrazones **11** were also cleaved using oxalic acid[12] with the same selectivities but in only 60% yield over 2 steps.

The loss of diastereomeric purity in the case of the (*S*,*S*,*S*) and (*R*,*R*,*R*) isomers of 6 and 7%, respectively, compared to the loss of 2 and 3% for the (*R*,*S*,*S*) and (*S*,*R*,*R*) isomers may be a result of a matching and mismatching of the reaction partners[13]. These results indicated a preservation of the enantiomeric purity of the products. The cleavage of the MOM protective group was achieved by applying bromodimethylborane[14] to obtain the corresponding serricornins in good yields. No epimerisation was observed in this reaction. Since it is possible to separate the different diastereomers by column chromatography as mentioned before, the products could be obtained in diastereomerically pure form. The cleavage of the MOM group with bromodimethylborane proceeds under very mild conditions at low temperature. This proved to be a very suitable cleavage method, giving good yields without the formation of by-products. The strong acidic conditions usually employed can not be used on serricornin, as it is known that dehydration takes place in the presence of only trace amounts of acid[3,15].

In conclusion, we have developed a short and versatile approach for the asymmetric synthesis of all possible 6,7-*syn*-isomers of serricornin in excellent diastereomeric and enantiomeric excess.

EXPERIMENTAL

All reactions were carried out under argon atmosphere. The solvents were purified and dried before use. Petroleum ether (40–60 °C) and pentane were distilled from CaH_2, THF and diethyl ether (ether) were distilled from Na/Pb alloy and benzophenone under Ar and CH_2Cl_2 was distilled from CaH_2 under Ar. SAMP (ref.[6]), BOMCl (ref.[16]) and Me_2BBr (ref.[14]) were synthesized according to literature procedures. All other chemicals were purchased from Aldrich, Acros, Merck and Fluka. Ozone was generated by a Fischer Ozone apparatus (M502). Optical rotations were measured at 25 °C on a Perkin–Elmer P 241 polarimeter using solvents of UVASOL quality and are given in 10^{-1} deg cm^2 g^{-1}. Infrared spectra were recorded on a Perkin–Elmer FT 1750 spectrometer (wavenumbers in cm^{-1}). Mass spectra were recorded on a Varian MAT 212 (EI 70 eV and CI 100 eV, isobutane), high resolution mass spectra on a Finigan MAT 95 spectrometer. Microanalyses were performed on a Heraeus CHN-O-Rapid. NMR spectra were measured on Varian Gemini 300 (^{1}H: 300 MHz, ^{13}C: 75 MHz), Varian Inova 400 (^{1}H: 400 MHz, ^{13}C: 100 MHz), Varian Unity 500 (^{1}H: 500 MHz, ^{13}C: 125 MHz) at

22 °C in $CDCl_3$ or C_6D_6 using tetramethylsilane as internal standard. Chemical shifts are given in ppm (δ-scale), coupling constants *J* in Hz. Gas chromatography on chiral stationary phases was performed on a Siemens Sichromat (column: Lipodex E®, 25 m, Chrompack). Preparative HPLC was carried out on Gilson Abimed (column: Hibar®, 250 mm × 25 mm, LiChrosorb Si 60, 7 μm, Merck). Thin layer chromatography was performed on silica gel F_{254} plates (Merck), with detection by UV (254 nm) or a solution of ammonium molybdate (5 g) and ceric sulfate (30 mg) in 10% sulfuric acid (100 ml). Preparative chromatography was done on silica gel 60 (40–63 μm, Merck).

Preparation of LDA Solutions. General Procedure

A solution of 1.2 equivalents (based on amount of the hydrazone) diisopropylamine in ether (5 ml/mmol hydrazone) or THF (3 ml/mmol hydrazone) was cooled under an inert atmosphere to 0 °C. At this temperature a solution of BuLi (1.6 M in hexane) was added and stirred for another 5 min.

Ozonolytic Cleavage of Hydrazones. General Procedure

A crude hydrazone was dissolved in CH_2Cl_2 (25–70 ml) and the mixture was cooled to –78 °C under an inert atmosphere. Ozone was passed through the solution until it changed the color from yellowish to a blue or grey shade. After the reaction was completed, Ar was passed through the solution until the color disappeared. This procedure is necessary to expunge surplus ozone. The mixture was warmed to room temperature and concentrated *in vacuo*. The resulting yellow oil was purified by flash chromatography to afford the products as a colorless oil.

(*S*)-1-{[(*R*)-1-Benzyloxy-2-methylpentan-3-ylidene]amino}-2-(methoxymethyl)pyrrolidine [(*S*,*R*)-**3**]

To a solution of LDA (6.00 mmol, procedure described above) in ether (25 ml) was added hydrazone (*S*)-**2** (992 mg, 5.00 mmol) at 0 °C. The resulting solution was stirred for 4 h at this temperature, then cooled to –115 °C and benzyloxymethyl chloride (BOMCl; 936 mg, 6.00 mmol) was added. The solution was allowed to warm to room temperature overnight and quenched with 20 ml of a buffer (pH 7)/15 ml THF. After stirring for 10 min, the aqueous layer was extracted with ether. The combined organic phases were washed with brine and dried over Na_2SO_4. The solution was filtered through a silica gel pad (5 mm) and concentrated *in vacuo*. The crude product (2.000 g) was employed in the next step without further purification.

A small amount of the crude product was purified by chromatography on a short column (4 cm silica gel, petroleum ether–ether 10 : 1) for characterization. R_F 0.23 (petroleum ether–ether 2 : 1). $[\alpha]_D$ +113.7 (*c* 0.97, $CHCl_3$), de = 94% (^{13}C NMR). ^1H NMR (500 MHz, C_6D_6): 0.88 (d, 3 H, *J* = 7.1, CH_3); 1.23 (t, 3 H, *J* = 7.3, CH_3); 1.58–2.02 (m, 4 H, $NCH_2CH_2CH_2$); 2.13 (dq, 2 H, *J* = 13.5, 7.3, CH_3CH_2); 2.53 (m, 1 H, NCHH); 2.94 (m, 1 H, NCHH); 3.13 (s, 3 H, OCH_3); 3.18–3.57 (m, 5 H, $NCHCH_2O$, CH_2O); 3.98 (m, 1 H, CH_3CH); 4.32 (m, 2 H, $C_{Ph}CH_2O$); 7.05–7.33 (m, 5 H, $C_{Ph}H$). NOE (500 MHz, C_6D_6): $CH_3CH \rightarrow$ *pro-S*-NCHH: 3%; $CH_3CHCH_2 \rightarrow CH_3CH_2$: 6%; *pro-S*-NCHH $\rightarrow CH_3CH$: 8%; *pro-R*-NCHH $\rightarrow$ NCH: 6%. ^{13}C NMR (125 MHz, C_6D_6): 11.35 (CH_3); 14.60 (CH_3); 22.35 ($NCH_2CH_2CH_2$); 24.53 (CH_3CH_2); 27.59 ($NCHCH_2$); 34.96 (CH_3CH); 55.90 (NCH_2); 58.81 (OCH_3); 66.76

(NCH); 72.70 (OCH_2Ph); 72.79 (CH_2O); 76.26 ($NCHCH_2O$); 127.62, 128.04, 128.52 (C_{Ph}); 139.20 ($C_{Ph,\ ipso}$); 173.08 (N=C). MS (EI): 318 (7, M^+); 274 (18, $MH^+ - CH_2OCH_3$); 273 (96, $M^+ - CH_2OCH_3$); 91 (100, $PhCH_2^+$); 70 (11); 56 (9). IR (neat): 1 950, 1 872, 1 808 (Ph); 1 631 (C=N); 1 100, 1 049 (s, C–O); 737, 698 (Ph). For $C_{19}H_{30}N_2O_2$ (318.5) calculated: 71.66% C, 9.50% H, 8.80% N; found: 71.89% C, 9.40% H, 8.34% N.

(*R*)-1-{[(*S*)-1-Benzyloxy-2-methylpentan-3-ylidene]amino}-2-(methoxymethyl)pyrrolidine [(*R*,*S*)-**3**]

To a solution of LDA (2.40 mmol, procedure described above) in ether (10 ml) was added hydrazone (*R*)-**2** (397 mg, 2.00 mmol) at 0 °C. Treatment with BOMCl (375 mg, 2.40 mmol) as described for (*S*,*R*)-**3** and subsequent workup provided 715 mg crude product, which was employed in the next step without further purification. A small amount of the crude product was purified by chromatography on a short column (4 cm silica gel, petroleum ether–ether 10 : 1) for characterization. $[\alpha]_D$ –112.7 (*c* 0.22, $CHCl_3$), de = 93% (^{13}C NMR). All spectroscopic data are identical with those given for (*S*,*R*)-**3**.

(*S*)-1-Benzyloxy-2-methylpentan-3-one [(*S*)-**4**]

A solution of crude hydrazone (*S*,*R*)-**3** (2.000 g) in CH_2Cl_2 (70 ml) was cleaved with ozone (as in the general procedure). Purification by chromatography (elution with petroleum ether–ether 10 : 1) provided 878 mg (4.26 mmol; 85%) colorless product. R_F 0.53 (petroleum ether–ether 2 : 1). $[\alpha]_D$ +24.7 (*c* 1.25, $CHCl_3$), ee = 94% (GC, Lipodex E). All other data are identical with those reported in literature[8].

(*R*)-1-Benzyloxy-2-methylpentan-3-one [(*R*)-**4**]

A solution of crude hydrazone (*R*,*S*)-**3** (655 mg) in CH_2Cl_2 (25 ml) was cleaved with ozone (as in the general procedure). Purification by chromatography (elution with petroleum ether–ether 10 : 1) provided 318 mg (1.54 mmol; 84%) colorless product. $[\alpha]_D$ –24.5 (*c* 1.50, $CHCl_3$), ee = 93% (GC, Lipodex E). All other data were identical with those given for (*S*)-**4**.

(2*S*,3*S*)-1-Benzyloxy-2-methylpentan-3-ol [(*S*,*S*)-**5**]

To a cold (–90 °C) solution of ketone (*S*)-**4** (1.204 g, 5.84 mmol) in CH_2Cl_2 (25 ml) were slowly added L-Selectride® (8.00 ml, 1.0 M solution in THF). The mixture was stirred for another 2 h and allowed to warm to –78 °C. The reaction was quenched with methanol (15 ml) and stirred for another 1 h while warming to room temperature. The volatile compounds were removed *in vacuo* and the residue was diluted with THF (10 ml). After adding 10% NaOH (5 ml) and 30% H_2O_2 (5 ml) the mixture was stirred overnight at room temperature. The aqueous phase was extracted with ether and the combined organic phases were washed with a buffer (pH 7) and brine. After drying with Na_2SO_4 and concentrating *in vacuo*, the crude oil was purified by chromatography on silica gel (elution with petroleum ether–ether 5 : 1) to give 1.126 g (5.41 mmol; 93%) colorless product. R_F 0.26 (petroleum ether–ether 2 : 1). *Syn*/*anti* = 6.5 : 1 (determined by ^{13}C NMR). ^1H NMR (300 MHz, $CDCl_3$, *syn*-isomer): 0.92 (d, 3 H, *J* = 7.1, CH_3); 0.94 (t, 3 H, *J* = 7.4, CH_3); 1.43 (m, 2 H, CH_2CH_3); 1.87 (m, 1 H, $CHCH_3$); 2.62 (s, 1 H, OH); 3.51 (m, 2 H, OCH_2CH); 3.65 (m, 1 H, CHOH); 4.49 (m, 2 H, CH_2Ph); 7.24–7.37 (m, 5 H, $C_{Ph}H$). ^{13}C NMR (75 MHz, $CDCl_3$, *syn*-isomer): 10.61 (CH_3);

10.71 (CH_3); 26.88 (CH_2CH_3); 37.49 ($CHCH_3$); 73.38, 74.80 (CH_2OCH_2Ph); 75.42 (CHOH); 127.57, 127.66, 128.41 (C_{ph}); 138.12 ($C_{ph,\ ipso}$). MS (CI): 210 (15); 209 (100, MH^+). IR (neat): 3 449 (OH); 1 949, 1 872, 1 808 (Ph); 1 096, 1 029 (C–O); 736, 698 (Ph). For $C_{13}H_{20}O_2$ (208.3) calculated: 74.96% C, 9.68% H; found: 74.47% C, 9.47% H.

(2*R*,3*R*)-1-Benzyloxy-2-methylpentan-3-ol [(*R*,*R*)-**5**]

A solution of ketone (*R*)-**4** (541 mg, 2.62 mmol) in CH_2Cl_2 (12 ml) was converted to **5** using L-Selectride® (4.00 ml) in the same manner as described for (*S*,*S*)-**5**. Purification by chromatography provided 499 mg (2.40 mmol; 91%) product. *Syn*/*anti* = 6.3 : 1 (determined by ^{13}C NMR). All other spectroscopic data were identical with those given for (*S*,*S*)-**5**.

(2*S*,3*S*)-1-Benzyloxy-3-(methoxymethoxy)-2-methylpentane [(*S*,*S*)-**6**]

Alcohol (*S*,*S*)-**5** (1.126 g, 5.41 mmol; *syn*/*anti* mixture) was dissolved in 2,6-lutidine (2.80 ml) and stirred at room temperature for 2.5 h. This solution was added to a solution of methoxymethyl chloride (MOMCl; 3.00 ml, 39.50 mmol) in CH_2Cl_2 (6 ml) containing catalytic amounts of 4-(dimethylamino)pyridine (DMAP). After stirring at room temperature for 6 h, the reaction was quenched with a buffer (15 ml, pH 7) and the organic material was extracted with CH_2Cl_2. The organic layer was washed with 1 M HCl solution until the aqueous layer became acidic, then once with a buffer (pH 7) and brine. After drying over Na_2SO_4 and evaporation under reduced pressure, the crude product was purified by column chromatography (elution with petroleum ether–ether 10 : 1). The product was obtained as colorless oil (1.300 g, 5.15 mmol; 95%). Only the desired *syn* product was characterized after HPLC purification. R_F 0.62 (petroleum ether–ether 2 : 1). $[\alpha]_D$ –8.0 (*c* 0.95, $CHCl_3$), de > 96% (determined by ^{13}C NMR), ee 94% (based on the ketone (*S*)-**4**). ^1H NMR (500 MHz, $CDCl_3$): 0.90 (t, 3 H, *J* = 7.5, CH_3); 0.93 (d, 3 H, *J* = 7.0, CH_3); 1.54 (m, 2 H, C**H**$_2$CH$_3$); 2.00 (m, 1 H, C**H**CH$_3$); 3.32 (dd, 1 H, *J* = 9.1, 6.5, OC**H**HCH); 3.34 (s, 3 H, OCH_3); 3.48 (dd, 1 H, *J* = 9.1, 6.8, OCH**H**CH); 3.56 (td, 1 H, *J* = 6.6, 3.4, C**H**OH); 4.48 (m, 2 H, CH_2Ph); 4.62 (s, 2 H, OCH_2O); 7.22–7.34 (m, 5 H, $C_{Ph}H$). ^{13}C NMR (125 MHz, $CDCl_3$): 10.26 (CH_3); 11.44 (CH_3); 24.68 (CH_2CH_3); 36.22 ($CHCH_3$); 55.51 (OCH_3); 72.83, 73.05 (CH_2OCH_2); 80.13 (CHOH); 96.49 (OCH_2O); 127.44, 127.59, 128.29 (C_{ph}); 138.62 ($C_{ph,\ ipso}$). MS (EI): decomposition. IR (neat): 1 950, 1870, 1 808 (Ph); 1 098, 1 039 (C–O); 737, 699 (Ph). For $C_{15}H_{24}O_3$ (252.4) calculated: 71.39% C, 9.59% H; found: 71.02% C, 9.61% H.

(2*R*,3*R*)-1-Benzyloxy-3-(methoxymethoxy)-2-methylpentane [(*R*,*R*)-**6**]

Alcohol (*R*,*R*)-**5** (258 mg, 1.24 mmol; *syn*/*anti* mixture) was converted to **6** with 2,6-lutidine (0.70 ml), MOMCl (1.00 ml, 13.17 mmol), catalytic amounts of DMAP and CH_2Cl_2 (0.5 ml) in the same manner as described for (*S*,*S*)-**6**. Purification by chromatography provided 287 mg (1.14 mmol; 92%) product. Only the desired *syn* product was characterized after HPLC purification. $[\alpha]_D$ +8.0 (*c* 1.03, $CHCl_3$), de > 96% (determined by ^{13}C NMR), ee = 93% (based on the ketone (*R*)-**4**). All other data were identical with (*S*,*S*)-**6**.

(2*S*,3*S*)-3-(Methoxymethoxy)-2-methylpentan-1-ol [(*S*,*S*)-**7**]

To a solution of (*S*,*S*)-**6** (1.103 g, 4.37 mmol) in ether (80 ml) was added Pd/C (30 mg; 10%) and the flask was equipped with a balloon containing H_2. The mixture was stirred overnight

at room temperature and was then filtered through a celite® pad. Evaporation of the solvent provided 709 mg (4.37 mmol, quant.) colorless oil, which was employed in the next step without further purification. R_F 0.16 (petroleum ether–ether 2 : 1). $[\alpha]_D$ +66.2 (*c* 1.63, $CHCl_3$), de > 96% (^{13}C NMR), ee = 94% (based on the ketone (*S*)-**4**). ^{1}H NMR (500 MHz, $CDCl_3$): 0.84 (d, 3 H, *J* = 7.0, CH_3); 0.93 (t, 3 H, *J* = 7.3, CH_3); 1.51–1.62 (m, 2 H, C**H**$_2$CH$_3$); 1.93 (m, 1 H, C**H**CH_3); 2.68 (s, 1 H, OH); 3.42 (s, 3 H, OCH_3); 3.52 (dd, 1 H, *J* = 11.0, 5.5, C**H**HOH); 3.61 (m, 1 H, C**H**OH); 3.62 (dd, 1 H, *J* = 11.0, 8.5, CH**H**OH); 4.68 (m, 2 H, OCH_2O). ^{13}C NMR (125 MHz, $CDCl_3$): 10.51 (CH_3); 10.70 (CH_3); 24.28 (CH_2CH_3); 37.71 ($CHCH_3$); 55.86 (OCH_3); 65.30 (CH_2OH); 81.16 (CHOH); 96.76 (OCH_2O). MS (CI): 164 (9); 163 (100, MH^+); 145 (8, $MH^+ - H_2O$). IR (neat): 3 425 (OH); 1 098, 1 039 (C–O). For $C_8H_{18}O_3$ (162.2) calculated: 59.23% C, 11.18% H; found: 58.80% C, 11.26% H.

(2*R*,3*R*)-3-(Methoxymethoxy)-2-methylpentan-1-ol [(*R*,*R*)-**7**]

A solution of (*R*,*R*)-**6** (187 mg, 0.74 mmol) in ether (30 ml) was treated analogously to (*S*,*S*)-**7**. Concentration *in vacuo* provided 114 mg (0.73 mmol; 95%) of the crude product. $[\alpha]_D$ –66.1 (*c* 1.12, $CHCl_3$), de > 96% (^{13}C NMR), ee = 93% (based on the ketone (*R*)-**4**). The other spectroscopic data are identical with those given for (*S*,*S*)-**7**.

(2*S*,3*S*)-3-(Methoxymethoxy)-2-methylpentyl Tosylate [(*S*,*S*)-**8**]

To a cold (0 °C) solution of alcohol (*S*,*S*)-**7** (675 mg, 4.16 mmol) in pyridine (10 ml) was added tosyl chloride (1.810 g, 9.50 mmol). The solution was stirred overnight at 0 °C, followed by the addition of a buffer (15 ml, pH 7). The aqueous layer was extracted with CH_2Cl_2 and the organic phase was washed with 1 M HCl solution until the washings became acidic. The organic phase was washed with a buffer (pH 7) and brine. Drying over Na_2SO_4, filtration over a silica gel pad (5 mm) and evaporation of the solvent provides 1.279 g of the crude product as a colorless oil. R_F 0.42 (petroleum ether–ether 2 : 1). This product was employed in the next step without characterization.

(2*R*,3*R*)-3-(Methoxymethoxy)-2-methylpentyl Tosylate [(*R*,*R*)-**8**]

The alcohol (*R*,*R*)-**7** (114 mg, 0.73 mmol) was converted with pyridine (4 ml) and tosyl chloride (268 mg, 1.41 mmol) in the same manner as described for (*S*,*S*)-**8**. The crude product (221 mg) was obtained as colorless oil. R_F 0.42 (petroleum ether–ether 2 : 1). This product was employed in the next step without any characterization.

(2*R*,3*S*)-1-Iodo-3-(methoxymethoxy)-2-methylpentane [(*R*,*S*)-**9**]

To a solution of crude tosylate (*S*,*S*)-**8** (1.279 g) in acetone (50 ml) was added NaI (3.030 g, 20.21 mmol) and a catalytic amount of $EtNiPr_2$. The mixture was refluxed for 6 h and evaporated after cooling to room temperature. The residue was taken up in water (15 ml)–ether (15 ml) and the aqueous layer was extracted twice with ether. The organic phase was washed with 5% $Na_2S_2O_3$ solution, brine and dried over Na_2SO_4. Concentration *in vacuo* and column chromatography (elution with petroleum ether–ether 10 : 1) provided 944 mg (3.47 mmol; 83%, 2 steps) colorless product. R_F 0.72 (petroleum ether–ether 2 : 1). $[\alpha]_D$ +15.5 (*c* 1.54, $CHCl_3$), de > 96% (^{13}C NMR), ee = 94% (based on the ketone (*S*)-**4**). ^{1}H NMR (500 MHz, $CDCl_3$): 0.91 (t, 3 H, *J* = 7.5, CH_3); 1.03 (d, 3 H, *J* = 6.7, CH_3); 1.50–1.59 (m, 2 H, C**H**$_2$CH$_3$);

1.94 (m, 1 H, C**H**CH_3); 3.09 (dd, 1 H, *J* = 9.8, 7.3, C**H**HI); 3.36 (dd, 1 H, *J* = 9.8, 5.8, CH**H**I); 3.39 (s, 3 H, OCH_3); 3.50 (m, 1 H, C**H**OH); 4.67 (m, 2 H, OCH_2O). ^{13}C NMR (125 MHz, $CDCl_3$): 9.94 (CH_3); 12.18 (CH_2I); 15.17 (CH_3); 24.09 (CH_2CH_3); 39.06 ($CHCH_3$); 55.70 (OCH_3); 81.78 (CHOH); 96.47 (OCH_2O). MS (CI): 273 (25, MH^+); 242 (7, $MH^+ - CH_3O$); 241 (100, $M^+ - CH_3O$). IR (neat): 1 101, 1 039 (C–O). For $C_8H_{17}IO_2$ (272.1) calculated: 35.31% C, 6.30% H; found: 35.24% C, 6.07% H.

(2*S*,3*R*)-1-Iodo-3-(methoxymethoxy)-2-methylpentane [(*S*,*R*)-**9**]

The tosylate (*R*,*R*)-**8** (221 mg) was treated with NaI (524 mg, 3.50 mmol) in the same manner as described for (*R*,*S*)-**9**. Purification by chromatography provided 150 mg (0.55 mmol; 79%, 2 steps) product. $[\alpha]_D$ –15.5 (*c* 1.17, $CHCl_3$), de > 96% (^{13}C NMR), ee = 93% (based on the ketone (*R*)-**4**). All spectroscopic data were identical with those given for (*R*,*S*)-**9**.

(*S*)-1-{[(4*S*,6*S*,7*S*)-7-(Methoxymethoxy)-4,6-dimethylnonan-3-ylidene]amino}-2-(methoxymethyl)pyrrolidine [(*S*,*S*,*S*,*S*)-**10**]

To a solution of LDA (1.20 mmol, prepared as mentioned above) in ether (8 ml) hydrazone (*S*)-**2** (198 mg, 1.00 mmol) was added at 0 °C. After stirring at this temperature for 4 h the solution was cooled to –115 °C. The iodide (*R*,*S*)-**9** (100 mg, 0.37 mmol; ee = 94%) was added at this temperature. The mixture was allowed to warm to room temperature overnight and was quenched with a buffer (20 ml, pH 7) and THF (20 ml). After stirring for 10 min the crude product was extracted with ether and the combined organic phases were washed with brine and dried over Na_2SO_4. The organic phase was filtered over a silica gel pad (5 mm) and evaporation of the solvent afforded 203 mg of the crude product (containing excess **2**). This was employed in the next step without further purification. R_F 0.22 (petroleum ether–ether 2 : 1). ^{1}H NMR (300 MHz, C_6D_6): 0.93 (t, 3 H, *J* = 7.4, CH_3); 0.94 (d, 3 H, *J* = 6.9, CH_3); 0.95 (d, 3 H, *J* = 6.9, CH_3); 1.23 (t, 3 H, *J* = 7.3, CH_3); 1.30–1.76 (m, 9 H, CH_3CH_2, $CHCH_2CH$, NCH_2CH_2CHH); 2.09 (m, 3 H, NCH_2CH_2CHH, CH_3CH_2); 2.43 (m, 1 H, NC**H**H); 3.02 (m, 1 H, NCH**H**); 3.21 (s, 3 H, OCH_3); 3.24 (s, 3 H, OCH_3); 3.28–3.65 (m, 4 H, C**H**OH, $NCHCH_2O$); 4.63 (m, 2 H, OCH_2O). ^{13}C NMR (75 MHz, C_6D_6): 9.36 (CH_3); 10.29 (CH_3); 13.51(CH_3); 16.78 (CH_3); 21.13 (CH_3CH_2); 22.53 (NCH_2CH_2); 23.38 (CH_3CH_2); 26.38 ($NCHCH_2$); 31.34, 32.56 (2 CH_3CH); 36.70 ($CHCH_2CH$); 54.02 (OCH_3); 54.40 (NCH_2); 57.47 (OCH_3); 65.55 (NCH); 75.52 ($NCHCH_2O$); 81.11 (CHOH); 95.32 (OCH_2O); 171.68 (C=N).

(*R*)-1-{[(4*R*,6*R*,7*R*)-7-(Methoxymethoxy)-4,6-dimethylnonan-3-ylidene]amino}-2-(methoxymethyl)pyrrolidine [(*R*,*R*,*R*,*R*)-**10**]

According to the procedure for synthesis of (*S*,*S*,*S*,*S*)-**10** hydrazone (*R*)-**2** (198 mg, 1.00 mmol) was treated with LDA (1.20 mmol) in ether (8 ml) and iodide (*S*,*R*)-**9** (100 mg, 0.37 mmol; ee = 93%). After workup, 210 mg of crude product (containing excess **2**) was obtained, which was employed in the next step without further purification. R_F 0.22 (petroleum ether–ether 2 : 1). The NMR data correspond with isomer (*S*,*S*,*S*,*S*)-**10**.

(*R*)-1-{[(4*R*,6*S*,7*S*)-7-(Methoxymethoxy)-4,6-dimethylnonan-3-ylidene]amino}-2-(methoxymethyl)pyrrolidine [(*R*,*R*,*S*,*S*)-**10**]

According to the procedure for synthesis of (*S*,*S*,*S*,*S*)-**10** hydrazone (*R*)-**2** (198 mg, 1.00 mmol) was treated with LDA (1.20 mmol) in ether (8 ml) and iodide (*R*,*S*)-**9** (149 mg, 0.55 mmol; ee = 94%). After workup, 302 mg of crude product (containing excess **2**) was obtained, which was employed in the next step without further purification. R_F 0.22 (petroleum ether–ether 2 : 1). ^{1}H NMR (300 MHz, C_6D_6): 0.93 (t, 3 H, *J* = 7.4, CH_3); 0.94 (d, 3 H, *J* = 7.1, CH_3); 1.03 (d, 3 H, *J* = 6.6, CH_3); 1.23 (t, 3 H, *J* = 7.4, CH_3); 1.40–1.74 (m, 9 H, CH_3CH_2, $CHCH_2CH$, NCH_2CH_2CHH); 1.98–2.49 (m, 4 H, NCH_2CH_2CHH, CH_3CH_2, NCHH); 2.99 (m, 1 H, NCHH); 3.20 (s, 3 H, OCH_3); 3.25 (s, 3 H, OCH_3); 3.26–3.63 (m, 4 H, CHOH, $NCHCH_2O$); 4.60 (m, 2 H, OCH_2O). ^{13}C NMR (75 MHz, C_6D_6): 10.86 (CH_3); 11.60 (CH_3); 15.56 (CH_3); 18.95 (CH_3); 22.46 (CH_3CH_2); 23.13 (NCH_2CH_2); 23.68 (CH_3CH_2); 27.74 ($NCHCH_2$); 32.52, 33.79 (2 CH_3CH); 37.89 ($CHCH_2CH$); 55.36 (OCH_3); 55.66 (NCH_2); 58.76 (OCH_3); 66.86 (NCH); 76.84 ($NCHCH_2O$); 83.45 (CHOH); 95.93 (OCH_2O); 172.49 (C=N).

(*S*)-1-{[(4*S*,6*R*,7*R*)-7-(Methoxymethoxy)-4,6-dimethylnonan-3-ylidene]amino}-2-(methoxymethyl)pyrrolidine [(*S*,*S*,*R*,*R*)-**10**]

According to the procedure for synthesis of (*S*,*S*,*S*,*S*)-**10** hydrazone (*S*)-2 (297 mg, 1.50 mmol) was treated with LDA (1.80 mmol) in THF (8 ml) and iodide (*S*,*R*)-**9** (200 mg, 0.73 mmol; ee = 94%). After workup, 383 mg of crude product (containing excess **2**) was obtained, which was employed in the next step without further purification. R_F 0.22 (petroleum ether–ether 2 : 1). The NMR data are identical with those given for (*R*,*R*,*S*,*S*)-**10**.

(4*S*,6*S*,7*S*)-7-(Methoxymethoxy)-4,6-dimethylnonan-3-one [(*S*,*S*,*S*)-**11**]

The crude hydrazone (*S*,*S*,*S*,*S*)-**10** (203 mg) was dissolved in CH_2Cl_2 (30 ml) and treated with ozone as described above. Purification by flash chromatography (elution with pentane–ether 10 : 1) afforded 73 mg (0.32 mmol; 86%, 2 steps) product as colorless oil. R_F 0.48 (petroleum ether–ether 2 : 1). $[\alpha]_D$ +2.2 (*c* 1.10, C_6H_6), de = 88% (^{13}C NMR), ee > 98%. ^{1}H NMR (500 MHz, C_6D_6): 0.80 (d, 3 H, *J* = 7.3, CH_3); 0.84 (t, 3 H, *J* = 7.5, CH_3); 0.93 (d, 3 H, *J* = 6.7, CH_3); 0.99 (t, 3 H, *J* = 7.3, CH_3); 1.35 (qdd, 1 H, *J* = 7.5, 13.5, 5.5, CH_3CHH); 1.45 (m, 2 H, CH_3CH, CHCHHCH); 1.56 (ddd, 1 H, *J* = 13.8, 8.5, 6.4, CHCHHCH); 1.67 (m, 1 H, CH_3CH); 2.09 (q, 2 H, *J* = 7.3, CH_3CH_2); 2.42 (m, 1 H, CH_3CH); 3.20 (s, 3 H, OCH_3); 3.25 (m, 1 H, CHOH); 4.49 (d, 1 H, *J* = 13.4, OCHHO); 4.53 (d, 1 H, *J* = 13.4, OCHHO). ^{13}C NMR (125 MHz): 8.06 (CH_3); 10.58 (CH_3); 14.91 (CH_3); 16.56 (CH_3); 23.92 (CH_3CH_2); 33.41 (CH_3CH); 33.93, 36.04 (CH_3CH_2, $CHCH_2CH$); 43.77 (CH_3CH); 55.41 (OCH_3); 82.95 (CHOH); 96.22 (OCH_2O); 212.87 (C=O). MS (EI): 169 (13, $MH^+ - C_2H_6O_2$); 168 (8, $M^+ - C_2H_6O_2$); 139 (16); 130 (69); 111 (10); 89 (25); 86 (10); 83 (16); 69 (10); 57 (47); 55 (12); 45 (100). IR (neat): 1 714 (C=O); 1 103, 1 039 (C–O). For $C_{13}H_{26}O_3$ (230.3) calculated: 67.79% C, 11.38% H; found: 67.38% C, 11.73% H.

(4*R*,6*R*,7*R*)-7-(Methoxymethoxy)-4,6-dimethylnonan-3-one [(*R*,*R*,*R*)-**11**]

The crude hydrazone (*R*,*R*,*R*,*R*)-**10** (210 mg) was dissolved in CH_2Cl_2 (30 ml) and treated with ozone as described above. Purification by flash chromatography (elution with pentane–ether 10 : 1) afforded 73 mg (0.32 mmol; 86%, 2 steps) product as colorless oil. $[\alpha]_D$

–0.9 (*c* 1.06, C_6H_6), de = 86% (^{13}C NMR), ee > 98%. All other data were identical with those reported for the (*S*,*S*,*S*)-**11**.

(4*R*,6*S*,7*S*)-7-(Methoxymethoxy)-4,6-dimethylnonan-3-one [(*R*,*S*,*S*)-**11**]

The crude hydrazone (*R*,*R*,*S*,*S*)-**10** (302 mg) was dissolved in CH_2Cl_2 (25 ml) and treated with ozone as described above. Purification by flash chromatography (elution with pentane–ether 10 : 1) afforded 100 mg (0.43 mmol; 80%, 2 steps) product as colorless oil. R_F 0.48 (petroleum ether–ether 2 : 1). $[\alpha]_D$ –28.4 (*c* 1.14, C_6H_6), de = 86% (^{13}C NMR), ee > 98%. ^{1}H NMR (400 MHz, C_6D_6): 0.83 (d, 3 H, *J* = 6.9, CH_3); 0.86 (t, 3 H, *J* = 7.4, CH_3); 0.91 (d, 3 H, *J* = 6.9, CH_3); 0.98 (t, 3 H, *J* = 7.3, CH_3); 1.02–1.38 (m, 2 H, CH_3CH_2); 1.48 (m, 1 H, CHC**H**HCH); 1.61 (m, 1 H, CH_3CH); 1.96 (m, 1 H, CHCH**H**CH); 2.11 (m, 2 H, CH_3CH_2); 2.47 (m, 1 H, CH_3CH); 3.22 (s, 3 H, OCH_3); 3.25 (m, 1 H, C**H**OH); 4.55 (s, 2 H, OCH_2O). ^{13}C NMR (100 MHz): 7.95 (CH_3); 10.48 (CH_3); 14.98 (CH_3); 17.63 (CH_3); 23.95 (CH_3CH_2); 33.33 (CH_3CH); 34.11, 36.51 (CH_3CH_2, $CHCH_2CH$); 43.68 (CH_3CH); 55.33 (OCH_3); 82.49 (CHOH); 96.05 (OCH_2O); 212.70 (C=O). All other data were identical with those reported for the (*S*,*S*,*S*)-**11**.

(4*S*,6*R*,7*R*)-7-(Methoxymethoxy)-4,6-dimethylnonan-3-one [(*S*,*R*,*R*)-**11**]

The crude hydrazone (*S*,*S*,*R*,*R*)-**10** (383 mg) was dissolved in CH_2Cl_2 (30 ml) and treated with ozone as described above. Purification by flash chromatography (elution with pentane–ether 10 : 1) afforded 155 mg (0.67 mmol; 92%, 2 steps) product as colorless oil. $[\alpha]_D$ +29.3 (*c* 1.21, C_6H_6), de = 90% (^{13}C NMR), ee > 98%. All other data were identical with those reported for the (*R*,*S*,*S*)-**11**.

(4*S*,6*S*,7*S*)-7-Hydroxy-4,6-dimethylnonan-3-one [(*S*,*S*,*S*)-**1**, Serricornin]

MOM-Protected serricornin (*S*,*S*,*S*)-**11** (73 mg, 0.32 mmol; de = 88%) was dissolved in CH_2Cl_2 (8 ml) and cooled to –78 °C. At this temperature Me_2BBr solution (1.50 ml, 0.75 mmol, 0.5 M in CH_2Cl_2) was added and the mixture was stirred for 1 h maintaining the temperature. The solution was transfered *via* a double-ended needle to a vigorously stirred mixture of saturated $NaHCO_3$ solution (5 ml) and THF (15 ml). After 10 min, ether (20 ml) was added and the organic phase was isolated. The aqueous layer was extracted once with ether and the combined organic layers were washed with a buffer (pH 7) and brine. Drying over Na_2SO_4 and evaporation of the solvent afforded the crude product. Purification by column chromatography (elution with pentane–ether 10 : 1–2 : 1) yielded two fractions. First 47 mg of desired product (*S*,*S*,*S*)-**1** (R_F 0.44–0.64, petroleum ether–ether 2 : 1) and second 3 mg of (*R*,*S*,*S*)-**1** (R_F 0.14, petroleum ether–ether 2 : 1). Total yield was 50 mg (0.27 mmol; 85%, de = 88%). ^{1}H NMR (400 MHz, C_6D_6): 0.73–2.40 (m, 21 H); 3.15 (m, 0.25 H, C**H**OH, open chain **1a**); 3.81 (m, 0.75 H, OCH, hemiacetal **1b**). ^{13}C NMR (100 MHz, C_6D_6, open chain **1a**): 8.05; 10.79; 13.61; 16.41; 27.44; 33.80; 35.69; 36.72; 43.64; 76.08; 213.21. ^{13}C NMR (100 MHz, C_6D_6, hemiacetal **1b**): 7.31; 10.70; 11.68; 16.74; 26.14; 30.19; 31.20; 32.99; 36.07; 72.50; 98.33. HR MS ($C_{11}H_{22}O_2$, 186.295): exact mass calculated for M – H_2O: 168.15141; found: 168.15152. All other spectroscopic data were identical with those given in the literature[3].

(4*R*,6*R*,7*R*)-7-Hydroxy-4,6-dimethylnonan-3-one [(*R*,*R*,*R*)-**1**]

MOM-Protected (*R*,*R*,*R*)-**11** (66 mg, 0.29 mmol; de = 86%) was reacted with Me_2BBr solution (0.70 ml, 0.49 mmol; 0.7 M in CH_2Cl_2) in CH_2Cl_2 (8 ml) as described for (*S*,*S*,*S*)-**1**. Chromatography yielded 41 mg of desired product and 3 mg of (*S*,*R*,*R*)-**1**. Total yield was 44 mg (0.24 mmol; 83%, de = 86%). All other data were identical with those given for (*S*,*S*,*S*)-**1**.

(4*R*,6*S*,7*S*)-7-Hydroxy-4,6-dimethylnonan-3-one [(*R*,*S*,*S*)-**1**]

MOM-Protected (*R*,*S*,*S*)-**11** (94 mg, 0.41 mmol; de = 92%) was reacted with Me_2BBr solution (1.50 ml, 0.75 mmol; 0.5 M in CH_2Cl_2) in CH_2Cl_2 (8 ml) as described for (*S*,*S*,*S*)-**1**. Chromatography yielded 59 mg of desired product (R_F 0.14, petroleum ether–ether 2 : 1) and 3 mg (*S*,*S*,*S*)-**1** (R_F 0.44–0.64, petroleum ether–ether 2 : 1). Total yield was 62 mg (0.33 mmol; 82%, de = 92%). $[\alpha]_D$ –14.0 (*c* 1.01, C_6H_6), de > 96% (^{13}C NMR), ee > 98%. ^{1}H NMR (400 MHz, C_6D_6): 0.83 (d, 3 H, *J* = 6.9, CH_3); 0.88 (d, 3 H, *J* = 6.9, CH_3); 0.92 (t, 3 H, *J* = 7.4, CH_3); 0.96 (t, 3 H, *J* = 7.1, CH_3); 1.01 (m, 1 H, CH_3CHHH); 1.24–1.46 (m, 3 H, CH_3CHH, $CHCHHCH$, CH_3CH); 1.89–2.20 (m, 4 H, CH_3CH_2, $CHCHHCH$, OH); 2.39 (m, 1 H, CH_3CH); 3.22 (m, 1 H, CHOH). ^{13}C NMR (100 MHz, C_6D_6): 8.00 (CH_3); 10.97 (CH_3); 13.98 (CH_3); 17.79 (CH_3); 27.39 (CH_2); 34.09 (CH_2); 36.27 (CH); 37.10 (CH_2); 44.00 (CH); 75.31 (CHOH); 213.92 (C=O). HR MS ($C_{11}H_{22}O_2$, 186.295): exact mass calculated for M – H_2O: 168.15141; found: 168.15194. All other data were in good correspondence with the data in the literature[3].

(4*S*,6*R*,7*R*)-7-Hydroxy-4,6-dimethylnonan-3-one [(*S*,*R*,*R*)-**1**]

MOM-Protected (*S*,*R*,*R*)-**11** (122 mg, 0.53 mmol; de = 90%) was reacted with Me_2BBr solution (1.20 ml, 0.84 mmol; 0.7 M in CH_2Cl_2) in CH_2Cl_2 (8 ml) as described for (*S*,*S*,*S*)-**1**. Chromatography yielded 88 mg of desired product and 5 mg of (*R*,*R*,*R*)-**1**. Total yield was 93 mg (0.50 mmol; 94%, de = 90%). $[\alpha]_D$ +13.7 (*c* 1.00, C_6H_6), de > 96% (^{13}C NMR), ee > 98%. All other data were identical with those given for (*R*,*S*,*S*)-**1**.

We thank J. Köbberling for helpful discussions concerning the cleavage of MOM-ethers, A. Müller for measuring the NMR spectra on Inova 400 and Unity 500, Dr J. Runsink for measuring the NOE effects and helpful discussions concerning the interpretation, K. Glensk and S. Küpper for performing IR and mass spectra (especially S. Küpper for the high resolution mass spectra), C. Dittrich for measuring elementary anlayses, D. Gilliam for performing GC spectra and S. Drehsen and S. Rother for separating diastereomers by preparative HPLC. We thank BASF AG, Degussa–Hüls AG and Bayer AG for donation of chemicals and DFG (SFB 380) for financial support.

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