'7, pp. 5657-5666, 1992

0040-4020/92 $5.00+.00
Pergamon Press Ltd

SPARTEINE COMPLEXES OF LITHIATED PRIMARY *O*-2-ALKENYL CARBAMATES STEREOCHEMISTRY OF THE LITHIUM-TITANIUM EXCHANGE AND APPLICATION FOR THE SYNTHESIS OF ENANTIOMERICALLY ENRICHED γ-LACTONES

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(*Received in Germany* 4 *March* 1992)

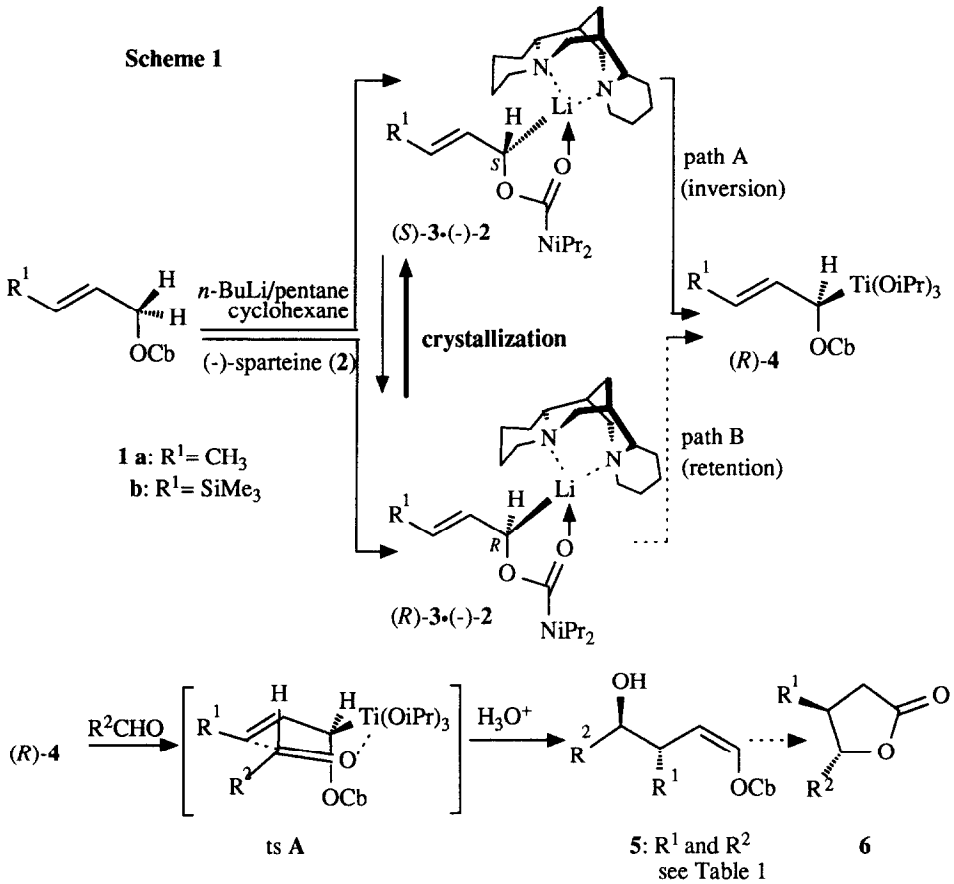
Summary. The preferentially formed (-)-sparteine complex from 1-lithio-2-butenyl *N,N*-diisopropylcarbamate has (*S*)-configuration at the metal bearing carbon atom, in contrary to our previous assumption. Transmetallation with titanium tetraisopropoxide and the carboxylation proceed with inversion. The addition of aldehydes occurs in a *anti*-S_E'-process. The enantioselective synthesis of homoaldol adducts and some corresponding γ-lactones is reported.

Recently we reported[1,2] that the deprotonation of (*E*)-2-butenyl 2-(*N,N*-diisopropyl)carbamate (**1a**) by means of *sec*-butyllithium/(-)-sparteine [(-)-**2**] gives rise to the predominant formation of one of the epimeric lithium carbanions **3a**/(-)-sparteine (Scheme 1). This was recognized by the formation of the enantiomerically enriched products **5a** with 80-90 % *ee* upon reaction of the allyltitanium intermediate **4**[3] with achiral aldehydes after metal exchange with titanium tetraisopropoxide (TIPT)[4]. The absolute configurations of **5** and of (*R*)-**4** are related through the pericyclic transition state **A**[5], which is the origin of an efficient 1,3-chirality transfer in the allylic part and the selection of the *re*-face in the carbonyl group. The titanium compound (*R*)-**4** could result from a stereospecific metal exchange either in (*S*)-**3a** with stereoinversion (path A) or in (*R*)-**3a** with retention (path B). We originally[1] gave the preference to (*R*)-**3a**/(-)-**2** and path B on the basis of the following reasons: A lithium/TMEDA carbanion derived from a secondary carbamate **1** (alkyl for the 1α-H), which is configurationally stable at low temperature, reacts with TIPT under stereoretention[6]. Furthermore, the aldehyde addition of the major lithium compound **3a**/(-)-**2** leads to the same enantiomer of the *anti*-addukt **5**[1]. Meanwhile, an X-ray structure analysis of the analogous crystalline lithium compound **3b**/(-)-**2** was performed[7]. Its (*S*)-configuration at the lithium-bearing carbon atom required a detailed investigation of the stereochemical problems associated with this approach.

Formation of the Lithium Compounds **3a** *and Titanation.* Unlike the lithium-sparteine carbanions of secondary allyl[8] or alkyl[9] carbamates, the diastereomeric complexes **3**/(-)-**2** are not configurationally stable and do interconvert in pentane solutions at -70°C. The equilibrium between (*S*)-**3a**/(-)-**2** and **3a**/(*R*)-(-)-**2** is disturbed by a second-order asymmetric transformation by preferential crystallization of one diastereomer, which is induced by the addition of cyclohexane[1]. This could be clearly demonstrated by the following experiment: The prochiral butenyl carbamate **1a** first was deprotonated under "achiral conditions" with *n*-BuLi/cyclohexane in the presence of one equiv. 1,2-dimethoxyethane (DME), and later (-)-sparteine was

added. When a crystallization occured, the stereochemical result was identical with that obtained by deprotonation in the presence of (-)-sparteine.

Scheme 1

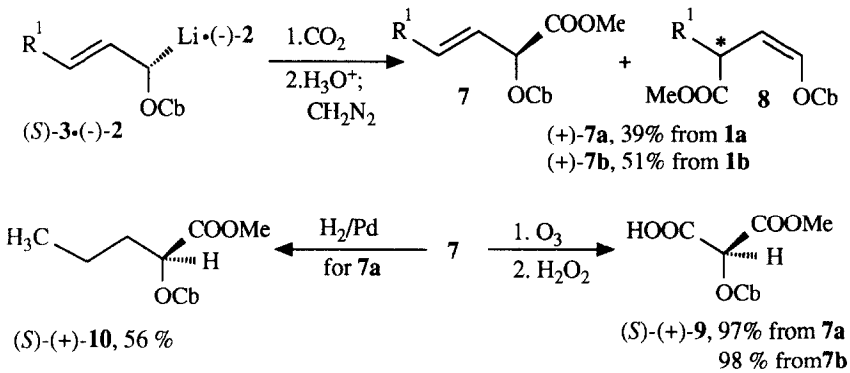


Otherwise, the enantiomeric excess of **5** was negligible. In order to achieve a high chirality transfer, the transmetallation has to proceed from the configurationally stable, solid lithium salt **3a**/(-)-**2**. Therefore a rapid addition of an excess of precooled TIPT is essential. The soluble titanium compound (*R*)-**4a**, which does not racemize below -30°C, adds smoothly to aldehydes. The reaction was also successfully applied by us to 2-alkenals as carbonyl components[10] and by *M. Julia* and coworkers[11] during a total synthesis of avermectin A.

This reaction sequence, starting from the 3-silyl-allyl carbamate (*Z*)-**1b**[7,12,13], gives homoaldol products with only approx. 40% *ee*. A further decreased configurational stability of the lithium compound **3b** presumably is caused by the electron-withdrawing silyl group, which facilitates ion-pair separation and 1,3-metallotropy. The special situation for the γ-silyl derivatives **3b** is also expressed by their rapid *Z*/*E* torsional isomerization[12,13].

Configuration of the Lithium Compound **3a**/(-)-**2**. Despite many efforts no crystals of the crotyl derivative **3a**/(-)-**2** suitable for an X-ray analysis could be prepared. For this reason, we envisaged a chemical correlation with the major diastereomer (*S*)-**3b**/(-)-**2** of known configuration[7]. Both suspensions of the preferentially formed lithium-sparteine complexes (*S*)-**3a,b**/(-)-**2** were reacted with an excess of dry carbon dioxide below -70°C and yielded (after methylation with diazomethane) the methyl esters (+)-**7a** (39 %), besides 30 % of the γ-product (+)-**8a** and (+)-**7b** (51 %), respectively. An ozonolysis followed by oxidative workup, (+)-**7a** and (+)-**7b** gave the same monomethyl malonate (*S*)-(+)-**9**[14]. Another sample of (+)-**7a** afforded on hydrogenation the pentanoate (*S*)-(+)-**10**[15]. Thus, the compounds (+)-**7a,b** and (+)-**9** also have (*S*)-configuration.

Scheme 2



From these results is evident that the carboxylation of (*S*)-**3b**/(-)-**2** proceeds with stereoinversion[16] and, under the reasonable assumption of the same stereochemical course in the analogous compound **3a**, also the (*S*)-configuration has to be assigned to the major diastereomer of the (-)-sparteine complex **3a**/(-)-**2**. When to the suspension of (*S*)-**3a**/(-)-**2** 7 equiv. of 2-methylpropanal (**11a**) were added, an inseparable mixture (63 %) of the *anti*- and the *syn*[17]-diastereomers **5a** and **14**[18] resulted in a ratio of 1 : 4 (Scheme 3). By ^{1}H-NMR analysis in the presence of Eu(hfc)$_3$ only **5a** is influenced, showing an enantiomeric excess of **5a** of 62 % over *ent*-**5a**. Surprisingly, the lithium compound (*S*)-**3a** and the titanate (*R*)-**4a**, although opposite in configuration, form the same major enantiomer, and as a consequence, the carbonyl additions must proceed through different mechanisms. The only explanation is the involvement of an open-chain anti-S_E' process in the lithium case, similar to the Lewis-acid catalysed reaction of allylsilanes and -stannanes[19], which to our best knowledge is unprecedented for allyllithium derivatives.

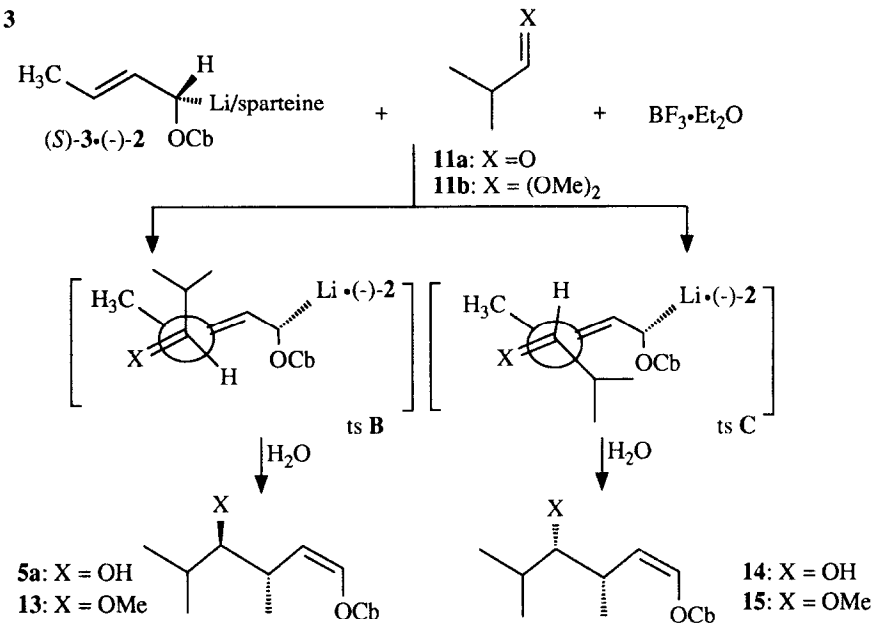
In order to exclude the participation of the pericyclic reaction pathway the experiment was repeated in the presence of boron trifluoride etherate, giving a similar result: 76 % of **5a** (42 % *ee*) and **14** in a ratio of 1 : 4.

Similarly, with isobutyraldehyde dimethylacetal/ boron trifluoride the appropriate methyl ethers **13** (42 % *ee*) and **15** (yield 76 %, ratio 1 : 4) were obtained. The identity of **13** was demonstrated by *O*-methylation of enantiomerically enriched **5a**.

From these results it must be concluded that: The thermodynamically favored lithium sparteine complex is (*S*)-**3**/(-)-**2**. It is attacked by carbonyl compounds by an *anti*-S_E' process. The titanation with TIPT proceeds with inversion of configuration at the metal-bearing carbon atom. We attribute the origin of the unusual stereochemical course to the bulky diamine ligand which extinguishes the ability of the lithium

cation to participate as a Lewis acid in these reactions.

Scheme 3



Stereoselective Lithiation of Further 2-Alkenyl Carbamates. As implicated by ts **A** (Scheme 1), the addition of the titanated allyl carbamates **4** to aldehydes proceeds stereospecifically with strict reagent-controlled[20] 1,3-chirality transfer to form exclusively the (*Z*)-*anti* products of type **5**[2]. Since the determination of the relative configuration in an unknown compound is easier than establishing directly its absolute configuration, we developed a method which is based on the first strategy[21,22].

The enantiomerically pure titanium intermediate (*R*)-**4** in its addition to (*S*)-2-benzyloxypropanal [(*S*)-**16**][23] should give exclusively the product **17**, whereas (*S*)-**4** must lead to the diastereomer **18**; thus, the ratio **17**/**18** roughly reflects the enantiomeric composition of **4**/*ent*-**4** (Scheme 4).

The transition states leading to **17** and **18** are diastereomeric and of different energies because a matched and a mismatched combination[17] are involved. The error arising from a different degree of conversion and competing side reactions[21b] can be corrected by performing the "diastereomeric" experiments using the aldehyde (*R*)-**16** to form the products *ent*-**18** and *ent*-**17**. Compared to the first experiment, matched and mismatched combinations here are interchanged, thus the mean value represents exactly the enantiomer composition of **4**. The diastereomers **17**/**18** are easily separated[22] and ^{1}H-NMR-spectroscopically assigned in their relative configurations[23] based on their different ability for intramolecular hydrogen bridging. As a consequence, not only the ratio, but also the absolute configuration of the major intermediate **4** is defined by the method. It was applied to several allyl carbamates **1a-d** after (-)-sparteine-assisted lithiation and metal exchange; the results are collected in Table 1[24].

It is noteworthy, that the sparteine complexes derived from 2-hexenyl carbamate **1c**, did not crystallize; hence the ratio 69 : 31 should reflect the relative thermodynamic stability of the diastereomers (*S*)-**3c**/(-)-**2** and (*R*)-**3c**/(-)-**2** in pentane solution.

A slight improvement was achieved by the utilization of the C_2-symmetric[25] ligand (-)-α-isosparteine **19**, which is available by epimerization of (-)-sparteine[26] (see below).

Scheme 4

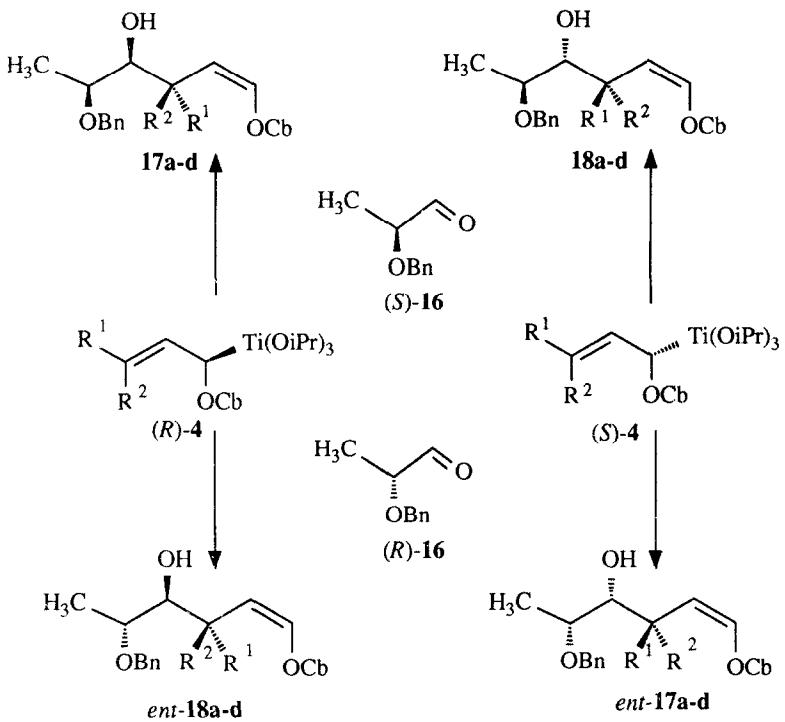
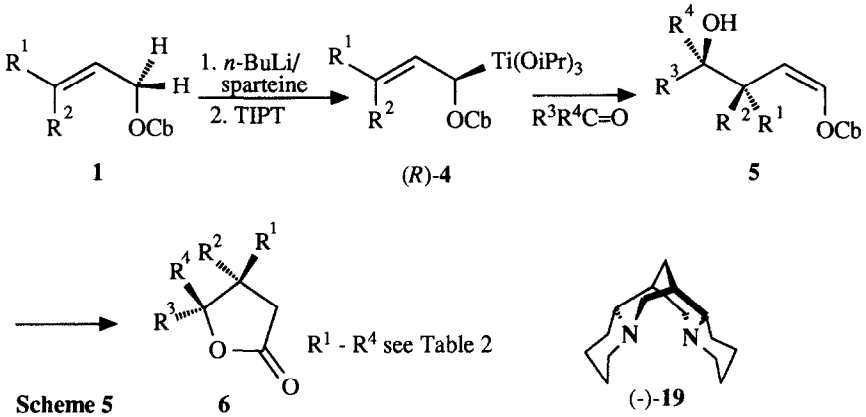


Table 1: Reaction of Enantiomerically Enriched α-Titanates **4** with (*S*)-**16** and (*R*)-**16**

1 - 4, 17, 18	R^1	R^2	Reaction with (*S*)-**16** yield (%)	ratio **17/18**	Reaction with (*R*)-**16** yield (%)	r. *ent*-**18**/*ent*-**17**	mean ratio	% *ee* in **4**
a	Me	H	94	96 : 4	93	85 : 15	90 : 10	80
b	$SiMe_3$	H	58	81 : 19	--	--	--	--
c	*n*-Pr	H	79	68 : 32	80	70 : 30	69 : 31	36
d	Me	Me	85	85 : 15	75	85 : 15	85 : 15	70

Synthesis of Enantiomerically Enriched γ-Lactones via Homoaldol Reaction. The addition of the racemic or the enantiomerically enriched titanates **4** to aldehydes or ketones devoid of stereogenic centers proceeds smoothly to form the respective homoaldol products **5** with the corresponding enantiomeric purity as single

diastereomers[1,27] (see Table 2). The compounds **5a-5d** were converted into the appropriate γ-lactones **6** by mercuric acetate assisted methanolysis[28] followed by Grieco oxidation[29]. Natural product **6c**, (+)-quercus lactone A, occurs in oak wood[30,31].



Scheme 5

The synthesis of the pheromone (+)-eldanolide, bearing a sensitive double bond in the side chain, requires another procedure which is reported in the subsequent paper[32].

Table 2: Synthesis of Enantiomerically Enriched Homoaldol Adducts and γ-Lactones

Educt	Product **5**								Lactone **6**			
	R^1	R^2	R^3	R^4		yield (%)[a]	$[\alpha]_D^{20}$ [b]	% ee[c]		yield (%)[a]	$[\alpha]_D^{20}$ [d]	% ee[e]
1a	Me	H	*i*Pr	H	**5a**	90	+16.1	90	**6a**[f]	89	+31.8	--
1a	Me	H	Me	H	**5b**	95	+22.0	80	[f]			
1a	Me	H	*n*Bu	H	**5c**	93	+39.2	84	**6c**[f]	90	+52.1	66
1a	Me	H	Me	Me	**5d**	92	+5.1	82	[f]			
1b	Me_3Si	H	*i*Pr	H	**5e**	56	+3.2	42	[f]			
1c	*n*Pr	H	*i*Pr	H	**5f**	82[m]	+2.8	31[m]	[f]			
1d	Me	Me	*i*Pr	H	**5g**	83	+4.2	76	[f]			

a) yield of isolated product after liquid chromatography; b) in MeOH, c = 1-3; c) determined with 7-20 Mol% $Eu(hfc)_3$; d) in MeOH, c = 2-2.5; e) determined by opt. rotation, f) ref. [25],m) with (-)-α-isosparteine 78% yield, 16% *ee*;

In summary, the methodology outlined above permits the simple generation of enantiomerically enriched allyltitanates. Besides, lactones **6**, various target molecules are accessible from the generally and readily available homoaldol products **5**[2,10]. The opposite enantiomeric series can be approached with the aid of easily prepared (+)-sparteine[33].

Experimental. All organometallic reactions were performed under Ar at -78°C with exclusion of air and moisture. Pentane and diethyl ether were distilled over $LiAlH_4$; (-)-sparteine [(-)-**2**] and (-)-α-isosparteine [(-)-**19**] were dried over CaH_2 prior to use. Tetra(isopropoxy)titanium (TIPT) was used after distillation under Ar. LC separations were carried out at 1-3 bar on "Silica Woelm 32-63" (Woelm Pharma GmbH & Co, Eschwege). Enantiomeric excesses were determined by 90-MHz-^{1}H-NMR spectroscopy with tris[(3-heptafluoropropylhydroxymethylen)-d-camphorato]europium(III), [Eu(hfc)$_3$]. In all cases shifts to lower field of the 1-H in compounds **5, 8** and **13** were observed. Optical rotations and *ee*-values of compounds **5** see Table 2. All new compounds gave satisfactory elemental analyses (C,H + 0.3%).

Deprotonation of the (E)-butenyl carbamate **1a** *to (S)-***3a**/(-)-**2**. Carbamate **1a** (2.0 mmol, diluted in 2 mL pentane) was added slowly to a solution of (-)-sparteine [(-)-**2**] (2.2 mmol) and *n*-BuLi (2.5 mmol; in hexane, 1.6N) in pentane/ cyclohexane (7 mL + 1.5 mL) and stirred vigorously. When *sec*-BuLi (1.3N in isopentane/cyclohexane) was used, no addition of cyclohexane was necessary. After 10 min a crystallization occured and stirring of the suspension was continued for 30 min.

Deprotonation of the carbamates **1c,d** *to* (*S*)-**3c,d**/(-)-**2**.
See procedure above for **1a**; *n*-BuLi; without cyclohexane; **1c**: 60 min (no cryst.); **1d**: 60 min (cryst. after 10 min).
Deprotonation of the (Z)-3-trimethylsilyl-2-propenyl carbamate **1b** *to* (*S*)-**3b**/(-)-**2**. The deprotonation of carbamate **1b** (1.0 mmol) was carried out in a mixture of pentane and diethyl ether (10 mL, 1:1) with (-)-sparteine (1.0 mmol) and *n*-BuLi (1.6 mmol; in hexane, 1.6N). After 20 h standing at -70°C (without stirring) for crystallization of the carbanion, the liquid phase was removed by a syringe.

Reaction of (*S*)-**3**/(-)-**2** *with electrophiles:*
Procedure **A** (with titanation): Precooled TIPT (4-10 mmol) was added very quickly at -70°C to the suspension of **3** and stirring was continued for 15 min. Aldehydes (4-6 mmol) were injected and the reaction mixture was allowed to warm to room temperature. It was poured onto a mixture of 2N aq. HCl (10 mL) and ether (20 mL). The aq. solution was extracted three times with ether (each 20 mL), the combined ethereal solns. were washed with aq. sat. $NaHCO_3$ (20 mL) and dried over Na_2SO_4. After evaporation of the solvent in vacuum, the residue was purified by LC (silica gel; diethyl ether/pentane).
Procedure **B**: Electrophiles (2-10 mmol, diluted in 5 mL pentane) were introduced quickly with a cooled syringe. Stirring at -70°C was continued for 30 min and work-up was performed as described above.

(1*Z*,3*S*,4*R*)-*4-Hydroxy-3,5-dimethyl-1-hexenyl N,N-diisopropylcarbamate* (**5a**)[13]. (*S*)-**3a**/(-)-**2** (*n*-BuLi) and 1.1 equiv. 2-methylpropanal (**11a**), procedure **A**, E/P (1:4), afforded 488 mg (90 %) of **5a**.

(1*Z*,3*S*,4*R*)-*4-Hydroxy-3-methyl-1-pentenyl N,N-diisopropylcarbamate* (**5b**)[13]. (*S*)-**3a**/(-)-**2** (*sec*-BuLi) and ethanal (10 equiv.), procedure **A**, E/P (1:4), afforded 492 mg (95 %) of **5b**.

(1*Z*,3*S*,4*R*)-*4-Hydroxy-3-methyl-1-octenyl N,N-diisopropylcarbamate* (**5c**)[13]. (*S*)-**3a**/(-)-**2** (*sec*-BuLi) and *n*-pentanal (1.1 equiv.), procedure **A**, E/P (1:4), afforded 530 mg (93 %) of **5c**.

(1*Z*,3*S*)-*4-Hydroxy-3,4-dimethyl-1-pentenyl N,N-diisopropylcarbamate* (**5d**)[13]. (*S*)-**3a**/(-)-**2** (*sec*-BuLi) and acetone (1.1 equiv.), procedure **A**, E/P (1:4), afforded 506 mg (92 %) of **5d**.

(1*Z*,3*S*,4*S*,5*S*)- *and* (1*Z*,3*R*,4*R*,5*S*)-*5-Benzyloxy-4-hydroxy-3-methyl-1-hexenyl N,N-diisopropylcarbamate* (**17a** *and* **18a**)[22]. (*S*)-**3a**/(-)-**2** (*sec*-BuLi) and (*S*)-2-benzyloxypropanal [(*S*)-**16**][24] (1.1 equiv.), procedure **A**, E/P (1:4), afforded 655 mg (90 %) of **17a** besides 35 mg (4 %) of **18a**; **17a:** $[\alpha]_D^{20}$ = +33.0 (MeOH, c = 2.0); R_F (1:1): 0.36; **18a:** $[\alpha]_D^{20}$ = +9.5 (MeOH, c = 2.2); R_F (1:1): 0.25.

(1*Z*,3*S*,4*S*,5*R*)- *and* (1*Z*,3*R*,4*R*,5*R*)-*5-Benzyloxy-4-hydroxy-3-methyl-1-hexenyl N,N-diisopropylcarbamate* (*ent*-**18a** *and ent*-**17a**)[22]. (*S*)-**3a**/(-)-**2** (*sec*-BuLi) and (*R*)-2-benzyloxypropanal [(*R*)-**16**][24] (1.1 equiv.), procedure **A**, E/P (1:4), afforded 578 mg (79 %) of *ent*-**18a** besides 102 mg (14 %) of *ent*-**17a**.

(1*Z*,3*S*,4*R*)-*4-Hydroxy-5-methyl-3-trimethylsilyl-1-hexenyl N,N-diisopropylcarbamate* (**5e**)[12]. (*S*)-**3b**/(-)-**2** (*n*-BuLi) and 1.1 equiv. 2-methylpropanal (**11a**), procedure **A**, E/P (1:4), afforded 370 mg (56 %) of **5e**.

(1*Z*,3*S*,4*S*,5*S*)- *and* (1*Z*,3*R*,4*R*,5*S*)-*5-Benzyloxy-4-hydroxy-3-trimethylsilyl-1-hexenyl N,N-diisopropylcarbamate* (**17b** *and* **18b**)[12]. (*S*)-**3a**/(-)-**2** and (*S*)-2-benzyloxypropanal [(*S*)-**16**] (1.5 equiv.), procedure **A**, E/P (1:4), afforded 406 mg (48%) of **17b** besides 84 mg (10 %) of **18b**; **17b:** $[\alpha]_D^{20}$ = +4.1 (MeOH, c = 0.4); R_F (1:1): 0.83; **18b:** $[\alpha]_D^{20}$ = -1.2 (MeOH, c = 0.6); R_F (1:1): 0.70.

(1*Z*,3*S*,4*R*)-*4-Hydroxy-5-methyl-3-propyl-1-hexenyl N,N-diisopropylcarbamate* (**5f**). (*S*)-**3c**/(-)-**2** (*n*-BuLi) and 1.5 equiv. 2-methylpropanal (**11a**), procedure **A**, E/P (1:4), afforded 493 mg (82 %) of **5f**.- ^{1}H-NMR ($CDCl_3$): δ = 0.85-1.05 (m,6,9-H_3,8-H_2); 1.251 (d,iPr-H_3); 1.25-1.50 (m,7-H_2); 1.588 (s,OH); 1.739 (dq,5-H); 2.776 (dddt,3-H); 3.177 (dd,4-H); 3.8-4.2 (m,NCH); 4.640 (dd,2-H); 7.174 (dd,1-H); $J_{1,2}$= 6.6 Hz; $J_{1,3}$= 0.8 Hz; $J_{2,3}$= 10.5 Hz; $J_{3,4}$= 4.0 Hz; $J_{3,7}$= 5.2 Hz; $J_{4,5}$= 6.0 Hz; $J_{5,6}$= 6.8 Hz; J_{iPr}= 6.8 Hz; ^{13}C-NMR ($CDCl_3$): δ = 14.17 and 17.15 (C-6); 19.77 (C-9); 20.18 (C-8); 20.95 (C-iPr); 30.96 (C-5); 34.38 (C-7); 39.07 (C-3); 46.34 (NCH); 78.87 (C-4); 111.19 (C-2); 137.22 (C-1); 152.80 (C=O). A 1 mmol experiment by use of (-)-α-isosparteine [(-)-**19**] (1.0 mmol) afforded 233 mg (78%) of **5f** with 16 % *ee*.

(1*Z*,3*S*,4*S*,5*S*)- *and* (1*Z*,3*R*,4*R*,5*S*)-*5-Benzyloxy-4-hydroxy-3-propyl-1-hexenyl N,N-diisopropylcarbamate* (**17c** *and* **18c**). (*S*)-**3c**/(-)-**2** and (*S*)-2-benzyloxypropanal [(*S*)-**16**] (1.5 equiv.), procedure **A**, E/P (1:4), afforded 422 mg (54%) of **17c** besides 195 mg (25 %) of **18c**; **17c:** $[\alpha]_D^{20}$ = -11.0 (MeOH, c = 1.0); R_F (1:1): 0.65;-^{1}H-NMR ($CDCl_3$): δ = 0.894 (t,14-H_3); 1.157 (d,6-H_3); 1.252 (d,iPr-H_3); 1.25-1.6 (m,12 und 13-H_2); 2.689 (s,OH); 2.62-2.80 (m,3-H); 3.446 (dd,4-H); 3.466 (dq,5-H); 3.7-4.2 (NCH); 4.405 and 4.646 (d,7-H_2); 4.809 (dd,2-H); 7.086 (dd,1-H); 7.2-7.4 (m,Phenyl-H); $J_{1,3}$= 0.5 Hz; $J_{14,13}$= 7.0 Hz; $J_{6,5}$= 5.8 Hz; J_{iPr}= 6.9 Hz; $J_{4,5}$= 6.0 Hz; $J_{2,3}$= 10.5 Hz; $J_{1,2}$= 6.6 Hz; J_{Bn}= 11.3 Hz; $J_{3,4}$= 4.5 Hz;^{13}C-NMR ($CDCl_3$): δ = 14.12 (C-14); 15.36 (C-6); 20.52 (C-13); 20.89 (C-iPr); 34.76 (C-12); 37.03 (C-3); 46.31 (NCH); 70.48 (C-7); 76.88 (C-5); 77.50 (C-4); 110.34 (C-2); 127.7-128.5 (C-9,10,11); 136.14 (C-1); 138.49 (C-8); 152.69 (C=O). **18c:** $[\alpha]_D^{20}$ = -32.1 (MeOH, c = 0.8); R_F (1:1): 0.42. -^{1}H-NMR ($CDCl_3$): δ = 0.863 (t,14-H_3); 1.1-1.6 (m,iPr- and 6-H_3,12- and 13-H_2); 1.984 (s,OH); 2.841 (m,3-H); 3.586 (dd,4-H); 3.681 (dq,5-H); 3.7-4.2 (NCH); 4.513 and 4.572 (d,7-H_2); 4.681 (dd,2-H); 7.176 (dd,1-H); 7.2-7.4 (m,Phenyl-H); $J_{1,3}$= 0.5 Hz; $J_{14,13}$= 7.0 Hz; $J_{6,5}$= 5.7 Hz; $J_{4,5}$= 3.1 Hz; $J_{2,3}$= 10.2 Hz; $J_{1,2}$= 6.5 Hz; J_{Bn}= 12.0 Hz; $J_{3,4}$= 4.7 Hz; ^{13}C-NMR ($CDCl_3$): δ = 14.20 (C-14); 15.94 (C-6); 20.36 (C-13); 20.98 (C-iPr); 34.14 (C-12); 37.97 (C-3); 46.31 (NCH); 70.87 (C-7); 76.22 (C-4); 78.01 (C-5); 111.13 (C-2); 127.5-128.5 (C-9,10,11); 136.81 (C-1); 138.79 (C-8); 152.83 (C=O).
(1*Z*,3*S*,4*S*,5*R*)- *and* (1*Z*,3*R*,4*R*,5*R*)-*5-Benzyloxy-4-hydroxy-3-propyl-1-hexenyl N,N-diisopropylcarbamate* (*ent*-**18c** *and ent*-**17c**). (*S*)-**3c**/(-)-**2** and (*R*)-2-benzyloxypropanal [(*R*)-**16**] (1.5 equiv.), procedure **A**, E/P (1:4), afforded 446 mg (56%) of *ent*-**18c** besides 186 mg (24 %) of *ent*-**17c**; *ent*-**18c**: $[\alpha]_D^{20}$ = +35.4 (MeOH, c = 2.1); R_F (1:1): 0.45; *ent*-**17c:** $[\alpha]_D^{20}$ = +10.1 (MeOH, c = 1.0); R_F (1:1): 0.64.

(1*Z*,4*R*)-*4-Hydroxy-3,3,5-trimethyl-1-hexenyl N,N-diisopropylcarbamate* (**5g**)[13]. (*S*)-**3d**/(-)-**2** (*n*-BuLi) and 2 equiv. 2-methylpropanal (**11a**), procedure **A**, E/P (1:4), afforded 473 mg (83 %) of **5g**.

(1*Z*,4*S*,5*S*)- *and* (1*Z*,4*R*,5*S*)-*5-Benzyloxy-4-hydroxy-3,3-dimethyl-1-hexenyl N,N-diisopropylcarbamate* (**17d** *and* **18d**). (*S*)-**3d**/(-)-**2** and (*S*)-2-benzyloxypropanal [(*S*)-**16**] (1.1 equiv.), procedure **A**, E/P (1:4), afforded 545 mg (72%) of **17d** besides 96 mg (13%) of **18d**; **17d:** $[\alpha]_D^{20}$ = +2.4 (MeOH, c = 1.0); R_F (1:1): 0.60;- ^{1}H-NMR ($CDCl_3$): δ = 1.0-1.8 (m,6-,12-,13-H_3,iPr-H_3); 1.650 (s,OH); 3.753 (ddd,4-H); 3.76 and 4.12 (m,NCH); 4.417 (d,7-H,one); 4.6-4.8 (m,one 7-H,5-H,2-H); 6.886 (d,1-H); 7.2-7.4 (m,Phenyl-H); $J_{1,2}$= 7.5 Hz; $J_{1,4}$= 1.0 Hz; $J_{4,5}$= 6.1 Hz; $J_{5,6}$= 6.0 Hz; J_{Bn}= 11.8 Hz; ^{13}C-NMR ($CDCl_3$): δ = 18.51 (C-6); 20.76 (C-iPr); 23.89 and 25.43 (C-12 and C-13); 39.59 (C-3); 46.26 (NCH); 70.65 (C-7); 73.75 (C-5); 80.86 (C-4); 116.16 (C-2); 127.4-128.6 (C-9,10,11); 134.40 (C-1); 138.21 (C-8); 151.74 (C=O). **18d:** $[\alpha]_D^{20}$ = +2.6 (MeOH, c = 0.8); R_F (1:1): 0.55; -^{1}H-NMR ($CDCl_3$): δ = 1.0-1.5 (m,6-,12-,13-H_3,iPr-H_3); 1.622 (s,OH); 3.746 (dd,4-H); 3.65 and 4.20 (m,NCH); 3.660 (dq,5-H); 4.493 and 4.551 (d,7-H_2); 4.757 (d,2-H); 6.809 (d,1-H); 7.2-7.4 (m,Phenyl-H); $J_{1,2}$= 7.5 Hz; $J_{1,4}$= 1.3 Hz; $J_{4,5}$= 3.0 Hz; $J_{5,6}$= 6.1 Hz; J_{Bn}= 11.7 Hz; -^{13}C-NMR ($CDCl_3$): δ = 14.96 (C-6); 20.77 (C-iPr); 25.48 and 25.96 (C-12 and C-13); 38.52 (C-3); 46.33 (NCH); 70.37 (C-7); 76.01 (C-5); 79.68 (C-4); 116.04 (C-2); 126.5-128.6 (C-9,10,11); 134.34 (C-1); 138.66 (C-8); 151.76 (C=O).

(1*Z*,4*S*,5*R*)- *and* (1*Z*,4*R*,5*R*)-*5-Benzyloxy-4-hydroxy-3,3-dimethyl-1-hexenyl N,N-diisopropylcarbamate* (*ent*-**18d** *and ent*-**17d**). (*S*)-**3d**/(-)-**2** and (*R*)-2-benzyloxypropanal [(*R*)-**16**] (1.1 equiv.), procedure **A**, E/P (1:4), afforded 481 mg (64%) of *ent*-**18c** besides 82 mg (11 %) of *ent*-**17c**; *ent*-**18c**: $[\alpha]_D^{20}$ = -2.7 (MeOH, c = 2.1); R_F (1:1): 0.53; *ent*-**17c:** $[\alpha]_D^{20}$ = -2.6 (MeOH, c = 0.6); R_F (1:1): 0.64.

(1*Z*,3*S*,4*R*)- *and* (1*Z*,3*S*,4*S*)-*4-Hydroxy-3,5-dimethyl-1-hexenyl N,N-diisopropylcarbamate* (**5a** *and* **14**)[13].
(*S*)-**3a**/(-)-**2** and 2-methylpropanal (**11a**) (14 mmol), procedure **B**, E/P (1:4), afforded 342 mg (63 %) of a mixture consisting **5a** and **14** in a ratio of 1:4 (by ^{1}H-NMR). Enantiomeric excess of **5a** determined by shift experiment with 25 Mol% of Eu(hfc)$_3$ to 62 % *ee*.
(*S*)-**3a**/(-)-**2** and 2-methylpropanal / boron trifluoride etherate (20 mmol), procedure **B**, E/P (1:4), afforded 412 mg (76 %) of a mixture consisting of **5a** and **14** in a ratio of 1:4. Enantiomeric excess of **5a** [25 Mol% Eu(hfc)$_3$]: 44% *ee*.

(1Z,3S,4R)- and (1Z,3S,4S)-4-Methoxy-3,5-dimethyl-1-hexenyl N,N-diisopropylcarbamate (**13** *and* **15**). (*S*)-**3a**/(-)-**2** and isobutyraldehyde dimethyl acetal (**11b**)/ boron trifluoride etherate (20 mmol), procedure **B**, E/P (1:4), afforded 203 mg (37 %) of a mixture consisting **13** and **15** in a ratio of 1:4. Enantiomeric excess of **13**: 42% *ee* [36 Mol% of $Eu(hfc)_3$]. **13** identified by methylation (NaH and MeJ) and ^{1}H-NMR-spectroscopy of enantiomerically enriched (88 % *ee*) pure **5a** [12 Mol% of $Eu(hfc)_3$]. **13**: ^{1}H-NMR ($CDCl_3$): δ = 0.869 and 0.948 (d,6-H_3); 1.070 (d,7-H_3); 1.246 (d,iPr-H_3); 1.747 (dqq,5-H); 2.658 (dd,4-H); 2.942 (dddq,3-H); 3.485 (s,8-H_3); 4.07 and 3.82 (m,NCH); 4.792 (dd,2-H); 7.005 (dd,1-H). $J_{6,5}$= 6.8 Hz; J_{iPr}= 6.6 Hz; $J_{5,4}$= 7.3 Hz; $J_{3,7}$= 7.0 Hz; $J_{4,3}$= 3.8 Hz; $J_{3,2}$= 10.0 Hz; $J_{3,1}$= 1.0 Hz; $J_{2,1}$= 6.6 Hz.-^{13}C-NMR ($CDCl_3$): δ = 19.37 and 19.61 (C-6); 20.45 (C-7); 21.69 (C-iPr); 32.43 (C-5); 33.93 (C-3); 47.11 (NCH); 62.14 (C-8); 91.92 (C-4); 113.62 (C-2); 135.43 (C-1); 153.71 (C=O).

Methyl (3E,2S)-2-(N,N-diisopropylcarbamoyloxy)pent-3-enoate and methyl (3Z,2S)-4-(N,N-diisopropylcarbamoyloxy-2-methyl)but-3-enoate (**7a** *and* **8a**). (*S*)-**3a**/(-)-**2** (4 mmol) was treated with an excess of dry carbon dioxide, the crude product was treated with an excess of diazomethane, procedure **B**, (1N in ether), E/P (1:4), afforded 408 mg (39%) **7a** and (30%) **8a**. **7a:** $[\alpha]_D^{20}$ = +30.4 (c = 0.5, MeOH), R_F = 0.52 (E/P 1:1),-^{1}H-NMR ($CDCl_3$): δ = 1.234 (d,iPr-H_3); 1.759 (ddd,5-H_3); 3.6 and 4.2 (m,NCH); 3.746 (s,6-H_3); 5.405 (ddq,2-H); 5.591 (ddq,3-H); 5.948 (ddq,4-H). $J_{2,4}$= 1.0 Hz; $J_{3,4}$= 15.2 Hz; $J_{3,5}$= 1.6 Hz; $J_{4,5}$= 6.5 Hz; $J_{2,3}$= 7.1 Hz; $J_{2,5}$= 1.0 Hz;-^{13}C-NMR ($CDCl_3$): δ = 17.89 (C-5); 20.86 (C-iPr); 46.24 (NCH); 52.14 (C-6); 73.50 (C-2); 124.13 (C-4); 131.77 (C-3); 154.47 (C=O); 170.53 (C-1).- **8a:** $[\alpha]_D^{20}$ = +64.8 (c = 1.0, MeOH); R_F = 0.41 (E/P, 1:1);-^{1}H-NMR ($CDCl_3$): δ = 1.230 (d,iPr-H_3); 1.248 (d,5-H_3); 3.620 (m,2-H); 3.684 (s,6-H_3); 3.7-4.2 (m,NCH); 4.849 (dd,3-H); 7.097 (dd,4-H). $J_{4,3}$= 6.4 Hz; $J_{3,2}$= 9.5 Hz; $J_{2,5}$= 7.1 Hz; $J_{4,2}$= 1.1 Hz:-^{13}C-NMR ($CDCl_3$): δ = 18.05 (C-5); 20.95 (C-iPr); 36.39 (C-2); 46.05 (NCH); 51.84 (C-6); 109.51 (C-3); 135.95 (C-4); 152.31 (C=O); 174.86 (C-1).

Methyl (3E,2S)-2-(N,N-diisopropylcarbamoyloxy)-4-trimethylsilyl-but-3-enoate (**7b**). (*S*)-**3b**/(-)-**2** (2 mmol) was treated with an excess of dry carbon dioxide, then excess of diazomethane (1N in ether), procedure **B**, E/P (1:4), afforded 320 mg (51%) of **7a**. $[\alpha]_D^{20}$ = +29.1 (MeOH, c = 1.0); R_F = 0.76 (1:1),-^{1}H-NMR ($CDCl_3$): δ = 0.087 (s,5-H_3); 1.2-1.4 (m,iPr-H_3); 3.759 (s,6-H_3); 3.81-4.06 (NCH); 5.521 (dd,2-H); 6.119 (m,3-H and 4-H); $J_{4,3}$= 15.9 Hz; $J_{2,3}$= 3.3 Hz; $J_{2,4}$= 1.1 Hz;- ^{13}C-NMR ($CDCl_3$): δ = -1.47 (C-5); 20.96 (C-iPr); 46.34 (NCH); 52.20 (C-6); 74.86 (C-2); 134.62 (C-4); 137.29 (C-3); 154.20 (C=O); 169.86 (C-1).

Methyl hydrogen (S)-2-(N,N-diisopropylcarbamoyloxy)malonate (**10**). Ozonolysis of **7a** (0.12 mmol) in 2 mL MeOH at -78°C and oxidative workup (H_2O_2/HCOOH) afforded 28 mg (98%) **10** , (E/P 3:1). $[\alpha]_D^{20}$ = +2.1 (c = 1.1, CH_2Cl_2) R_F= 0.12 (E/P, 1:1);-^{1}H-NMR ($CDCl_3$): δ = 1.1-1.4 (m,iPr-H_3); 3.864 (s,3-H_3); 3.8-4.2 (m,NCH); 5.601 (s,1-H); 7.4-8.3 (m,4-OH);- MHz-^{13}C-NMR ($CDCl_3$): δ = 20.57 (C-iPr); 46.42 (NCH); 53.29 (C-3); 72.11 (C-1); 154.19 (C-7); 165.74 und 167.70 (C-2 und C-4).
Ozonolysis of **7b** (0.63 mmol) in 2 mL MeOH at -78°C and oxidative workup (H_2O_2/HCOOH) afforded 151 mg (96%) **10** , (E/P 3:1). $[\alpha]_D^{20}$ = +2.8 (c = 4.5, CH_2Cl_2) R_F= 0.13 (E/P, 1:1),
Methyl (S)-2-(N,N-diisopropylcarbamoyloxy)pentanoate (**9**). **7a** (0.62 mmol) in 3 mL abs. EtOH was stirred for 24 h with Pd/C (0.62 mmol) under H_2. Aqueous workup and chromatography with E/P (1:4) afforded 104 mg (65 %) **9**. $[\alpha]_D^{20}$ = +51.2 (c = 0.6, MeOH), R_F = 0.71 (E/P, 1:1); ^{1}H-NMR ($CDCl_3$): δ = 0.957 (t,5-H_3); 1.230 (m,iPr-H_3); 1.463 (ddq,4-H_2); 1.822 (dddd,3-H_2); 3.6-4.3 (m,NCH); 3.733 (s,6-H_3); 5.024 (dd,2-H). $J_{2,3A}$= 5.3 Hz; $J_{2,3B}$= 6.4 Hz; $J_{3A,4}$= 4.6 Hz; $J_{3B,4}$= 6.3 Hz; $J_{4,5}$= 7.3 Hz;-^{13}C-NMR ($CDCl_3$): δ = 13.73 (C-5); 18.76 (C-4); 20.98 (C-iPr); 33.61 (C-3); 46.12 (NCH); 51.87 (C-6); 72.43 (C-2); 154.99 (C=O); 171.92 (C-1).
(3S,4R)-3,5-Dimethyl-4-hexanolide (**6a**)[25]. Optical active **5a** (1.6 mmol, 83% *ee*) in 8 mL of dry MeOH was stirred with $MeSO_3H$ (1 equiv.) and $Hg(OAc)_2$ (1 Mol%) for 2h at room temperature. The solvent was evaporated in vacuum and the residue was dissolved in 11 mL of methylene chloride. The mixture was treated with 20 mol% of boron trifluoride etherate and 1.1 equiv. of MCPBA. After stirring for 3h 0.1 mL dimethyl sulfide was added and the mixture was poured to a mixture of ether (50 mL) and water (15 mL). The aq. solution was extracted three times with ether (each 20 mL), the combined etheral solns. were washed with aq. sat. $NaHCO_3$ (20 mL) and dried over Na_2SO_4. After evaporation of the solvent in vacuum, the residue was purified by LC (E/P 1:4) and yielded 197 mg (87%) of **6a**; $[\alpha]_D^{20}$ = +31.5 (MeOH, c = 2.5); R_F = 0.30 (E/P 1:1);-^{1}H-NMR ($CDCl_3$): δ = 0.99 (d,7-H_3); 1.01 (d,6-CH_3); 1.16 (d,4-CH_3); 1.87 (qqd,6-H); 2.18 (dd, 3-H); 2.36 (dddq,4-H); 2.70 (dd,3'-H); 3.85 (dd,5-H); $J_{7,6}$= 6.9 Hz; $J_{6,5}$= 5.6 Hz; $J_{3,4}$= 8.0 Hz; $J_{3',4}$= 8.6 Hz; $J_{6,6\text{-Me}}$= 6.9 Hz;$J_{3',3}$= 17.5 Hz; $J_{5,4}$= 6.6 Hz; $J_{4,4\text{-Me}}$= 6.7 Hz;-^{13}C-NMR ($CDCl_3$): δ = 17.33 (4-CH_3); 18.68 (C-7); 19.21 (6-CH_3); 31.63 (C-6); 32.50 (C-4); 37.22 (C-3); 92.02 (C-5); 176.41 (C-2).

(3S,4R)-3-Methyl-4-octanolide [(+)-quercus lactone A] (**6c**).[30] The analogous procedure with optical active **5c** (1.6 mmol, 84% *ee*) afforded 224 mg (90%) of **6c**; $[\alpha]_D^{20}$ = +52.1 (MeOH, c = 0.95); R_F = 0.38 (E/P 1:1).

Acknowledgement. - Generous support by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie is gratefully acknowledged.

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