Chiral Homoenolate Equivalents, V[◇]

Hydroxyalkylation of Lithiated 3-[(*S*)-2-(Methoxymethyl)pyrrolidino]-1,3-diphenylpropene – An Asymmetric Homoaldol Reaction

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The hydroxyalkylation of lithiated 3-[(*S*)-2-(methoxymethyl)-pyrrolidino]-1,3-diphenylpropene (**2**) with aldehydes is completely regioselective giving homoaldol adducts in good yields. The simple diastereoselectivity is low with typical ratios ranging between 1:1 and 1:3 with the *syn* isomer predominating. The induced diastereoselectivity is much higher and is strongly solvent-dependent. The reaction predominantly proceeds according to a metalloretentive mechanism from the *si* side of the allylic system in THF as well as in TBME. The induced diastereoselectivity obtained by the use of the less solvating TBME is considerably higher than in the strongly solvating THF, selectivities of up to 97% *ee* being reached.

Alkylation of metallated chiral allylamines with (*S*)-2-(methoxymethyl)pyrrolidine (SMP) as the aliphatic amino component leads to 3-chiral enamines and, after hydrolysis, to 3-chiral aldehydes[2] and ketones[3]. The enantiomeric excess is quite good, and the course of induction can be controlled by the choice of the solvent. In some cases both configurations can be generated with equal selectivity without changing the chiral auxiliary. Therefore, it was interesting to test the reaction of metallated allylamines with carbonyl compounds in order to achieve an asymmetric homoaldol reaction[4].

Asymmetric homoaldol reactions are scarce, one of the few examples being the addition of benzaldehyde to optically active stannanes[5] with an almost complete transfer of chirality. In order to obtain high diastereoselectivities in homoaldol reactions of lithiated allyl compounds, lithium is exchanged for titanium[4]. Enantioselective lithiation[4,6] of an enantiomerically pure secondary 2-alkenylcarbamate or deprotonation of primary alkenylcarbamates in the presence of (−)-sparteine[6a,7], followed by a lithium/titanium exchange results in homoaldol products with >95% *ee* after reaction with aldehydes and ketones.

Hydroxyalkylation of achiral metallated allylamines[8a,b] and enamines[8b,c] leads to 4-hydroxy enamines. After acid-promoted cleavage of the amino group, a cyclisation follows, and dihydrofurans are obtained with moderate diastereoselectivity. Reactions of metallated chiral allylamines, which represent aldehyde homoenolate equivalents, with aldehydes result in tetrahydrofurans without loss of the amino group. The resulting diastereomeric ratios are also moderate and cannot be increased by use of titanium derivatives[9].

This work describes the reaction of the lithiated allylamine **2** with different aldehydes and thus contributes further to the field of reactions of chiral homoenolate equivalents.

Deprotonation and Hydroxyalkylation

3-Lithio-1-[(*S*)-2-(methoxymethyl)pyrrolidino]-1,3-diphenylpropene (**2**) is generated[3b,c] by treatment of allylamine **1** with 1 equiv. of *n*BuLi at 0°C in tetrahydrofuran (THF; 1 h) or in *tert*-butyl methyl ether (TBME; 12 h). If the potassium salt is desired, 2 equiv. of *t*BuOK is added to the solution of the lithium compound after metallation. Further stirring for 1 h results in the formation of the potassium compound.

Reaction of **2** with different aldehydes leads to the 4-(lithiooxy) enamines **3** which were not isolated. Hydrolysis with 2 N HCl produces the 4-hydroxy ketones **4** which are in equilibrium with their cyclic tautomers **5** that under these conditions partially dehydrate to 2,3-dihydrofurans **6**. Distillation completes the dehydration process, and the pure 2,3-dihydrofurans **6** can be obtained. However, these compounds are not suitable for the determination of enantiomeric purity because no separated signals for monitoring could be induced with chiral lanthanide shift reagents. It turned out to be more useful to protect the alcoholate group of the adduct **3** by acetylation[2a]. Then the (*E*) enamines **7** are obtained as the only products, as can be seen from the typical C-2 ^{13}C-NMR shifts occurring at δ = 99.3−103.1[3b,c,10]. Addition of acetyl chloride increases the

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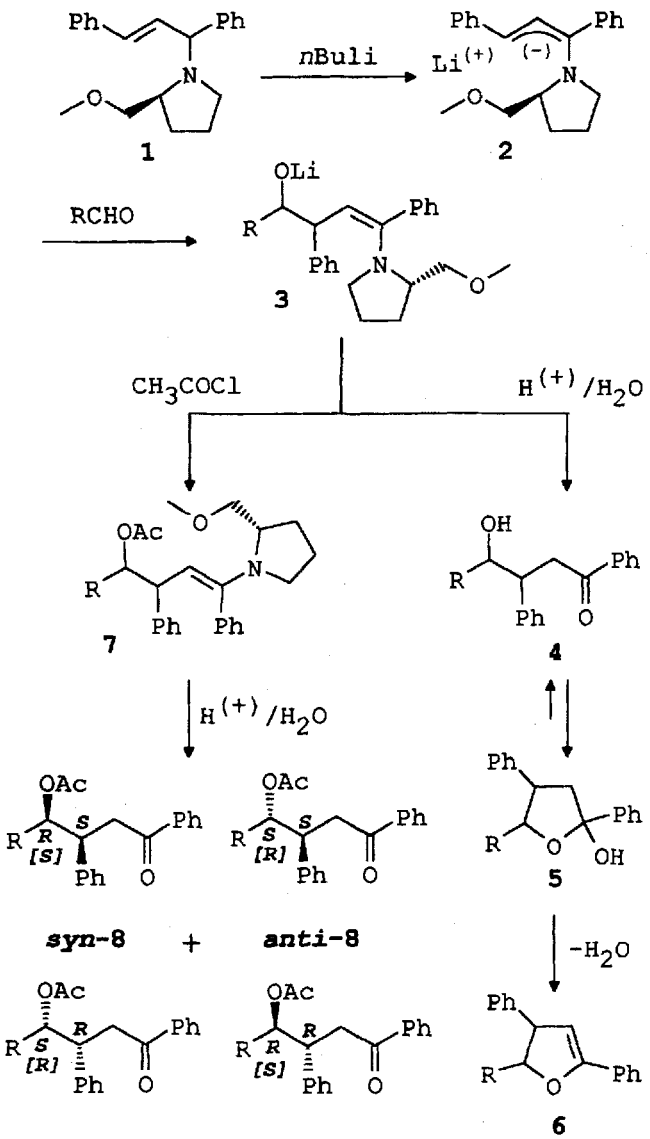
polarity of the solution and permits the isomerisation[3b,c] of the (*Z*) enamines **3** obtained first to the more stable (*E*) isomers **7**.

Scheme 1



a: R = Ph **b**: R = tC_4H_9
c: R = iC_3H_7 **d**: R = C_2H_5
e: R = nC_3H_7 **f**: R = nC_6H_{13}
g: R = iC_4H_9 **h**: R = iC_5H_{11}
i: R = cC_6H_{11} **j**: R = H

The (*E*) enamines **7** were isolated after the addition of anhydrous methanol followed by removal of all solvents in vacuo and are suitable for the determination of the induced diastereoselectivity (see below).

When **7** is hydrolysed with 2 N HCl, the 4-acetoxy ketones **8** are obtained as mixtures of the *syn* and *anti* diastereomers[11]. The observed selectivity is low; the ratio varying from approximately 1:1 to 1:3, depending slightly on the reaction conditions employed. The chemical yields are fairly good (Table 1). If enolisable aldehydes are used, the yield can be remarkably increased by the addition of 1 equiv. of LiBr[12] to the aldehyde before reaction (Table 1, entry 17).

Table 1. Chiral 4-acetoxy-1,3-diphenyl ketones **8**

Entry	8	R	Solvent	Temp. [°C]	Yield [%]	Ratio[a] *syn*:*anti*	*ee* [%] *syn*	*ee* [%] *anti*
1	a	Ph	THF	-78	74	50:50	9[c]	9[c]
2	a	Ph	THF/HMPT	-78	84	54:46	36[c]	18[c,e]
3	a	Ph	TBME	0	80	59:41	>90[c,d]	>90[c,d]
4	a	Ph	TBME/LiBr	0	66	68:32	>90[c]	>90[c]
5	a	Ph	TBME/(K^+)[f]	-78	91	18:82[b]	13[c]	9[c]
6	a	Ph	TBME/LiI	0	52	43:57[b]	>90[c]	>90[c]
7	b	tC_4H_9	TBME	0	73	84:16	>90[c]	>90[c]
8	b	tC_4H_9	TBME/LiBr	0	50	95:5	–	–
9	c	iC_3H_7	THF	-78	64	60:40	44[d]	59[d]
10	c	iC_3H_7	TBME	0	72	61:39	93[d]	93[d]
11	c	iC_3H_7	TBME	-78	70	38:62[b]	95[d]	88[d]
12	c	iC_3H_7	TBME	+30	66	66:34	61[d]	78[d]
13	c	iC_3H_7	TBME/LiBr	0	74	58:42	>90[c]	>90[c]
14	c	iC_3H_7	diethyl ether	0	79	72:28	>90[d]	94[d]
15	d	C_2H_5	THF	-78	69	60:40	22[d]	–
16	d	C_2H_5	TBME	0	66	56:44	>90[d]	>90[d]
17	d	C_2H_5	TBME/LiBr	0	76	53:47	>90[c,d]	>90[c,d]
18	e	nC_3H_7	THF	-78	69	67:33	35[d]	1[d]
19	e	nC_3H_7	TBME	0	76	58:42	94[d]	85[d]
20	e	nC_3H_7	TBME	-78	69	51:49	–	–
21	e	nC_3H_7	TBME/LiI	0	68	50:50	–	–
22	e	nC_3H_7	TBME/LiI	-78	61	37:63[b]	>90[d]	88[d]
23	f	nC_6H_{13}	THF	-78	70	64:36	45[d]	10[d]
24	f	nC_6H_{13}	TBME	0	77	56:44	>90[d]	>90[d]
25	g	iC_4H_9	THF	-78	62	61:39	27[d]	17[d]
26	g	iC_4H_9	TBME	0	77	59:41	97[d]	93[d]
27	h	iC_5H_{11}	THF	-78	71	55:45	37[d]	44[d]
28	h	iC_5H_{11}	TBME	0	79	57:43	94[d]	89[d]
29	i	cC_6H_{11}	THF	-78	60	65:35	49[d]	68[d]
30	i	cC_6H_{11}	TBME	0	72	63:37	>90[d]	>90[d]
31	j	H	TBME	0	45	–	48[g]	

[a] Determined by integration of the signals of the acetoxy group in the ^{1}H-NMR spectra of **8** (400 MHz; $CDCl_3/TMS_{int}$). – [b] Reversed simple diastereoselectivity. – [c] Determined by the signal height of the methyl signals of the acetoxy group in the ^{1}H-NMR spectra of **8** (100 MHz; $CDCl_3/TMS_{int}$), shift reagent: $Pr(hfc)_3$. – [d] Determined by integration of the vinylic signals in ^{1}H-NMR spectra of **7** (400 MHz; $CDCl_3/TMS_{int}$). – [e] Reversed course of asymmetric induction. – [f] K^+ used as counterion. – [g] Determined by the signal height of C-4 in the ^{13}C-NMR spectrum of **8** (25 MHz; $CDCl_3/TMS_{int}$), shift reagent: $Pr(hfc)_3$.

Simple Diastereoselectivity

The simple diastereoselectivity of the reaction could be determined by ^{1}H-NMR spectroscopy for the acetoxy ketones **8** by using the sharp singlet of the acetoxy group located at about $\delta = 2$.

In addition, the assignment of the relative configuration was possible on the basis of the magnitude of the coupling constants beween the protons at C-3 and C-4, which resonate at about $\delta = 5-6$. Two constants were observed; one of the order of magnitude of 4–5 Hz, the other being 9–10 Hz. From the work of House et al.[13] the coupling constants of 2,3-chiral aldol products are known. The *anti* coupling constant is nearly twice as large (6–9 Hz) as the *syn* coupling constant (2–4 Hz). This behaviour seems to be valid for homoaldol products, too. In one case, Hoppe

et al.[14] found an *anti* coupling constant of 3.2 Hz and a *syn* coupling constant of 1.8 Hz. In analogy to these results, we therefore assign the *syn* configuration to the isomer exhibiting the smaller coupling constant. The acetoxy ketone **8** isomer with the larger coupling constant then possesses the *anti* configuration. The 3-H/4-H coupling constant may only be determined in the case of adducts with α-branched aldehydes (**8b**, **8c**, **8h**, **8i**). No separation of the 4-H signals of the *syn* and *anti* isomers could be achieved with the β-branched (**8g**) or the unbranched aldehydes (**8d**–**f**). In these cases we used chemical shift differences for the assignment.

For the acetoxy ketones **8b**, **8c**, **8h**, and **8i**, a *syn*/*anti* assignment of the acetoxy singlet at about δ = 2 is possible on the basis of the 4-H signal intensities. With all aliphatic compounds, the signals of the *syn* diastereomers are located downfield compared to the signals of the *anti* diastereomers. If one assumes that the relative acetoxy proton signal positions for the *syn* and *anti* isomers are not changed by less branched alkyl groups, assignment of the *syn* and *anti* configurations to **8d**, **8e**, **8f**, and **8g** is possible.

This assumption was shown to be valid in the case of the acetoxy ketone **8e**. Here decoupling experiments reveal two 4-H doublets with different coupling constants. Comparison of the signal intensities results in an assignment of the downfield signal of the acetoxy protons to *syn*-**8e**.

The stereochemical assignment for the benzaldehyde adduct **8a** is only tentative. In this case, the difference in the observed coupling constants is small (7.7/8.6 Hz), and the chemical shifts of the acetoxy group reveal a behaviour opposite to that of the aliphatic derivatives with the lower coupling derivative resonating downfield.

The simple diastereomeric ratios listed in Table 1 favour the *syn* isomers slightly (entries 2–4, 7–10, 12–21, 23–30). All attempts to increase the selectivity were less successful. The choice of solvent and/or addition of LiBr (entries 4, 8, 13, 17) to the aldehyde before addition has little influence on the diastereomeric ratios. On the other hand, addition of LiI or a decrease of the temperature or a combination of both leads to a predominance of the *anti* isomer in TBME (entries 6, 11, 22). However, since compound **2** could not be completely dissolved in TBME at −78 °C a heterogeneous reaction occurred.

The *anti*-**8a** diastereomer can be obtained in high excess by using the potassium instead of the lithium compound in TBME (entry 5).

As expected, the size of the alkyl group influences the selectivity; the smaller the group, the smaller the ratio (e.g. entries 10, 16, 19). High selectivity in favour of the *syn* diastereomer was observed only with the bulky *tert*-butyl group.

Preparative separation of the diastereomers with HPLC is possible. For example, compound **8a** can be separated under the following conditions: LiChrosorb RP 18, CH_3CN/H_2O (50:50).

Induced Diastereoselectivity

The induced diastereoselectivity of the homoaldol reaction of enamines **7** was determined by ^{1}H-NMR spectroscopy. Alternatively, the use of chiral shift reagents like-tris[3-(2,2,3,3,4,4,4-heptafluoro-1-hydroxybutylidene)-*d*-camphorato]praseodym(III) [Pr(hfc)$_3$] with the acetoxy ketones **8** was found to be less successful, since partial overlapping of the acetoxy signals with the shift reagent signals in the ^{1}H-NMR spectra occurs and, in addition, a high concentration of Pr(hfc)$_3$ is necessary.

Because the enamines **7** are very easily hydrolysed, they can only be isolated by nonaqueous workup before being analysed. The ^{1}H-NMR spectra obtained show four doublets for the vinyl proton (see Table 2). The stereocentre of the SMP group of **7** is fixed; therefore, the diastereomeric ratios of the enamines **7** reflect the enantiomeric ratios of the acetoxy ketones **8**. The well-known *syn*/*anti* ratios of **8** allowed the assignment of the two upfield signals of **7** to the *syn* diastereomer.

Table 2. Signals (main diastereomers marked italic) of the vinylic protons in the ^{1}H-NMR spectra of **7** (400 MHz, C_6D_6/TMS$_{int}$)

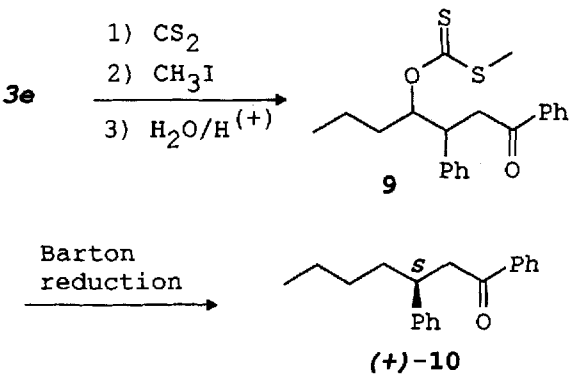
		H_{vinyl}			
7	R	*syn*		*anti*	
		δ	*J* [Hz]	δ	*J* [Hz]
a	Ph	4.56	10.6	4.94	10.6
		4.57	*10.5*	*4.95*	*10.4*
c	iC_3H_7	4.62	10.1	4.80	10.4
		4.67	*10.4*	*4.90*	*10.4*
d	C_2H_5	4.65	10.4	4.86	10.9
		4.73	*10.5*	*4.93*	*10.5*
e	nC_3H_7	4.67	10.3	4.83	10.4
		4.74	*10.5*	*4.90*	*10.5*
f	nC_8H_{13}	4.66	10.4	4.81	10.6
		4.73	*10.6*	*4.89*	*10.6*
g	iC_4H_9	4.70	10.3	4.82	10.6
		4.76	*10.5*	*4.89*	*10.6*
h	iC_5H_{11}	4.63	10.1	4.79	10.5
		4.69	*10.4*	*4.86*	*10.4*
i	cC_6H_{11}	4.65	10.2	4.81	10.4
		4.69	*10.4*	*4.93*	*10.5*

Absolute Configuration

No example could be found in the literature for homoaldol products of 1,3-diphenyl ketones with known absolute configuration. However, the configuration of some 3-alkylated 1,3-diphenyl ketones is known[3b,c,15]. Thus, the assignment of the absolute configuration in the case of acetoxy ketones **8** becomes possible by reduction of the protected hydroxyl group. The often discussed problems[16,17] encountered in the deoxygenation of a secondary alcohol can be solved by using two variants of the Barton reaction[18–21]. Reduction of compound **8e** was performed with both methods. The 4-(lithiooxy) enamine **3e**, generated in TBME, was treated with CS_2 to give the corresponding dithiocarbonate **9** after alkylation with methyl iodide followed by hydrolysis (*syn*:*anti* = 66:34). The crude dithiocarbonate **9** was then reduced with nBu$_3$SnH · Et$_3$B[18,19] or with tris(trimethylsilyl)silane (TTMSS)[20,21] in the presence of azoisobutyronitrile (AIBN) yielding the 1,3-diphenylheptanone **10**. The latter variant is more attractive because higher yields were obtained. Both methods afford **10** with a positive specific optical rotation {Sn variant: $[\alpha]_D^{22}$ = +9.72 (*c* = 1.780, CCl_4) ≡ 52% *ee*; Si variant: $[\alpha]_D^{22}$ = +10.23 (*c* = 2.619, CCl_4) ≡ 54% *ee*}. Based on the known data[3b,c], C-3 of ketone **10** and thus in acetoxy ketone **8** has the (*S*) configuration.

The enantiomeric excess obtained after deoxygenation is lower as compared to that found by the enamine method (Table 1, entry 19). To exclude the possibility that the *syn* and the *anti* isomer possess different absolute configurations at C-3, thus causing a lower optical purity after reduction, we investigated the reduction of **9**, formed in TBME/LiI. The application of these conditions resulted in a reversed simple diastereoselectivity (*syn*:*anti* = 41:59) leading to ketone **10** also with (3*S*) configuration {$[\alpha]_D^{22}$ = +8.48 (*c* = 2.276, CCl_4) ≡ 45% *ee*). The enantiomeric excess again decreases during deoxygenation (Table 1, entry 22).

Scheme 2



It is obvious from these experiments that the high induction found occurs at C-3 in the homoaldol product **8e**. The absolute configuration at this carbon atom is (3*S*). The observed decrease in the enantiomeric excess after deoxygenation may be the result of the known radical mechanism of the reduction[18,20], which perhaps generates a stereochemically unstable benzyl radical in a side reaction.

In the ^{1}H-NMR spectrum of the corresponding enamine **7e**, the more intensive part of the vinyl signal for the *syn* isomer as well as for the *anti* isomer is shifted downfield. The same behaviour is observed in the ^{1}H-NMR spectra of **7a**, **c**–**i**; the more intensive peaks of the signal of the vinyl proton of the *syn* and *anti* isomers are shifted downfield in all cases. This considerably leads to the assumption that all the acetoxy ketones **8a**, **c**–**i** behave uniformly and possess predominantly (3*S*) configuration. Because of the well-known relative configuration, the absolute configuration of the predominating enantiomer of the *unlike syn* diastereomers **8c**–**i** can thus be assigned to (3*S*,4*R*) and the *like anti* diastereomers to (3*S*,4*S*). In the case of **8a** (R = Ph), the priority sequence of the substituents at C-4 is changed as compared to **8c**–**i**. Here the designation in parenthesis is (tentatively) valid (see Scheme 1).

Influence of Aldehyde Structure, Temperature, Additives and Solvent on the Asymmetric Induction

To improve the asymmetric induction, we first varied the size of the aldehyde employed, but observed no significant influence (see Table 1). Only in THF is the enantiomeric excess of the *syn* isomers slightly higher than that of the *anti* isomers when β-branched or unbranched aldehydes are used (Table 1, entries 18, 23, 25). On the other hand, α-branched aldehydes reverse this effect (Table 1, entries 9, 27, 29).

If TBME is employed as the solvent, temperature has no influence in the range from −78 to 0°C (Table 1, entries 10, 11). Only the reaction at +30°C results in a decreased enantiomeric excess (Table 1, entry 12). This behaviour parallels completely that found in alkylation reactions of **2**[3]. In contrast to this is the significant effect of temperature on the simple diastereoselectivity (Table 1, entry 11).

At least the addition of lithium halides does not significantly influence the induction obtained (Table 1, entries 4, 6, 8, 13, 17, 22).

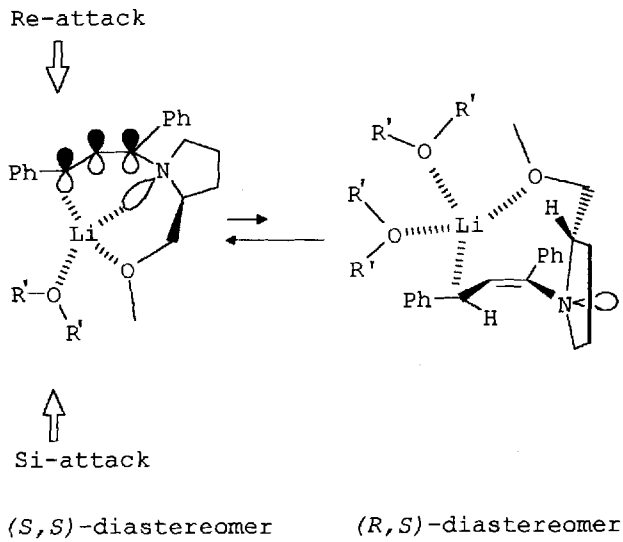
As observed in similar alkylation reactions[3], only the solvent has a significant influence on the asymmetric induction for this homoaldol reaction. The use of THF results in asymmetric induction up to 68% *ee*. In TBME, the selectivity is increased up to 97% *ee* (see Table 1). Low induction was observed in TBME only with formaldehyde (Table 1, entry 31). This may be attributed to the more polar reaction medium caused by partial oligomerisation of the electrophile to give a complexing polyether.

Discussion

The structure of 3-lithio-1-[(*S*)-2-(methoxymethyl)pyrrolidino]-1,3-diphenylpropene (**2**) in solution as well as in the solid state was extensively studied[3,22].

On the basis of the ^{1}H-, ^{13}C-, and ^{6}Li-NMR data as well as X-ray structure analysis, determination of aggregation, UV data, and MNDO calculations, the following picture has evolved (see Scheme 3). In less solvating solvents like diethyl ether or TBME as well as in the solid state, only the (*S*,*S*) diastereomer was found. On the other hand, an equilibrium of two diastereomeric (1-aminoallyl)metal compounds was shown to be present in solvents with better complexing ability like THF or with the use of the larger potassium as the counterion. The ratio of the (*S*,*S*) diastereomer to the (*R*,*S*) diastereomer is about 90:10. The amino substituent is located in the *endo* position in both isomers.

Scheme 3



X-ray results[22] as well as UV spectroscopy[2a] demonstrate that, for the (*S,S*) diastereomer, the planes of the allyl system and the amino group are twisted with respect to each other. The nitrogen lone pair in the (*S,S*) diastereomer is directed inside; therefore, the chelating methoxymethyl group of SMP lies on the *si* side of the allylic plane. The lithium is coordinated by the oxygen and the nitrogen atom in SMP and, in addition, by the allylic C-3 in such a manner that a (*S*)-configurated chiral centre is created. Perhaps one solvent molecule could occupy the forth coordination site on lithium.

Semiempirical calculations revealed a structure for the second *endo* isomer in which the nitrogen lone pair is directed outward with the chelating methoxy group now located on the *re* side of the allylic plane. The lithium is coordinated only by the oxygen atom of SMP and the allylic C-3, so that C-3 possesses an (*R*)-configured chiral centre. As experimentally observed, this structure should be favoured by stronger external solvation since the internal solvation is weakened by the loss of the N–Li contact. Probably, two solvent molecules are now coordinated to lithium.

Electrophilic assistance, i.e. coordination of the lithium ion with the carbonyl oxygen, may precede the addition of the aldehyde. A six-membered cyclic transition-state structure[4,6,23], often proposed in carbonyl addition reactions, is excluded here because of the experimentally observed exclusive selectivity at C-3 of this homoaldol reaction. A charge density-controlled reaction of the allyl anion seems more likely[24].

Precoordination of the aldehyde is supported by the stereochemistry observed. The (*S,S*) diastereomer is the only one found in TBME[3]. Alkylation in this solvent occurs with inversion of configuration, giving the (*R*)-configured centre. Hydroxyalkylation on the other hand occurs with retention of configuration. Therefore, the allylic system is attacked by the aldehyde in a metalloretentive mode, as expected from a precoordinated species.

Reaction in the presence of lithium halides (Table 1, entries 4, 6, 8, 13, 17, 22) seems to argue against such a model. Here the aldehyde oxygen is already complexed with the lithium halide, and coordination with the allylic lithium should be unfavourable. However, a decrease in the asymmetric induction was not observed. The assumption of a doubly complexed carbonyl group by coordination of the aldehyde-LiX complex with the counterion of the allylic system may explain the observed results.

The use of a more polar solvent like THF or the application of a larger counterion like potassium results in the formation of some (*R,S*) diastereomer. The aldehyde may therefore attack the allylic system from the *re* side as well, and the asymmetric induction should decrease, as was observed (see Table 1). The use of the solvent combination THF/HMPT even leads to a reversed course of induction in the case of the *anti* isomer (Table 1, entry 2).

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Experimental

Melting points: Tottoli apparatus (Büchi). – Elemental analyses: Elementanalysator MOD 1106 (Carlo Erba). – HPLC: Gynkotek Model 480, *L* = 25 cm, *id* = 8 mm; Knauer Differentialrefraktometer; Knauer UV-Photometer (254 nm). – GC: HRGC Mega 5300 (Carlo Erba), OV-101, *L* = 10 m, *id* = 0.25 mm. – Specific optical rotations: Polarimeter 141 (Perkin-Elmer); $[\alpha]_D^T$ in [degree · $cm^2 \cdot 10^{-1} \cdot g^{-1}$]. – Kugelrohr distillation: Glasrohrofen GKR-50 (Büchi). – MS: Mat-311, Mat-311A (Varian). – ^1H NMR: Varian XL 100, Bruker AM 400; ^{13}C NMR: Varian XL 100, Bruker AM 400; internal standard TMS (δ = 0.00), firstorder analysis of multiplets; partly overlapping peaks of aromatic carbon atoms in ^{13}C-NMR spectra are not considered. – The boiling pressures given are only approximate; the boiling points are the oven temperatures and are about 20°C too high.

Reagents and Solvents: Argon (99.99%, Firma Messer-Griesheim), dried and scrubbed clean from CO_2 by $CaCl_2$, and KOH was used for reactions necessitating the exclusion of moisture and air. – *THF and diethyl ether:* Commercial ethers were stored for a few days over solid KOH. The ethers were then decanted, distilled over fresh KOH, refluxed over Na/benzophenone, distilled and stored in brow bottles under Ar and over Na. – *TBME* was refluxed over Na/benzophenone, distilled and stored in a brown bottle under Ar and over Na. – *Benzene and toluene:* The solvents were extracted with conc. H_2SO_4 until the H_2SO_4 was only slightly yellow. After refluxing over Na/benzophenone and distillation, they were stored under Ar and over Na. – *HMPT* was stirred for 3 d over CaH_2, distilled and stored under Ar and over CaH_2. – *Methanol:* 1 l of methanol and 0.5 g of Mg filings were refluxed. After the metal had completely dissolved with foaming (ca. 30 min), 4.5 g of additional Mg was added in small portions. The methanol was then refluxed for 3 h, distilled and stored under Ar. – *Potassium tert-butylate* was heated at 100°C with continuous stirring in an oil-pump vacuum for 8–10 h and then stored under Ar. – *Acetyl chloride and aldehydes* were distilled in a Vigreux column (20 cm) and stored under Ar. – C_6D_6 was stored under Ar and over molecular sieves (3 Å). – *n-Butyllithium* in hexane was obtained from the Metallgesellschaft Frankfurt. The content was determined by titration with diphenylacetic acid[25]. – *LiBr* and *LiI* were heated at 100°C with stirring in an oil-pump vacuum for 8 h and stored under Ar in the dark. – *Phenylmagnesium bromide* was prepared according to ref.[26]. – *(L)-Proline* was obtained from DEGUSSA AG, Wolfgang, and was dried over silica gel for 7 d. – *SMP* was synthesised according to ref.[2a]. – *2-[(S)-2-(Methoxymethyl)pyrrolidino]-4-phenyl-3-butenenitrile and 3-[(S)-2-(methoxymethyl)pyrrolidino]-1,3-diphenylpropene* (**1**) were synthesised according to ref.[3b].

Addition of Aldehydes to Allylamine **1** *Yielding 4-(Lithiooxy) Enamines* **3**. – *General Procedure A:* An evacuated and heated 100-ml two-necked flask with a thermometer and a three-way cock is flushed with Ar and charged with a solution of 1.54 g (5 mmol) of allylamine **1** in 10 ml of anhydrous solvent (see Table 1). 5 mmol of *n*BuLi in hexane (1.6 M) is then added dropwise within 5 min at 0°C. After stirring (THF: 1 h; TBME: 12 h), a solution of 6.25 mmol of aldehyde in 3 ml of anhydrous solvent is added dropwise with stirring at the given temp. (see Table 1). Stirring is continued over a 2-h period until a yellow solution is obtained. If the potassium salt is desired, the solution of the lithium salt in TBME is cooled to –78°C, and 1.14 g (10 mmol) of *t*BuOK in 30 ml of anhydrous TBME is added, and the mixture is stirred for 1 h. If the aldehyde is activated with LiX (X = Br, I), a mixture of 6.25

mmol of aldehyde and 6.25 mmol of LiX in 30 ml of anhydrous solvent is added to the solution of **2** at the given temp.

General Procedure B: As Genral Procedure A, but on a 2-mmol scale.

4-Acetoxy Enamines **7**. – *General Procedure:* 0.16 g (2 mmol) of acetyl chloride is added to a stirred solution of **3** obtained according to procedure B. The solution is then warmed up to room temp., and stirring is continued for 2 h (LiCl precipitates in TBME and diethyl ether). Half of the solvent is then removed and 5 ml of anhydrous methanol is added. After stirring for 1–2 h, all solvents are fully removed in an oil-pump vacuo. Part of the residue is dissolved in 1.5 ml of C_6D_6, and an NMR analysis is performed.

4-Acetoxy-1,3-diphenyl Ketones **8**. – *General Procedure:* 0.39 g (5 mmol) of acetyl chloride is added to a stirred solution of **3** obtained by procedure A. The reaction mixture is then warmed up to room temp., and stirring is continued for 2 h (LiCl precipitates in TBME and diethyl ether). 10 ml of the solvent used and 50 ml of diethyl ether are then added. After acidification with 10 ml of 2 N HCl, the reaction mixture is further stirred for 2 h at room temp. The organic layer is washed with water (3 × 20 ml) and the aqueous phase extracted with diethyl ether (3 × 30 ml). The combined organic layers are dried with $MgSO_4$, concentrated in vacuo, and the residue is purified by kugelrohr distillation yielding a mixture of *syn* and *anti* acetoxy ketones.

4-Acetoxy-1,3,4-triphenyl-1-butanone (**8a**): General procedure A, solvent TBME with the use of 1.54 g (5 mmol) of allylamine **1**, 0.66 g (6.25 mmol) of benzaldehyde and 0.39 g (5 mmol) of acetyl chloride yields 1.41 g (80%) of a yellow-orange solid (*syn*:*anti* = 60:40). B.p. 110°C/0.01 Torr, m.p. 136°C. – ^{1}H NMR ($CDCl_3$/TMS_{int}): δ = 1.87 (s, *syn*), 1.93 (s, *anti*), (3H, $COCH_3$); ABX spin system, 3.13–3.40 AB part (*syn*), J_{AX} = 5.0, J_{BX} = 8.8, J_{AB} = 17.1 Hz, 3.39–3.52 AB part (*anti*), J_{AX} = 7.8, J_{BX} = 5.7, J_{AB} = 16.8 Hz, 3.9–4.1 X part (*syn* and *anti*), (3H, $CHCH_2$); 5.96 (d, *anti*, *J* = 8.6 Hz), 6.07 (d, *syn*, *J* = 7.7 Hz), (1H, OCH); 7.0–7.6 (m, 13H, $H_{aromat.}$); 7.7–7.8, 7.9–8.0 (2 m, 2H, H_o of COPh). – ^{13}C NMR ($CDCl_3$/TMS_{int}): δ = 20.9 (*syn*), 21.0 (*anti*), ($COCH_3$); 40.6 (CH_2); 46.3 (*syn*), 47.1 (*anti*), (CH_2CH); 78.3 (*syn*), 79.3 (*anti*), (OCH); 137.0 (*syn*), 137.1 (*anti*), 138.6 (*syn*), 138.8 (*anti*), 140.0 (*syn*), 140.2 (*anti*), (C_i^1, C_i^3 and C_i^4); 169.8 (*syn*), 170.1 (*anti*), (OC=O); 197.6 (*syn*), 198.0 (*anti*), (C=O). – $C_{24}H_{22}O_3$ (358.4): calcd. C 80.42, H 6.19; found C 80.48, H 6.18.

4-Acetoxy-5,5-dimethyl-1,3-diphenyl-1-hexanone (**8b**): General procedure A in TBME with the use of 1.54 g (5 mmol) allylamine **1**, 0.54 g (6.25 mmol) of pivalaldehyde, and 0.39 g (5 mmol) of acetyl chloride yields 1.23 g (73%) of a light yellow, highly viscous liquid. According to ^{1}H NMR, **8b** is a mixture of diastereomers *syn*:*anti* = 83:17. B.p. 105°C/0.006 Torr. – ^{1}H NMR ($CDCl_3$/TMS_{int}): δ = 0.82 [s, 9H, $C(CH_3)_3$]; 1.81 (s, *anti*), 2.11 (s, *syn*), (3H, $OCOCH_3$); 2.9–3.0, 3.2–3.5 (m, 2H, CH_2); 3.8–4.0 (m, 1H, CH_2CH); 5.09 (d, *syn*, *J* = 3.0 Hz), 5.20 (d, *anti*, *J* = 8.3 Hz), (1H, OCH); 7.1–7.6 (m, 8H, $H_{aromat.}$); 7.8–7.9 (m, 2H, H_o of COPh). – ^{13}C NMR ($CDCl_3$/TMS_{int}): δ = 20.7 (*anti*), 21.0 (*syn*), ($OCOCH_3$); 26.6 (*anti*), 26.8 (*syn*), [$C(CH_3)_3$]; 35.9 (*syn*), 36.0 (*anti*), [$C(CH_3)_3$]; 41.1 (*syn*), 42.2 (*anti*), (CH_2CH); 43.4 (*anti*), 44.5 (*syn*), (CH_2); 82.2 (*syn*), 83.3 (*anti*), (CHO); 171.0 (*syn*), 171.3 (*anti*), (OC=O); 197.9 (*syn*), 198.1 (*anti*), (C=O). – $C_{22}H_{26}O_3$ (338.4): calcd. C 78.07, H 7.74; found C 78.17, H 7.66.

4-Acetoxy-5-methyl-1,3-diphenyl-1-hexanone (**8c**): General procedure A, solvent TBME with the use of 1.54 g (5 mmol) of allylamine **1**, 0.45 g (6.25 mmol) of 2-methylpropanal, 0.543 g (6.25 mmol) of LiBr, and 0.39 g (5 mmol) of acetyl chloride yields 1.20 g (74%) of a light yellow, highly viscous liquid. According to ^{1}H NMR, **8c** is a mixture of diastereomers *syn*:*anti* = 56:44. B.p. 85°C/0.01 Torr. – ^{1}H NMR ($CDCl_3$/TMS_{int}): δ = 0.81 (d, *anti*, *J* = 6.9 Hz), 0.85 (d, *syn*, *J* = 6.7 Hz), 0.90 (d, *anti*, *J* = 6.7 Hz), 1.00 (d, *syn*, *J* = 6.7), [6H, $(CH_3)_2CH$]; 1.5–1.8 [m, 1H, $(CH_3)_2CH$]; 1.96 (s, *anti*), 2.04 (s, *syn*), (3H, $OCOCH_3$); 3.2–3.4 (m, 2H, CH_2); 3.7–3.9 [m, 1H, CH(Ph)]; 5.07 (d/d, *syn*, J_{43} = 4.7, J_{45} = 8.1 Hz), 5.21 [d/d, *anti*, J_{43} = 9.9, J_{45} = 3.1 Hz, 1H, CH(OAc)]; 7.1–7.6 (m, 8H, $H_{aromat.}$); 7.8–7.9 (m, 2H, H_o of COPh). – ^{13}C NMR ($CDCl_3$/TMS_{int}): δ = 15.4, 18.2, 19.4, 20.1, 20.9 [$OCOCH_3$ and $(CH_3)_2CH$]; 29.2 (*anti*), 30.0 (*syn*), [$(CH_3)_2CH$]; 41.9 (*anti*), 42.3 (*syn*), (CH_2); 42.0 (*syn*), 43.2 (*anti*), [CH(Ph)]; 80.6 (*anti*), 80.7 (*syn*), [CH(OAc)]; 170.8 (*syn*), 171.3 (*anti*), ($OCOCH_3$); 197.8 (*syn*), 198.3 (*anti*), (C=O). – $C_{21}H_{24}O_3$ (324.4): calcd. C 77.75, H 7.46; found C 78.02, H 7.31.

4-Acetoxy-1,3-diphenyl-1-hexanone (**8d**): General procedure A in TBME with the use of 1.54 g (5 mmol) of allylamine **1**, 0.36 g (6.25 mmol) of propanal, and 0.39 g (5 mmol) of acetyl chloride yields 0.99 g (64%) of a light yellow, viscous liquid. According to ^{1}H NMR, **8d** is a mixture of diastereomers *syn*:*anti* = 58:42. B.p. 87°C/0.01 Torr. – ^{1}H NMR ($CDCl_3$/TMS_{int}): δ = 0.80 (t, *anti*, *J* = 7.4 Hz), 0.87 (t, *syn*, *J* = 7.4 Hz), (3H, CH_3CH_2); 1.3–1.6 (m, 2H, CH_3CH_2); 1.95 (s, *anti*), 2.02 (s, *syn*), (3H, $OCOCH_3$); 3.2–3.5 (m, 2H, CH_2C=O); 3.6–3.8 (m, 1H, $OCHCHCH_2$); 5.16 (m_c, 1H, OCHCH); 7.1–7.6 (m, 8H, $H_{aromat.}$); 7.8–8.0 (m, 2H, H_o of COPh). – ^{13}C NMR ($CDCl_3$/TMS_{int}): δ = 9.3 (*anti*), 10.1 (*syn*), (CH_3CH_2); 21.0 ($OCOCH_3$); 25.0 (*syn*), 25.4 (*anti*), (CH_3CH_2); 40.8 (*syn*), 41.6 (*anti*), (CH_2CO); 43.7 (*syn*), 44.9 (*anti*), ($OCHCHCH_2$); 77.6 (*syn*), 78.2 (*anti*), ($OCHCHCH_2$); 170.8 (*syn*), 171.1 (*anti*), (OC=O); 198.0 (*syn*), 198.3 (*anti*), (C=O). – $C_{20}H_{22}O_3$ (310.4): calcd. C 77.39, H 7.14; found C 77.63, H 7.19.

4-Acetoxy-1,3-diphenyl-1-heptanone (**8e**): General procedure A with the use of 1.54 g (5 mmol) of allylamine **1**, 0.45 g (6.25 mmol) of *n*-butanal, and 0.39 g (5 mmol) of acetyl chloride yields 1.23 g (76%) of a light yellow, viscous liquid. According to ^{1}H NMR, **8e** is a mixture of diastereomers *syn*:*anti* = 56:44. B.p. 100°C/0.01 Torr. – ^{1}H NMR ($CDCl_3$/TMS_{int}): δ = 0.78 (t, *anti*, *J* = 7.2 Hz), 0.85 (t, *syn*, *J* = 7.2 Hz), (3H, $CH_3CH_2CH_2$); 1.1–1.5 [m, 4H, $CH_3(CH_2)_2CH$]; 1.94 (s, *anti*), 2.01 (s, *syn*), (3H, $OCOCH_3$); 3.2–3.4 (m, 2H, CH_2CO); 3.6–3.8 [m, 1H, CH(Ph)]; 5.24 [m_c, 1H, CH(OAc)]; 7.1–7.6 (m, 8H, $H_{aromat.}$); 7.9–8.0 (m, 2H, H_o of COPh). – ^{13}C NMR ($CDCl_3$/TMS_{int}); δ = 13.8 ($CH_3CH_2CH_2$); 18.4 (*anti*), 19.0 (*syn*), ($CH_3CH_2CH_2$); 21.0 ($OCOCH_3$); 34.1 (*syn*), 34.8 (*anti*), ($CH_3CH_2CH_2$); 40.7 (*syn*), 41.5 (*anti*), (CH_2CO); 44.1 (*syn*), 45.4 (*anti*), [CH(Ph)]; 76.1 (*syn*), 76.9 (*anti*), [CH(OAc)]; 170.7 (*syn*), 171.0 (*anti*), (OC=O); 198.0 (*syn*), 198.2 (*anti*), (C=O). – $C_{21}H_{24}O_3$ (324.4): calcd. C 77.75, H 7.46; found C 77.95, H 7.18.

4-Acetoxy-1,3-diphenyl-1-decanone (**8f**): General procedure A in TBME with the use of 1.54 g (5 mmol) of allylamine **1**, 0.71 g (6.25 mmol) of heptanal, and 0.39 g (5 mmol) of acetyl chloride yields 1.41 g (77%) of a light yellow wax. According to ^{1}H NMR, **8f** is a mixture of diastereomers *syn*:*anti* = 59:41. B.p. 120°C/0.01 Torr. – ^{1}H NMR ($CDCl_3$/TMS_{int}): δ = 0.82 (t, *anti*, *J* = 7.3 Hz), 0.84 (t, *syn*, *J* = 6.7 Hz), [3H, $CH_3(CH_2)_5$]; 1.0–1.3 [m, 8H, $CH_3(CH_2)_4$]; 1.42 [m_c, 2H, $CH_3(CH_2)_4CH_2$]; 1.94 (s, *anti*), 2.01 (s, *syn*), (3H, $OCOCH_3$); 3.25–3.39 (m, 2H, $CHCH_2CO$); 3.6–3.8 [m, 1H, CH(Ph)], 5.18–5.25 [m, 1H, CH(OAc)]; 7.1–7.6 (m, 8H, $H_{aromat.}$); 7.8–8.0 (m, 2H, H_o of COPh). – ^{13}C NMR ($CDCl_3$/TMS_{int}): δ = 14.0 [$CH_3(CH_2)_5$]; 21.0 (*anti*), 21.1 (*syn*), ($OCOCH_3$); 2 × 22.5, 25.0 (*anti*), 25.6 (*syn*), 2 × 29.0, 31.6 (*anti*), 31.7 (*syn*), 32.0 (*syn*), 32.6 (*anti*), [$(CH_2)_5$]; 40.7 (*syn*), 41.5 (*anti*), ($CHCH_2CO$); 44.0 (*syn*), 45.3 (*anti*), [CH(Ph)]; 76.4 (*syn*), 77.1

(*anti*), [*C*H(OAc)]; 170.7 (*syn*), 171.0 (*anti*), (OC=O); 198.0 (*syn*), 198.3 (*anti*), (C=O). – $C_{24}H_{30}O_3$ (366.5): calcd. C 78.65, H 8.25; found C 78.73, H 7.97.

4-Acetoxy-6-methyl-1,3-diphenyl-1-heptanone (**8g**): General procedure A in TBME with the use of 1.54 g (5 mmol) of allylamine **1**, 0.54 g (6.25 mmol) of 3-methylbutanal, and 0.39 g (5 mmol) of acetyl chloride yields 1.30 g (77%) of a yellow, viscous liquid. According to ^{1}H NMR, **8g** is a mixture of diastereomers *syn*:*anti* = 63:37. B.p. 105°C/0.01 Torr. – ^{1}H NMR ($CDCl_3$/TMS_{int}): δ = 0.78, 0.80 (2 d appears as t, *anti*, each J = 6.7 Hz), 0.84 (d, *syn*, J = 6.5 Hz), 0.88 (d, *syn*, J = 6.7 Hz), [6H, $(CH_3)_2$CH]; 1.1–1.7 [m, 3H, $(CH_3)_2CHCH_2$]; 1.93 (s, *anti*), 2.00 (s, *syn*), (3H, OC-OCH_3); 3.2–3.5 (m, 2H, $CHCH_2CO$); 3.63 (m_c, *anti*), 3.69 (m_c, *syn*), [1H, C*H*(Ph)]; 5.30–5.37 [m, C*H*(OAc)]; 7.1–7.6 (m, 8H, $H_{aromat.}$); 7.8–8.0 (m, 2H, H_o of COPh). – ^{13}C NMR ($CDCl_3$/TMS_{int}): δ = 21.0 (*anti*), 21.1 (*syn*), 21.5 (*anti*), 22.0 (*syn*), 23.1 (*syn*), 23.5 (*anti*), 24.5 (*anti*), 24.7 (*syn*), [$OCOCH_3$ and $(CH_3)_2CH$]; 40.6 (*syn*), 41.0 (*syn*), 41.3 (*anti*), 42.0 (*anti*), ($CHCH_2CO$ and $CHCH_2CH$); 44.3 (*syn*), 45.9 (*anti*), [CH(Ph)]; 74.6 (*syn*), 75.4 (*anti*), [*C*H(OAc)]; 170.6 (*syn*), 171.0 (*anti*), (OC=O); 197.9 (*syn*), 198.2 (*anti*), (C=O). – $C_{22}H_{26}O_3$ (338.4): calcd. C 78.07, H 7.74; found C 78.10, H 7.85.

4-Acetoxy-5-ethyl-1,3-diphenyl-1-heptanone (**8h**): General procedure A in TBME with the use of 1.54 g (5 mmol) of allylamine **1**, 0.63 g (6.25 mmol) of 2-ethylbutanal, and 0.39 g (5 mmol) of acetyl chloride yields 1.39 g (79%) of a light yellow, highly viscous liquid. According to ^{1}H NMR, **8h** is a mixture of diastereomers *syn*:*anti* = 56:44. B.p. 110°C/0.02 Torr. – ^{1}H NMR($CDCl_3$/TMS_{int}): δ = 0.78 (t, *anti*, J = 7.0 Hz), 0.81 (t, *syn*, J = 7.4 Hz), 0.82 (t, *anti*, J = 7.4 Hz), 0.92 (t, *syn*, J = 7.4 Hz), [6H, $(CH_3CH_2)_2CH$]; 1.0–1.7 [m, 5H, $(CH_3CH_2)_2CH$]; 1.91 (s, *anti*), 1.96 (s, *syn*), (3H, $OCOCH_3$); 3.2–3.4 (m, 2H, $CHCH_2CO$); 3.82 (m_c, *syn*), 3.88 (m_c, *anti*), [1H, C*H*(Ph)]; 5.31 (d/d, *syn*, J_{43} = 5.7, J_{45} = 6.6 Hz), 5.41 (d/d, *anti*, J_{43} = 10.1, J_{45} = 1.7 Hz) [1H, C*H*(OAc)]; 7.1–7.6 (m, 8H, $H_{aromat.}$); 7.8–7.9 (m, 2H, H_o of COPh). – ^{13}C NMR($CDCl_3$/TMS_{int}): δ = 10.4 (*syn*), 11.0 (*syn*), 11.5 (*anti*), 12.0 (*anti*), [$(CH_3CH_2)_2CH$]; 20.7 (*syn*), 21.0 (*anti*), 21.6 (*syn*), 22.8 (*anti*), [$(CH_3CH_2)_2CH$]; 20.8 (*syn*), 20.9 (*anti*), (OC-OCH_3); 42.0 (*syn*), 42.1 (*syn*), 42.5 (*anti*), 43.1 (*anti*), [$(CH_3CH_2)_2CH$ and CH(Ph)]; 42.0 (*anti*), 42.3 (*syn*), ($CHCH_2CO$); 77.4 (*syn*), 77.8 (*anti*), [*C*H(OAc)]; 170.7 (*syn*), 171.3 (*anti*), (OC=O); 197.9 (*syn*), 198.4 (*anti*), (C=O). – $C_{23}H_{28}O_3$ (352.5): calcd. C 78.37, H 8.01; found C 78.47, H 8.00.

4-Acetoxy-4-cyclohexyl-1,3-diphenyl-1-butanone (**8i**): General procedure A in TBME with the use of 1.54 g (5 mmol) of allylamine **1**, 0.70 g (6.25 mmol) of cyclohexanecarbaldehyde, and 0.39 g (5 mmol) of acetyl chloride yields 1.30 g (72%) of a light yellow, highly viscous liquid. According to ^{1}H NMR; **8i** is a mixture of diastereomers *syn*:*anti* = 64:36. B.p. 115°C/0.01 Torr. – ^{1}H NMR ($CDCl_3$/TMS_{int}): δ = 0.9–1.9 (m, 11H, C_6H_{11}); 1.94 (s, *anti*), 2.04 (s, *syn*), (3H, $OCOCH_3$); 3.2–3.4 (m, 2H, $CHCH_2CO$); 3.8–3.9 [m, 1H, C*H*(Ph)]; 5.11 (d/d, *syn*, J_{43} = 4.5, J_{45} = 8.3), 5.15 (d/d, *anti*, J_{43} = 9.2, J_{45} = 3.8) [1H, C*H*(OAc)]; 7.1–7.6 (m, 8H, $H_{aromat.}$); 7.8–7.9 (m, 2H, H_o of COPh). – ^{13}C NMR ($CDCl_3$/TMS_{int}): δ = 2 × 20.9 ($OCOCH_3$); 25.6 (*syn*), 25.8 (*syn*), 26.0 (*anti*), 26.1 (*anti*), 2 × 26.2, 26.3 (*anti*), 28.3 (*syn*), 29.6 (*syn*), 30.5 (*anti*), [$(CH_2)_5$]; 39.2 (*anti*), 39.3 (*syn*), [$(CH_2)_4CHCH_2$]; 41.3 (*anti*), 42.2 (*syn*), ($CHCH_2CO$); 41.3 (*syn*), 42.3 (*anti*) [CH(Ph)]; 79.8 (*syn*), 80.5 (*anti*) [*C*H(OAc)]; 170.8 (*syn*), 171.2 (*anti*), (OC=O); 197.9 (*syn*), 198.3 (*anti*), (C=O). – $C_{24}H_{28}O_3$ (364.5): calcd. C 79.09, H 7.74; found C 79.04, H 7.62.

4-Acetoxy-1,3-diphenyl-1-butanone (**8j**): General procedure A in TBME with the use of 1.54 g (5 mmol) of allylamine **1**, 5 ml of a solution of 0.2 mol of thermally cracked paraformaldehyde in 120 ml of TBME, and 0.39 g (5 mmol) of acetyl chloride yields 0.63 g (45%) of a colourless, viscous liquid. B.p. 105°C/0.01 torr. – ^{1}H NMR ($CDCl_3$/TMS_{int}): δ = 1.96 (s, 3H, $OCOCH_3$); ABMXY spin system, 3.34 (part A, d/d, 1H, $HCHCO$), 3.44 (part B, d/d, 1H, $HCHCO$), 3.79 (part M, d/d/d/d appears as quint, 1H, CH_2CHCH_2), 4.26 (part X, d/d, 1H, $HCHOAc$), 4.32 (part Y, d/d, 1H, $HCHOAc$), J_{AB} = 17.1, J_{AM} = 7.0, J_{BM} = 6.7, J_{XY} = 10.9, J_{XM} = 7.3, J_{YM} = 6.3, J_{AY} = J_{AX} = J_{BX} = J_{BY} = 0 Hz; 7.1–7.6 (m, 8H, $H_{aromat.}$); 7.9–8.0 (m, 2H, H_o of COPh). – ^{13}C NMR ($CDCl_3$/TMS_{int}): δ = 20.8 (CH_3); 40.1 (CH); 41.5 (CH_2CO); 67.6 (CH_2OAc); 170.8 (OC=O); 197.9 (C=O). – $C_{18}H_{18}O_3$ (282.3): calcd. C 76.57, H 6.43; found C 76.89, H 6.34.

2,3-Dihydro-2,3,5-triphenylfuran (**6a**): 0.66 g (6.25 mmol) of benzaldehyde, 10 ml of TBME, and 50 ml of diethyl ether are added to a solution of **3** obtained according to general procedure A in TBME. After acidification with 10 ml of 2 N HCl, the reaction mixture is stirred for 2 h at room temp. The organic layer is then extracted with water (3 × 20 ml), and the combined aqueous phases are reextracted with diethyl ether (3 × 30 ml). The combined organic layers are dried with $MgSO_4$ and concentrated in vacuo. Purification of the residue by kugelrohr distillation yields 1.04 g (70%) of **6a** as a yellow solid. According to ^{1}H NMR, **6a** is a mixture of diastereomers[27] *cis*:*trans* = 67:23. B.p. 120°C/0.01 Torr, m.p. 75–105°C. – ^{1}H NMR ($CDCl_3$/TMS_{int}): δ = 4.21 (d/d, *trans*, $J_{3,4}$ = 2.8, $J_{2,3}$ = 6.8 Hz), 4.52 (d/d, *cis*, $J_{3,4}$ = 2.8, $J_{2,3}$ = 9.8 Hz), (1H, $CHCHCH$=C); 5.48 (d, *trans*, J = 2.8 Hz), 5.62 (d, *cis*, J = 2.8 Hz), (1H, CH=C); 5.47 (d, *trans*, J = 6.8 Hz), 6.00 (d, *cis*, J = 9.8 Hz), (1H, OCH); 6.89–7.43 (m, 13H, $H_{aromat.}$); 7.71–7.78 (m, 2H, H_o of C=CPh). – ^{13}C NMR ($CDCl_3$/TMS_{int}): δ = 54.4 (*cis*), 59.0 (*trans*), (C-3); 87.2 (*cis*), 90.8 (*trans*), (C-2); 98.8 (*trans*), 100.0 (*cis*), (C-4); 130.6, 130.7, 138.0 (*cis*), 139.5 (*trans*), 142.6 (*cis*), 143.9 (*trans*), (C_i^2, C_i^3, and C_i^5); 156.3 (*trans*), 157.0 (*cis*), (C-5). – $C_{22}H_{18}O$ (298.4): calcd. C 88.56, H 6.08; found C 88.16, H 6.14. – Calcd. 298.1358; found 298.1368.

Dithiocarbonate **9**: A solution of 0.46 g (6 mmol) of CS_2 in 3 ml of TBME is added to the stirred solution of **3e** obtained according to the general procedure A with TBME. The solution is then warmed up to room temp., and stirring is continued for 2 h. After cooling to 0°C, 0.85 g (6 mmol) of methyl iodide is added and the mixture again warmed up to room temp. Stirring is continued for 2 h and is followed by the addition of 10 ml of TBME and 50 ml of diethyl ether. After acidification with 10 ml of 1 N HCl, the reaction mixture is stirred for a further 2 h at room temp. The organic layer is extracted with water (3 × 20 ml), and the combined aqueous phases are reextracted with diethyl ether (3 × 30 ml). The combined organic layers are dried with $MgSO_4$ and concentrated in vacuo. The viscous yellow-orange residue is directly reduced as the crude product because decomposition occurs upon distillation.

Reduction of the Dithiocarbonate **9** *to (3S)-(+)-1,3-Diphenyl-1-heptanone* (**10**). – *Variant A:* 6.4 ml (6.4 mmol) of a 1 M solution of triethylborane in hexane is added at room temp. under Ar to a mixture of 2.15 g (5.8 mmol) of **9**, 1.86 g (6.4 mmol) of nBu_3SnH, and 20 ml of benzene in a 100-ml one-necked flask equipped with a three-way cock. After stirring for 30 min, 1.28 g of KF[28] and 13 ml of water are added, and the heterogeneous mixture is stirred vigorously. The organic layer is separated and the aqueous layer extracted with ethyl acetate (2 × 20 ml). The combined organic layers are dried with $MgSO_4$, the solvent is evaporated, and the tin compounds are separated from the residue by CC (silica gel/hexane). The remaining ketone **10** is eluted by ethyl acetate and the solution dried with $MgSO_4$. After removal of the solvent, the resi-

due is distilled (86 °C/0.01 Torr). The purity after distillation is only ≤87% (GC), thus necessitating additional purification by HPLC [LiChrosorb RP 18 (7 μm); CH_3CN/H_2O, 75:25]. 89 mg of **10** is obtained as a colourless solid. $[\alpha]_D^{22} = +9.72$ ($c = 1.780$, CCl_4) ≡ 52% *ee*.

Variant B: A mixture of 1.78 g (4.8 mmol) of **9**, 1.71 g (5.72 mmol) of tris(trimethylsilyl)silane (TTMSS), 0.082 g (0.5 mmol) of azoisobutyronitrile (AIBN), and 20 ml of toluene is placed in a 100-ml one-necked flask equipped with a reflux condenser and stirred for 2 h under Ar at 85–105 °C. After addition of 1 g of KF and 10 ml of water at room temp., the mixture is stirred vigorously. The work-up is as described above. 291 mg of **10** is obtained as a colourless solid. $[\alpha]_D^{22} = +10.23$ ($c = 2.619$, CCl_4) ≡ 54% *ee*. – According to gas chromatography and NMR spectroscopy, the compounds obtained are identical with the compound described in ref.[3b,c].

[1] [1a] A. Kramer, Diplomarbeit, University of Gießen, **1990**. – [1b] A. Kramer, Dissertation, University of Gießen, **1995**.

[2] [2a] G. Zimmermann, Dissertation, University of Gießen, **1985**. – [2b] H. Ahlbrecht, D. Enders, L. Santowski, G. Zimmermann, *Chem. Ber.* **1989**, *122*, 1995–2004. – [2c] L. Santowski, Dissertation, University of Gießen, **1992**.

[3] [3a] H. Sommer, Diplomarbeit, University of Gießen, **1986**. – [3b] H. Sommer, Dissertation, University of Gießen, **1990**. – [3c] H. Ahlbrecht, H. Sommer, *Chem. Ber.* **1990**, *123*, 829–836.

[4] Review: D. Hoppe, *Angew. Chem.* **1984**, *96*, 930–946; *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 932.

[5] [5a] V. J. Jephcote, A. J. Pratt, E. J. Thomas, *J. Chem. Soc., Chem. Commun.* **1984**, 800–802. – [5b] V. J. Jephcote, A. J. Pratt, E. J. Thomas, *J. Chem. Soc., Chem. Commun.* **1989**, 1521–1527; *J. Chem. Soc., Perkin Trans. 1*, **1989**, 1529–1535. – [5c] B. W. Gung, D. T. Smith, M. A. Wolf, *Tetrahedron Lett.* **1991**, *32*, 13–16 – [5d] B. W. Gung, A. J. Peat, B. M. Snook, D. T. Smith, *Tetrahedron Lett.* **1991**, *32* 453–456. – [5e] J. A. Marshall, D. M. Yashunsky, *J. Org. Chem.* **1991**, *56*, 5493–5495. – [5f] P. Bravo, P. Carrera, G. Resnati, C. Ticozzi, *J. Chem. Soc. Chem. Commun.* **1984**, 19–20. – [5g] H. Roder, G. Helmchen, E. Peters, K. Peters, H. v. Schnering, *Angew. Chem.* **1984**, *96*, 895–898. – [5h] S. Kano, T. Yokomatsu, S. Shibuya, *Tetrahedron Lett.* **1991**, *32*, 233–236. – [5i] H. Gais, H. Müller, J. Decker, R. Hainz, *Tetrahedron Lett.* **1995**, *36*, 7433–7436. – [5j] P. Beak, H. Du, *J. Am. Chem. Soc.* **1993**, *115*, 2516–2518.

[6] [6a] T. Krämer, D. Hoppe, *Tetrahedron Lett.* **1987**, *28*, 5149–5152. – [6b] D. Hoppe, T. Krämer, J. Schwark, O. Zschage, *Pure Appl. Chem.* **1990**, *62*, 1999–2006.

[7] [7a] D. Hoppe, O. Zschage, *Angew. Chem.* **1989**, *101*, 67–69; *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 69. – [7b] O. Zschage, D. Hoppe, *Tetrahedron* **1992**, *48*, 5657–5666.

[8] [8a] H. Ahlbrecht, G. Rauchschwalbe, *Synthesis* **1973**, 417–420. – [8b] G. Rauchschwalbe, Dissertation, University of Gießen, **1974**. – [8c] G. Rauchschwalbe, H. Ahlbrecht, *Synthesis* **1974**, 663–665.

[9] C. Sanner, Diplomarbeit, University of Gießen, **1985**.

[10] H. O. Kalinowski, S. Berger, S. Braun, *^{13}C-NMR-Spektroskopie*, Georg Thieme Verlag, Stuttgart, **1984**, p. 264.

[11] [11a] S. Masamune, S. A. Ali, D. L. Snitman, D. S. Garvey, *Angew. Chem.* **1980**, *92*, 573–575; *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 557. – [11b] S. Masamune, T. Kaiho, D. S. Garvey, *J. Am. Chem. Soc.* **1982**, *104*, 5521–5523. – [11c] D. Seebach, V. Prelog, *Angew. Chem.* **1982**, *94*, 696–702; *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 654.

[12] About the influence of Li^+ on the reactivity of carbonyl compounds see: [12a] J. L. Pierre, H. Handel, R. Perraud, *Tetrahedron* **1975**, *31*, 2795–2798. – [12b] H. Handel, J. L. Pierre, *Tetrahedron* **1975**, *31*, 2799–2802. – [12c] H. Handel, J. L. Pierre, *Tetrahedron Lett.* **1976**, 2029–2032. – [12d] A. Loupy, J. Seyden-Penne, P. Tchoubar, *Tetrahedron Lett.* **1976**, 1677–1680. – [12e] O. Eisenstein, J. M. Lefour, C. Minot, *Tetrahedron Lett.* **1976**, 1681–1684.

[13] H. O. House, D. S. Crumrine, A. Y. Teranishi, H. D. Olmstead, *J. Am. Chem. Soc.* **1973**, *95*, 3310–3324.

[14] D. Hoppe, R. Hanko, A. Brönneke, F. Lichtenberg, E. v. Hülsen, *Chem. Ber.* **1985**, *118*, 2822–2851.

[15] [15a] T. J. Leitereg, D. J. Cram, *J. Am. Chem. Soc.* **1968**, *90*, 4011–4018. – [15b] T. Imamoto, T. Mukaiyama, *Chem. Lett.* **1980**, 45–46. – [15c] K. Soai, T. Hayasaka, S. Ugajin, S. Yokoyama, *Chem. Lett.* **1988**, 1571–1572.

[16] D. H. R. Barton, W. B. Motherwell, *Pure Appl. Chem.* **1981**, *53*, 15–31.

[17] W. Hartwig, *Tetrahedron* **1983**, *39*, 2609–2645.

[18] D. H. R. Barton, S. W. McCombie, *J. Chem. Soc., Perkin Trans. 1*, **1975**, 1574–1585.

[19] K. Nozaki, K. Oshima, K. Utimoto, *Bull. Chem. Soc. Jpn.* **1990**, *63*, 2578–2583.

[20] M. Ballestri, C. Chatgilialoglu, K. B. Clark, D. Griller, B. Giese, B. Kopping, *J. Org. Chem.* **1991**, *56*, 678–683.

[21] D. Schummer, G. Höfle, *Synlett* **1990**, 705–706.

[22] H. Ahlbrecht, G. Boche, K. Harms, M. Marsch, H. Sommer, *Chem. Ber.* **1990**, *123*, 1853–1858.

[23] [23a] R. W. Hoffmann, *Angew. Chem.* **1982**, *94*, 569–580; *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 555. – [23b] Y. Yamamoto, K. Marujama, *Heterocycles* **1982**, *18*, 357–386.

[24] R. Gompper, H.-U. Wagner, *Angew. Chem.* **1976**, *88*, 389–401; *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 321.

[25] W. G. Kofron, M. Baclawski, *J. Org. Chem.* **1976**, *41*, 1879–1880.

[26] [26a] K. Nützel in *Methoden der organischen Chemie (Houben-Weyl)*, vol. XIII/2a, Georg Thieme Verlag, Stuttgart, **1973**, p. 54. – [26b] Organikum, VEB Deutscher Verlag der Wissenschaften, Berlin, **1977**, p. 623.

[27] G. Dana, A. Zysman, *Bull. Soc. Chim. Fr.* **1975**, 1951–1956.

[28] J. E. Leibner, J. Jacobus, *J. Org. Chem.* **1979**, *44*, 449–450.

[96070]