Highly Enantioselective Conjugate Addition of $AlMe_3$ to Linear Aliphatic Enones by a Designed Catalyst

Paul K. Fraser and Simon Woodward*[a]

Abstract: 2-Hydroxy-2′-alkylthio-1,1′-binaphthyl compounds are catalytic promoters of the 1,4-addition of $AlMe_3$ to linear aliphatic enones in THF at -40 to $-48\,^{\circ}C$ in the presence of $[Cu(MeCN)_4]BF_4$. At ligand loadings of 5–20 mol%, enantioselectivities of 80–93% are realised for most substrates. To attain these values, the use of highly pure $AlMe_3$ is mandatory. The presence of methylalumoxane (MAO), derived by hydrolysis, leads to reduced enantioselectivity and a conjugate addition product.

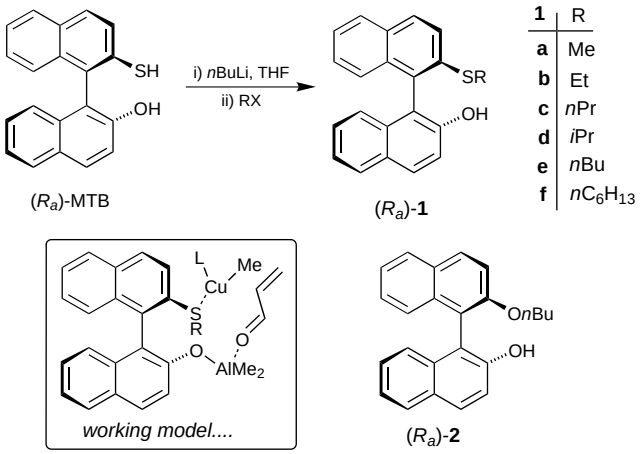
Keywords: alanes · asymmetric catalysis · cuprates · S ligands · thioethers

Introduction

The last five years have seen dramatic breakthroughs in what is possible in the area of catalytic asymmetric 1,4-addition of alkyl organometallic nucleophiles to enones. Both the practical[1] and mechanistic[2] aspects of these reactions are the subjects of extensive reviews. Most of the successful asymmetric versions of this chemistry have made use of diorgano zinc reagents, especially $ZnEt_2$, a trend started by Alexakis (Cu catalysis) and Soai (Ni catalysis).[3] Viable ligand classes affording >90% enantiomeric excess (*ee*) for the addition of ZnR_2 to cyclopentanones,[4] cyclohexanones[5] and chalcones[6] are now available. However, relatively few publications describing highly enantioselective addition of organometallics to linear aliphatic enones have appeared. Very recently, Hoveyda disclosed a modular phosphinodipetidic ligand capable of delivering 80–95% *ee* in the addition of ZnR_2 (R = Me, Et, $(CH_2)_nFG$) to this class of enones.[7] This publication leads us to disclose full details of our own studies into highly selective asymmetric 1,4-addition of $AlMe_3$ in this arena.

Results and Discussion

Ligand synthesis: We chose the ligands (R_a)-**1a–f** as initial chiral moderators in the copper-catalysed conjugate addition of $AlMe_3$ to nonenone **3a** fashioning (+)-(*R*)-4-methylnonen-2-one (*R*)-**4a**. We have proposed that the presence of both *hard* (alkoxide) and *soft* (thioether) donors facilitates the formation of bimetallic catalyst structures containing aluminium and copper (as in the working model in Scheme 1).[8] The ligands **1** are easily obtained by treating monothiobinaphthol (MTB)[9] with appropriate alkylating agents (Scheme 1) and their enantiopurity assayed by HPLC. Ligand



Scheme 1. Designed ligands for asymmetric conjugate addition and a working model (L represents a number of possible cuprate structures).

1e has been reported previously;[10] it was used in the majority of our studies and was of ≥95% *ee*. To allow us to probe the necessity of having a group to direct the addition of the cuprate in the transition state, the butyl ether ligand (R_a)-**2** was also prepared by standard Mitsunobu chemistry with *n*BuOH in the presence of triphenylphosphine (TPP) and diethyl azodicarboxylate (DEAD) in THF.[11]

"Magic bottle" effects: Our initial investigations in this area had revealed that the ligand **1e** (20 mol%) promoted 1,4-

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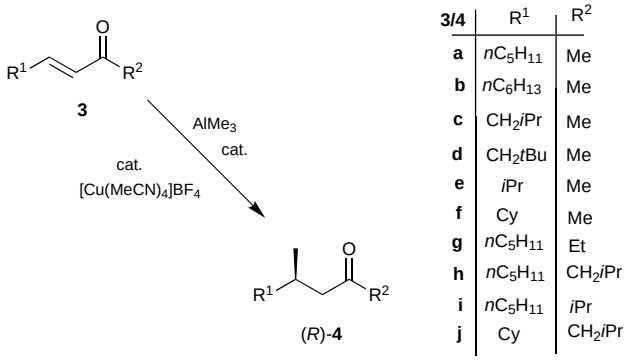
addition of $AlMe_3$ to nonenone **3a** to afford **4a** in 79% chemical yield (*cy*) and 71% *ee* in the presence of $[Cu(MeCN)_4]BF_4$ (Scheme 2).[10] These studies were carried out with a solution of $AlMe_3$ in hexane (Aldrich, 2.0 M). Subsequently we discovered that under these conditions (−20 °C, 20 mol% **1e**) the *cy* and, to a lesser extent, the *ee* were highly dependent on the individual source of $AlMe_3$ used and how it had aged. Representative examples of the behaviour of three commercial Aldrich sources (Bottles 1–3) are shown in Table 1.



3/4	R^1	R^2
a	nC_5H_{11}	Me
b	nC_6H_{13}	Me
c	CH_2iPr	Me
d	CH_2tBu	Me
e	*i*Pr	Me
f	Cy	Me
g	nC_5H_{11}	Et
h	nC_5H_{11}	CH_2iPr
i	nC_5H_{11}	*i*Pr
j	Cy	CH_2iPr

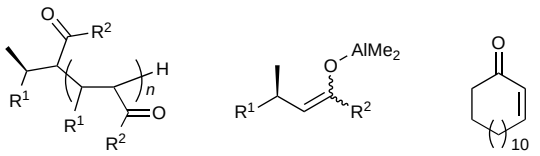
Scheme 2. Substrates for asymmetric conjugate addition.

Table 1. Source effects in asymmetric conjugate additions of $AlMe_3$ to nonenone **3a**, catalysed by (R_a)-**1e** and $[Cu(MeCN)_4]BF_4$.[a]

$AlMe_3$ source	Additional conditions	Conversion of **2** [%]	Yield (*cy*) **4a** [%]	*ee* (*R*)-**4a** [%]
Bottle 1[b]	–	88	79	71
Bottle 2[c]	–	77	36	69
Bottle 3[d]	–	78	48	54
Bottle 3[d]	+1.0 equiv H_2O[e]	13	< 5	< 5
Bottle 3[d]	+1.0 equiv EtOH[f]	70	29	70
Bottle 3[d]	5 mol% MAO[g]	91	42	73
Bottle 3[d]	50 mol% MAO[g]	83	39	54
Bottle 3[d]	Aged[h]	80	31	63
MAO[g] 1.7 equiv	100 mol%	81	33	31
Bottle 4[i]	–	75	57	79

[a] Carried out in THF at −20 °C, joint slow addition (20 min) of $AlMe_3$ (1.7 equiv, 1.0 M in THF/hexane) and **3a** (0.85 M in THF) followed by further stirring (20 min); $[Cu(MeCN)_4]BF_4$ (10 mol%), **1e** (20 mol%). [b] Initial 2.0 M in hexane (Aldrich) $AlMe_3$ source; see ref. [10]. [c] Second 2.0 M in hexane (Aldrich) $AlMe_3$ source. [d] Third 2.0 M in hexane (Aldrich) $AlMe_3$ source. [e] Added to $AlMe_3$ to fashion in situ "$AlMe_2(OH)$"-derived hydrolysis products. [f] Added to $AlMe_3$ to fashion "$AlMe_2(OEt)$". [g] Commercial MAO, 2.0 M in toluene (Aldrich) remainder $AlMe_3$ (Bottle 3). [h] Behaviour 5 months after initial opening. [i] Freshly prepared from 98% pure (Strem) $AlMe_3$ diluted in hexane (distilled from $LiAlH_4$) to 2.0 M.

In the absence of additives, the conversion of **3a** is always high, but most commercial bottles of $AlMe_3$ in hexane lead to low chemical yields of **4a**. Variable performance of nominally identical bottles of commercial organometallic reagents has been noted since the earliest days of asymmetric conjugate additions, but is rarely explicitly cited in the literature.[12] Efforts were made to identify the features of the "magic bottle" effect in our particular case. Firstly, GC-MS studies of the crude reaction mixtures revealed that significant amounts of the missing mass balance could be accounted for through the formation of the double addition product **5a** ($n = 1$) as shown by GC-MS. There were also hints in GPC chromatograms for these reaction mixtures of the presence of higher



5 n = 1, 2... **6** **7**

oligomeric products ($n > 1$). We reasoned that the variability in the commercial hexane solutions of $AlMe_3$ could be due to variable contamination by methylalumoxane (MAO)[13] and related hydrolysis products. A number of facts support this hypothesis. Firstly, as all commercial bottles of $AlMe_3$ start to age, the *ee* of the derived **4a** increases but its yield falls as more **5a** is formed. Finally, with highly aged commercial $AlMe_3$ both the *ee* and yield become inferior. This behaviour can be mimicked by deliberate addition of commercial MAO to fresh $AlMe_3$ (Table 1). Small concentrations are beneficial to the enantioselectivity but large excesses degrade the catalyst performance. The MAO-induced *ee* improvement in the catalytic reaction is apparently not due to kinetic resolution of the initial aluminium enolate **6a**; this is based on the fact that the *ee* of **4a** is not dependent on the extent of reaction. Additionally, when isolated **4a** is subjected to the reaction conditions it is re-isolated in reduced yield but identical *ee*. Deliberate addition of excess water to the initial $AlMe_3$ is unhelpful, but the presence of alkoxides also slightly improves the enantioselectivity of the catalytic system. Finally, noncommercial sources of $AlMe_3$ in hexane (prepared from high purity neat $AlMe_3$) give both improved enantioselectivity and yield of **4a**. Neat $AlMe_3$ is typically supplied at a 98+% purity level, the major impurities being $AlMe_nCl_{3-n}$ ($n = 1, 2$) and traces of MAO. Having identified the origin of the problem, we endeavoured to find conditions that exploited this discovery.

Temperature effects and initial optimisation: We speculated that the undesired multiple Michael addition reactions leading to **5a** might be due to a high reactivity for the intermediate aluminium enolate **6a**, and that its loss might be further promoted by extrinsic MAO presence leading to **5a**. If this is the case, using pure ($AlMe_3$ solutions prepared "in house") and lowering the reaction temperature should improve the stability of **6a**, and hence the yield of **4a**. While keeping a fixed reaction time (20 min addition of reagents followed by 20 min of further stirring) the *cy* and *ee* were studied as a function of temperature (Table 2). Encouragingly, while *cy* fell (as expected), at low temperature the mass balance for the reaction significantly improved; this indicated that degradation of **6a** to **5a** was minimised below −40 °C. As expected, the *ee* value of the derived (*R*)-**4a** also rose at the lower temperatures. An additional benefit of these conditions is that the catalytic reaction became rather more robust with respect to the $AlMe_3$ source. Commercial hexane solutions, aged and

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Table 2. Temperature dependency of the *ee* and *cy* for $AlMe_3$ (1.7 equiv) addition to **3a** (10 mol% $[Cu(MeCN)_4]BF_4$, 20 mol% **1e**, 40 min total reaction time).[a]

Temperature [°C]	Conversion [%]	Yield (*cy*) **4a** [%]	*ee* (*R*)-**4a** [%]
−20	78	47	71
−30	71	45	81
−40	56	40	85
−50	34	26	87

[a] Carried out in THF at −20 °C, joint slow addition (20 min) of $AlMe_3$ (1.7 equiv, 1.0 M in THF/hexane) (from Aldrich >97% $AlMe_3$) and **3a** (0.85 M in THF) followed by further stirring (20 min); $[Cu(MeCN)_4]BF_4$ (10 mol%), **1e** (20 mol%).

pure (prepared "in house" from neat $AlMe_3$) now gave similar results. However, the most carefully prepared pure $AlMe_3$ solutions always gave the best *ee* values (typically 2–5% higher than the commercial solutions of $AlMe_3$ in hexane). With these results in hand, attempts were made to optimise the catalytic reaction at these new low temperatures.

At −40 or −46 °C, changing the Cu^I/**1e** ratio had no effect on the *ee* of **4a** derived from the catalytic reaction in the range 1:1 to 1:2. In order to maximise the conversion at these low temperatures, the copper loading was increased to 18 mol% while keeping the loading of **1e** at 20 mol%. By running the reaction for extended periods, it proved possible to enter a synthetically useful regime with nonenone and many other substrates (Table 3). Synthetically viable enantioselectivities are attained except in the case where R^2 is α-branched. When either R^1 or R^2 is a *tert*-butyl group, the catalytic reaction stops. In all cases, except **4e** and **4i**, the (+)-isomer is obtained from (R_a)-**1e**. We have previously assigned (+)-**4a** to the (*R*) stereoisomer based on the degradation of **3a** to (+)-2-methylheptan-1-ol.[10] The optical rotations of ketones **4** and their derived products are, however, generally rather small and variable. For the ketones (*R*)-**4**, as the size of R^2 increases compared with R^1, the size of the $[\alpha]_D$ value first drops and then reverses. For example, (*R*)-methylheptan-2-one (**4**; $R^1 = n$Pr, R^2 = Et) has $[\alpha]_D^{24} = -16.8$ ($c = 4.26$ in hexane)[14] while (*R*)-**4a** ($R^1 = nC_5H_{11}$, R^2 = Me) gives $[\alpha]_D^{20} = +8.7$ ($c = 1.17$ in $CHCl_3$, 94% *ee*).[7] To be absolutely sure of the correlation, our original degradation was repeated on the high *ee* **4a** attained here and compared with authentic (*S*)-(−)-2-methylheptan-1-ol prepared independently by Evans auxiliary technology.[15] The latter yielded the opposite enantiomer to that from (R_a)-**1e**-based catalysis, as expected. As a final check, **3b** was treated with $AlMe_3$ by using ligand (R_a)-**1e** in the expectation that it would give (+)-**4b**, which is known, through a literature correlation,[16] to correspond to *R*; this also proved to be the case. Based on these facts, we have also assigned *R* configurations to **4a–d, f** and **g**. For **4e** and **4h–j**, the rotation values do not allow confidence in the assignment without specific degradation to known compounds.

Table 3. Asymmetric conjugate addition of $AlMe_3$ to various enones under 20 mol% **1e** catalysis.[a]

Enone	R^1	R^2	Conv.[b] [%]	*cy* **4**[c] [%]	*ee* **4** [%] (config.)
3a	nC_5H_{11}	Me	>96	(82)	85–87 (+)-*R*
3b	nC_6H_{13}	Me	>96	58	86 (+)-*R*
3c	CH_2iPr	Me	>96	63	87 (+)-*R*
3d	CH_2tBu	Me	>96	46	93 (+)-*R*
3e	*i*Pr	Me	>97	55 (97)	90–93 (−)
3f	Cy	Me	>96	58	92 (+)-*R*
3g	nC_5H_{11}	Et	>96	52	80–83 (+)-*R*
3h	nC_5H_{11}	CH_2iPr	>96	55	85 (+)
3i	nC_5H_{11}	*i*Pr	>96	62	76 (−)
3j	Cy	CH_2iPr	>96	64	89 (+)

[a] Carried out in THF at −40 or −46 °C, joint slow addition (20 min) of $AlMe_3$ [1.7 equiv; 2.0 M in hexane prepared from Strem $AlMe_3$ (>98%)] and **3** followed by further stirring (18 h); $[Cu(MeCN)_4]BF_4$ (18 mol%), **1e** (20 mol%). [b] Conversion based on GC assay. [c] Isolated, GC yields versus internal standards in parentheses.

Optimisation at low catalyst loadings: Having attained viable levels of enantioselectivity, we sought to overcome the need for high ligand loadings in this system. We reasoned that at lower catalyst loadings the reaction could be driven to completion by use of larger excesses of terminal organometallic, a trick we had previously employed in catalysis with carbene ligands.[17] A series of runs confirmed the efficiency of this approach (Table 4). However, exploration of variation of the solvent or copper source led to no further improvement (Table 5). It is readily apparent that application of conditions that are efficacious in closely related modern systems[18] are less helpful here. Finally, we probed the effect of ligand structure on the outcome of the catalysis under these new conditions (Table 6). Interestingly, under the low-temperature

Table 4. Variation of excess $AlMe_3$ in addition to **3a** under 5 mol% **1e** catalysis.[a]

$AlMe_3$ [equiv]	Conv.[b] [%]	*cy*[c] [%]	*ee* [%] (config.)
1.1	54	20	70 (+)-*R*
1.7	62	27	83 (+)-*R*
2.2	87	51	86 (+)-*R*
3.2	89	41	82 (+)-*R*
4.2	89	33	74 (+)-*R*

[a] Carried out in THF at −46 °C, joint slow addition (20 min) of $AlMe_3$ [2.0 M in hexane prepared from Strem $AlMe_3$ (98%)] and **3a** followed by further stirring (18 h); $[Cu(MeCN)_4]BF_4$ (5 mol%), **1e** (5 mol%). [b] Conversion based on GC. [c] GC yields versus internal standard.

Table 5. Solvent and copper-source effects in $AlMe_3$ in addition to **3a** under 5 mol% **1e** catalysis.[a]

Variation	Conv.[b] [%]	*cy*[c] [%]	*ee* [%] (config.)
A. Solvent			
THF	87	51	86 (+)-*R*
THP	86	86	73 (+)-*R*
DME	91	50	37 (+)-*R*
Et_2O	91	43	42 (+)-*R*
MeCN	11	<5	<5
toluene	98	50	<5
B. Cu source[d]			
$[Cu(MeCN)_4]BF_4$	87	51	86 (+)-*R*
Cu(OTf)	77	23	39 (+)-*R*
$Cu(OTf)_2$	73	33	47 (+)-*R*
$Cu(O_2CC_4H_3S)$[e]	76	30	59 (+)-*R*

[a] Carried out in THF at −46 °C, joint slow addition (20 min) of $AlMe_3$ [2.2 equiv of 2.0 M in hexane prepared from Strem $AlMe_3$ (98%)] and **3a** followed by further stirring (18 h); $[Cu(MeCN)_4]BF_4$ (5 mol%), **1e** (5 mol%), solvent as indicated. [b] Conversion based on GC. [c] GC yields versus internal standard. [d] All runs in THF. [e] Thiophene-2-carboxylate.

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Table 6. Ligand effects in $AlMe_3$ addition to **3a** under 5 mol% catalysis.[a]

Ligand (R group)	Conversion[b] [%]	*cy*[c] [%]	*ee* [%] (config.)
1a (Me)	87	34	79 (+)-*R*
1c (*n*Pr)	87	41	84 (+)-*R*
1d (*i*Pr)	63	24	70 (+)-*R*
1e (*n*Bu)	84	51	86 (+)-*R*
1f (nC_6H_{13})	80	33	82 (+)-*R*
2 (*n*Bu)	< 5	< 5	< 5

[a] Carried out in THF at −46 °C, joint slow addition (20 min) of $AlMe_3$ [2.0 M in hexane prepared from Strem $AlMe_3$ (98%)] and **3a** followed by further stirring (18 h); $[Cu(MeCN)_4]BF_4$ (5 mol%), **1** or **2** (5 mol%). [b] Conversion based on GC. [c] GC yields versus internal standard.

conditions, the favoured ligand architectures appear to possess an *n*-alkyl chain of medium length in the thioether of **1**. Under the "old" conditions (catalysis at −20 °C, 20 mol% **1**) all of the thioethers **1a–e** had delivered ~70% *ee* irrespective of structure. Consistent with the design model, the presence of the thioether is mandatory; use of the closely related ether (R_a)-**2** instead gave poor catalyst performance: both the yield and *ee* of the derived **4a** were minimal.

Practicalities, limitations and mechanistic insights: The final optimised conditions were applied to a smaller range of the original substrates **3**. Although the *ee* remains at the selectivity of the 18 mol% version of the reaction, the chemical yield is reduced. For example, **3a** still delivers enantiomeric excesses of 82–86%, but the chemical yield is reduced to 42–48% (GC vs. internal standards). Similarly **3c** also showed a high selectivity of 83%, but reduced chemical yield was obtained (~50% isolated). In both cases the missing mass is shown to be present as oligomeric products (GC-MS). The new 5 mol% catalyst system was applied to the synthesis of (*R*)-muscone by addition to enone **7**. Muscone was obtained in 39% isolated yield and 77% *ee*. The latter figure, while outside the synthetically useful range, is one of the highest attained in direct catalytic approaches to this molecule.[19] To broaden practical application of the procedure we have investigated two methods that do not involve the use of cryostatic cooling apparatus or syringe pumps. By using cyclohexanone/dry ice baths it is possible to maintain a temperature of −45(±5) °C for reasonable periods. Preparation of the catalyst at −78 °C followed by sequential dropwise addition of $AlMe_3$ and neat enone **3a**, and then further stirring at −46 °C for 3 hours allowed isolation of **4a** in 22% yield and 90% *ee*. Alternatively, if all of the reaction components were added to $[Cu(MeCN)_4]BF_4$/**1e** in THF at −78 °C, and the reaction mixture was allowed to warm to room temperature over 18 hours, then **4a** could be obtained in 50–55% yield (69–79% *ee*) from **3a**. The results for these methods were slightly variable from run to run due to differing rates of warming in the cold baths employed.

The substrate range of our present catalyst system also deserves some comment. While the addition of pure $AlMe_3$ solutions to a wide variety of aliphatic enones robustly delivers synthetically useful *ee* values and chemical yields, attempted additions to benzylideneacetone, enones bearing a conjugated vinyl function (e.g. **3**: R^1 = (*E*)-CH=CHEt), or nitroalkenes have not been successful. In all cases only the starting Michael acceptor has been isolated. However, we have seen that when α,β-unsaturated esters and cyclic ethers are present in the starting aliphatic enone these are tolerated, and the catalyst chemospecifically adds only to the enone. Attempted additions of $AlEt_3$ have, thus far, led only to the formation of conjugate addition products in lower yield and unacceptable enantioselectivity (*ee* < 5%). This intolerance of $AlEt_3$ strongly suggests that the structure of the active catalyst incorporates an AlR_3-dependent substrate binding pocket.

Conclusion

Optimisation of the reaction conditions has led to a practical system for the addition of $AlMe_3$ to linear aliphatic enones by using $[Cu(MeCN)_4]BF_4$ and binaphthol-derived thioether **1e**. Few other catalytic systems are available for this transformation that deliver these levels of stereoselectivity, and only one other is known that employs organo aluminium reagents.[20] The substrate selectivity profile of the $[Cu(MeCN)_4]BF_4$/**1e** catalyst is unusual, and further work is required to unmask the exact nature of the catalyst responsible.

Experimental Section

General: Infrared spectra were recorded by using Perkin–Elmer 983G infrared and Perkin–Elmer 882 infrared spectrophotometers. Proton and ^{13}C NMR spectra were recorded on either Jeol (JNM-GX270) or Bruker (AM400, AV400 or DRX500) spectrometers with $CHCl_3$ (7.27 ppm) or tetramethylsilane (0.00 ppm) as standard; *J* values are given in Hz. All spectra were recorded at ambient temperature unless otherwise noted. Mass spectra were obtained on Finnigan-MAT1020 or Autospec VG (electron impact ionisation, EI), Finnigan-QMS (electrospray ionisation, ESI), VG-ZAB, or Autospec VG (fast atom bombardment, FAB). Elemental analyses were performed by using a Fisons Instruments EA1108CHN elemental analyser. Optical rotations were measured on a JASCO polarimeter model DIP-370 in units of 10^{-1} ° $cm^2 g^{-1}$ (*c* in g per 100 cm^3).

All reactions involving air-sensitive materials were carried out under argon by using standard Schlenk techniques. Reaction solvents were distilled under argon from appropriate agents immediately prior to use: THF from either Na benzopheneone or $LiAlH_4$, hexane from $LiAlH_4$. Light petroleum refers to the fraction with b.p. 40–60 °C. Solutions of $AlMe_3$ in hexane were prepared from neat $AlMe_3$ (neat, 98% Strem) and stored in Schlenk storage flasks. The quality of commercial $AlMe_3$ solutions (2.0 M, Aldrich) was found to be batch dependent in this chemistry. The MTB precursor to ligands **1a–f** is known,[9] but the following improvements were made to its synthesis: the BINOL was best treated with $Me_2NC{=}SCl$ and $Me_2NC{=}CCl$ in two separate steps (EtOH is the best recrystallisation solvent for the first step; CH_2Cl_2/hexane for the latter). The thiophene by-product formation (to 7-thiadibenzo[*c*,*g*]fluorine) in the Newmann–Kwart rearrangement was minimised by use of crystalline (not powdered) precursors and prior removal of all traces of occluded solvent. Any thiophene formed was easily removed as a first crop from EtOH. These improvements increased the rotation of the rearranged product from +144 to $[\alpha]_D^{298} = +159$ ($c = 2.0$ in $CHCl_3$). The enantiopurity of ligands **1a–f** was confirmed by HPLC analysis on a Daicel-AD column. The following compounds are available by literature procedures: $[Cu(MeCN)_4]BF_4$,[21] **1e**,[22] **3c**,[23] **3i**.[23] Isomeric 5-methylhex-4-en-2-one was removed from commercial **3e** by selective MCPBA epoxidation followed by flash chromatography. All other compounds were used as supplied.

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General preparation of ligands 2a–d: *n*BuLi (425 μL, of a 2.5 M hexane solution, 1.09 mmol) was added dropwise to a stirring solution of MTB[9] (0.30 g, 0.99 mmol) in THF at 0 °C under an inert atmosphere. Neat alkyl halide (1.09 mmol) was added, the solution was allowed to warm to room temperature and monitored by TLC (dichloromethane/light petroleum 1:1). When the reaction was complete (1 h – 1 d), the reaction mixture was quenched with HCl (2 M, 5 mL) and extracted with dichloromethane, washed with brine and dried over $MgSO_4$. Purification by flash column chromatography (dichloromethane/light petroleum 1:1) yielded low-melting-point solids or oils whose spectroscopic properties were consistent with the desired formulation.

(R_a)-(−)-*S*-Methyl-2-hydroxy-2′-mercapto-1,1′-binaphthyl (1a): Yield 60 %; low-melting-point solid; $[\alpha]_D^{24} = -26.5$ ($c = 1.02$ in $CHCl_3$); ^{1}H NMR (400.1 MHz, $CDCl_3$) $\delta = 2.44$ (s, 3H; Me), 4.81 (br s, 1H; OH), 6.97 (d, $J =$ 8.3 plus small unresolved long-range couplings, 1H; $H_{8or8'}$), 7.08 (d, $J = 8.3$ plus small unresolved long-range couplings, 1H; $H_{8or8'}$), 7.26 (ddd, $J = 8.3$, 6.8, 1.3, 1H; $H_{6,7,6'or7'}$), 7.30 (ddd, $J = 8.3$, 6.8, 1.3, 1H; $H_{6,7,6'or7'}$), 7.34 (ddd, $J =$ 8.2, 6.8, 1.3, 1H; $H_{6,7,6'or7'}$), 7.37 (d, $J = 8.8$, 1H; $H_{3or3'}$), 7.45 (ddd, $J = 8.1$, 6.8, 1.3, 1H; $H_{6,7,6'or7'}$), 7.60 (d, $J = 8.8$, 1H; $H_{3or3'}$), 7.89 (d, $J = 8.1$, plus small unresolved long-range couplings, 1H; $H_{5or5'}$), 7.92 (d, $J = 8.2$, plus small unresolved long-range couplings, 1H; $H_{5or5'}$), 7.96 (d, $J = 8.8$, 1H; $H_{4or4'}$), 8.04 (d, $J = 8.8$, 1H; $H_{4or4'}$); ^{13}C NMR (67.8 MHz, $CDCl_3$) $\delta = 15.6$ (Me), 116.7, 117.8, 123.0, 123.9, 124.6, 125.1, 125.8 (3C), 127.1, 127.8, 128.5, 129.5, 130.1, 130.8, 131.7, 133.4, 133.6, 139.1, 151.2; IR (KBr disc): $\tilde{\nu}_{max} = 3530$ (m, br, OH), 3425 (m, br, OH), 1618 (m), 1595 (m), 1206 (m), 1140 (m), 812 cm^{-1} (s); ES: *m*/*z* (%): 317 (100) [M^++H]; found (HRMS, ES) = 317.0997 [M^++H], $C_{21}H_{17}OS$ requires *M* 317.1000. This compound has been reported, but no spectroscopic details have appeared to our knowledge.[24]

(R_a)-(−)-*S*-Ethyl-2-hydroxy-2′-mercapto-1,1′-binaphthyl (1b): Yield 62 %; low-melting-point solid; $[\alpha]_D^{24} = -19.5$ ($c = 1.06$ in $CHCl_3$); ^{1}H NMR (400.1 MHz, $CDCl_3$) $\delta = 1.21$ (t, $J = 7.1$, 3H; CH_2Me), 2.88 (m, 2H; CH_2Me), 4.81 (br s, 1H; OH), 6.95 (d, $J = 8.2$ plus small unresolved long-range couplings, 1H; $H_{8or8'}$), 7.13 (d, $J = 8.2$ plus small unresolved long-range couplings, 1H; $H_{8or8'}$), 7.21 (ddd, $J = 8.2$, 6.8, 1.3, 1H; $H_{6,7,6'or7'}$), 7.25 (ddd, $J = 8.2$, 6.8, 1.3, 1H; $H_{6,7,6'or7'}$), 7.30 (ddd, $J = 8.0$, 6.8, 1.3, 1H; $H_{6,7,6'or7'}$), 7.34 (d, $J = 8.8$, 1H; $H_{3or3'}$), 7.41 (ddd, $J = 8.1$, 6.8, 1.3, 1H; $H_{6,7,6'or7'}$), 7.59 (d, $J = 8.8$, 1H; $H_{3or3'}$), 7.85 (d, $J = 8.1$, plus small unresolved long-range couplings, 1H; $H_{5or5'}$), 7.86 (d, $J = 8.2$, plus small unresolved long-range couplings, 1H; $H_{5or5'}$), 7.91 (d, $J = 8.8$, 1H; $H_{4or4'}$), 7.94 (d, $J = 8.8$, 1H; $H_{4or4'}$); ^{13}C NMR (67.8 MHz, $CDCl_3$) $\delta = 14.1$ (Me), 26.2 (CH_2), 116.8, 117.6, 123.5, 124.2, 124.4, 125.0, 125.6, 126.7, 127.4, 128.2 (3C), 129.1, 129.6, 130.3, 131.6, 133.2, 133.5, 137.6, 150.8; IR (KBr disc): $\tilde{\nu}_{max} = 3501$ (w, C–H), 3500 (s, br, OH), 3417 (m, br, OH), 2961 (w, C–H), 2924 (w, C–H), 2862 (w, C–H), 1618 (s), 1595 (s), 1501 (s), 1203 (s), 1143 (s), 969 (m), 814 (s), 747 cm^{-1} (m); ES *m*/*z* (%): 331 (100) [M^++H]; found (HRMS, FAB) = 330.1065 [M^+]; $C_{22}H_{18}OS$ requires *M* 330.1078. This compound has been reported, but no spectroscopic details have appeared to our knowledge.[24]

(R_a)-(−)-*S*-Propyl-2-hydroxy-2′-mercapto-1,1′-binaphthyl (1c): Yield 72 %; colourless oil; $[\alpha]_D^{24} = -8.6$ ($c = 3.42$ in $CHCl_3$); ^{1}H NMR (400.1 MHz, $CDCl_3$) $\delta = 0.90$ (t, $J = 7.4$, 3H; Me), 1.59 (sextet, $J = 7.4$, 2H; central CH_2), 2.86 (m, 2H; SCH_2), 4.78 (br s, 1H; OH), 6.96 (d, $J = 8.2$ plus small unresolved long-range couplings, 1H; $H_{8or8'}$), 7.13 (d, $J = 8.2$ plus small unresolved long-range couplings, 1H; $H_{8or8'}$), 7.22 (ddd, $J = 8.2$, 6.8, 1.3, 1H; $H_{6,7,6'or7'}$), 7.28 (ddd, $J = 8.2$, 6.8, 1.3, 1H; $H_{6,7,6'or7'}$), 7.32 (ddd, $J = 8.0$, 6.8, 1.3, 1H; $H_{6,7,6'or7'}$), 7.35 (d, $J = 8.8$, 1H; $H_{3or3'}$), 7.43 (ddd, $J = 8.1$, 6.8, 1.3, 1H; $H_{6,7,6'or7'}$), 7.64 (d, $J = 8.8$, 1H; $H_{3or3'}$), 7.87 (d, $J = 8.1$, plus small unresolved long-range couplings, 1H; $H_{5or5'}$), 7.89 (d, $J = 8.2$, plus small unresolved long-range couplings, 1H; $H_{5or5'}$), 7.93 (d, $J = 8.8$, $H_{4or4'}$), 7.98 (1H; d, $J = 8.8$, 1H; $H_{4or4'}$); ^{13}C NMR (67.8 MHz, $CDCl_3$) $\delta = 13.4$ (Me), 22.5 (CH_2), 34.2 (CH_2), 117.6, 123.4, 124.4 (2C), 125.0, 125.7, 126.7, 127.4, 128.1, 128.2 (3C), 128.4, 129.1, 129.6, 130.3, 131.7, 133.3, 137.8, 150.8; IR ($CHCl_3$ solution): $\tilde{\nu}_{max} = 3537$ (s, OH), 2966 (s, C–H), 2933 (m, C–H), 2874 (w, C–H), 1621 (s), 1596 (s), 1466 (m), 1381 (s), 1355 (s), 1145 (s), 1120 (m), 970 (m), 862 cm^{-1} (w); ES: *m*/*z* (%): 345 (100) [M^++H]; found (HRMS, FAB) = 344.1231 [M^+], $C_{23}H_{20}OS$ requires *M* 344.1235.

(R_a)-(−)-*S*-(1-methyl)ethyl-2-hydroxy-2′-mercapto-1,1′-binaphthyl (1d): Yield 35 %; low-melting-point solid; $[\alpha]_D^{24} = -4.1$ ($c = 1.06$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) $\delta = 1.19$ (d, $J = 6.7$, 3H; $CHMe_{2\alpha}$), 1.25 (d, $J =$ 6.7, 3H; $CHMe_{2\beta}$), 3.53 (septet, $J = 6.7$, 1H; SCH), 4.76 (br s, 1H; OH), 6.95 (d, $J = 8.2$ plus small unresolved long-range couplings, 1H; $H_{8or8'}$), 7.13 (d, $J = 8.2$ plus small unresolved long-range couplings, 1H; $H_{8or8'}$), 7.22 (ddd, $J = 8.2$, 6.8, 1.3, 1H; $H_{6,7,6'or7'}$), 7.28 (ddd, $J = 8.3$, 6.8, 1.3, 1H; $H_{6,7,6'or7'}$), 7.31 (ddd, $J = 8.2$, 6.8, 1.3, 1H; $H_{6,7,6'or7'}$), 7.35 (d, $J = 8.9$, 1H; $H_{3or3'}$), 7.44 (ddd, $J = 8.2$, 6.8, 1.2, 1H; $H_{6,7,6'or7'}$), 7.70 (d, $J = 8.8$, 1H; $H_{3or3'}$), 7.87 (d, $J = 8.2$, plus small unresolved long-range couplings, 1H; $H_{5or5'}$), 7.90 (d, $J = 8.2$, plus small unresolved long-range couplings, 1H; $H_{5or5'}$), 7.94 (d, $J = 8.9$, 1H; $H_{4or4'}$), 7.98 (d, $J = 8.8$, 1H; $H_{4or4'}$); ^{13}C NMR (125.8 MHz, $CDCl_3$) $\delta = 22.9$ ($CHMe_{2\alpha}$), 23.3 ($CHMe_{2\beta}$), 36.4, 117.3, 117.6, 123.5, 124.6, 125.4, 126.0, 126.3, 126.7, 127.5, 128.3 (2C), 129.2, 129.6, 129.8, 130.3, 132.0, 133.5, 133.7, 137.5, 150.7; IR (KBr disc): $\tilde{\nu}_{max} = 3510$ (w, br, OH), 3429 (w, br, OH), 2960 (w, C–H), 2903 (s, C–H), 2863 (C–H), 1618 (m), 1598 (m), 1205 (m), 1144 (m), 813 (m), 747 cm^{-1} (m); FAB: *m*/*z* (%): 344 (20) [M^+], 307 (30), 154 (100); found (HRMS, FAB) = 344.1231 [M^+], $C_{23}H_{20}OS$ requires *M* 344.1235.

(R_a)-(−)-*S*-Hexyl-2-hydroxy-2′-mercapto-1,1′-binaphthyl (1f): Yield 52 %; low-melting-point solid; $[\alpha]_D^{24} = -9.9$ ($c = 1.19$ in $CHCl_3$); ^{1}H NMR (500.1 MHz, $CDCl_3$) $\delta = 0.88$ (t, $J = 7.1$, 3H; $(CH_2)_3Me$), 1.25 – 1.38 (m, 6H; $(CH_2)_3$Me), 1.59 (distorted quintet, $J = \sim 6.0$, 2H; SCH_2CH_2), 2.92 (m, 2H; SCH_2), 4.83 (br s, 1H; OH), 7.00 (d, $J = 8.3$ plus small unresolved long-range couplings, 1H; $H_{8or8'}$), 7.18 (d, $J = 8.2$ plus small unresolved long-range couplings, 1H; $H_{8or8'}$), 7.27 (ddd, $J = 8.2$, 6.8, 1.3, 1H; $H_{6,7,6'or7'}$), 7.32 (ddd, $J = 8.3$, 6.8, 1.3, 1H; $H_{6,7,6'or7'}$), 7.36 (ddd, $J = 8.2$, 6.8, 1.3, 1H; $H_{6,7,6'or7'}$), 7.39 (d, $J = 8.9$, 1H; $H_{3or3'}$), 7.48 (ddd, $J = 8.2$, 6.8, 1.2, 1H; $H_{6,7,6'or7'}$), 7.62 (d, $J = 8.8$, 1H; $H_{3or3'}$), 7.91 (d, $J = 8.2$, plus small unresolved long-range couplings, 1H; $H_{5or5'}$), 7.94 (d, $J = 8.2$, plus small unresolved long-range couplings, 1H; $H_{5or5'}$), 7.97 (d, $J = 8.9$, 1H; $H_{4or4'}$), 8.00 (d, $J = 8.8$, 1H; $H_{4or4'}$); ^{13}C NMR (100.6 MHz, $CDCl_3$) 14.2 (Me), 22.7 (CH_2), 28.7 (CH_2), 29.3 (CH_2), 31.5 (CH_2), 32.5 (CH_2), 117.1, 117.8, 123.7, 124.6, 124.7, 125.3, 125.9, 126.9, 127.6, 128.4 (2C), 128.5, 129.3, 129.8, 130.5, 131.9, 133.5, 133.7, 138.1, 151.0; IR (KBr disc): $\tilde{\nu}_{max} = 3548$ (w, OH), 2945 (w, C–H), 2926 (w, C–H), 2856 (w, C–H), 1622 (m), 1582 (m), 1507 (m), 1432 (m), 1338 (m), 1267 (m), 1251 (m), 967 (s), 820 (s), 810 (s), 746 cm^{-1} (s); ES: *m*/*z* (%): 387 (100) [M^+], found (HRMS) = 386.1699 [M^+], $C_{23}H_{20}OS$ requires *M* 386.1704.

(R_a)-(−)-*O*-Butyl-2-hydroxy-2′-hydroxy-1,1′-binaphthyl (2): Triphenylphosphine (0.734 g, 2.80 mmol) in dry THF (25 mL) and diethyl azodicarboxylate (DEAD) (0.44 mL, 2.80 mmol) were added to a stirring solution of (R_a)-BINOL (0.80 g, 2.80 mmol) and *n*BuOH (1.28 mL 13.97 mmol). Yield 70 %; low-melting-point solid (when synthesised, we found genuine (±)-**2** to be a white solid of m.p. 94 – 95 °C); $[\alpha]_D^{24} = +7.6$ ($c = 1.2$ in $CHCl_3$, > 98 % *ee*); ^{1}H NMR (400.1 MHz, $CDCl_3$); 0.76 (t, $J = 7.3$, 3H; Me), 1.14 (sextet, $J = 7.3$, 2H; $MeCH_2$), 1.52 (quintet, $J = 6.8$, 2H; CH_2Et), 4.04 (m, 3H; $ArOCH_2n$Pr), 5.23 (br s, 1H; OH), 7.19 (d, $J = 8.3$, 1H; $H_{8or8'}$), 7.27 – 7.45 (m, 7H, Ar), 7.92-7.96 (m, 2H; $H_{5and5'}$), 7.97 (d, $J = 8.8$, 1H; $H_{4or4'}$), 8.02 (d, $J = 9.0$, 1H; $H_{4or4'}$); ^{13}C NMR (100.6 MHz, $CDCl_3$) $\delta = 13.6$ (Me), 18.8 (CH_2), 31.3 (CH_2), 69.5 (CH_2), 115.4, 115.7, 116.5, 117.6, 123.2, 124.2, 125.1, 125.2, 126.3, 127.2, 128.1, 128.2, 129.2, 129.6, 129.7, 130.8, 134.0, 134.2, 151.4, 155.6; IR (diffuse reflectance): $\tilde{\nu}_{max} = 3472$ (m, OH), 3417 (w, OH), 2969 (w, C–H), 2957 (w, C–H), 1619 (m), 1590 (m), 1505 (m), 1379 (m), 1272 (m), 1205 (m), 1179 (m), 1081 (m, C-O), 814 cm^{-1} (s). Racemic **2** has appeared, but apparently no spectroscopic details have been published.[25]

Enone preparation by LDA-enolate chemistry: Diisopropylamine (3.34 mL, 23.8 mmol) in THF (30 mL) was cooled to −78 °C, and *n*BuLi (12.0 mL, 2.0 M, 23.8 mmol) was added. The solution was stirred for 30 min before addition of ketone (23.8 mmol) in THF (0.7 mL). After 30 min, neat aldehyde (23.8 mmol) was added dropwise. The solution was stirred for a further 30 min at −78 °C before the cooling bath was removed, and stirring was continued at ambient temperature for 10 mins. Water (20 mL) was added, and the layers were separated, the organic phase was dried ($MgSO_4$), and the solvent was removed. The residue was dissolved in diethyl ether, conc. HCl (*ca* 5 mL) was added, and the elimination of the alcohol was monitored by TLC. Flash column chromatography (diethyl ether/pentane 1:8) or Kugelrohr distillation followed. Typically 55 – 70 % isolated yield was obtained.

Enone preparation by Wittig chemistry: The aldehyde (20.7 mmol) and Ph_3P=CH(COMe) (21.7 mmol) were heated to reflux in THF (40 mL) for 6 h – overnight, the solution was cooled, and the solvent was removed. The enone was extracted from the white precipitate with pentane (5 × 10 mL), and the pentane was removed under reduced pressure. The resulting oil was purified by column chromatography (hexane/Et_2O 23:2). Typically 55 – 75 % isolated yield was obtained.

0947-6539/03/0903-0780 $ 20.00+.50/0 *Chem. Eur. J.* **2003**, *9*, No. 3

(*E*)-6,6-Dimethylhept-3-en-2-one (3d): Yield 50%; oil; ^{1}H NMR (400.1 MHz, $CDCl_3$) $\delta = 0.94$ (s, 9H; *t*Bu), 2.11 (dd, $J = 7.8$, 1.3, 2H; CH_2), 2.25 (s, 3H; *Me*CO), 6.06 (dt, $J = 15.8$, 1.3 1H; =*CH*CO), 6.82 (dt, 15.8, 7.8, 1H; CH_2CH=); ^{13}C NMR (125.8 MHz, $CDCl_3$) $\delta = 27.4$, 29.8 (*t*Bu), 31.9, 47.3 (Me), 133.7 (=CH), 146.2 (=CH), 198.9 (C=O); IR (liquid film): $\tilde{\nu}_{max} = 2958$ (s, C–H) 2868 (m, C–H), 1698 (m), 1676 (s, C=O), 1628 (m), 1474 (m), 1431 (w), 1394 (w), 1365 (s), 1261 (m), 1251 (m), 1236 (m), 1185 (w), 982 cm^{-1} (m); found (HRMS, EI) = 140.11976 [M^+], $C_9H_{16}O$ requires *M* 140.12012. Only limited literature data are available for this compound.[26]

(*E*)-4-Cyclohexylbut-3-en-2-one (3f): Oil; ^{1}H NMR (400.1 MHz, $CDCl_3$) $\delta = 1.10$–1.38 (m, 5H; Cy), 1.68–1.80 (m, 5H; Cy), 2.15 (m, 1H; $(CH_2)_2CH$CH=), 2.25 (s, 3H; Me), 6.05 (dd, $J = 16.1$, 1.3, 1H; =*CH*CO), 6.74 (dd, 16.1, 6.8, 1H; Cy*CH*=); ^{13}C NMR (100.6 MHz, $CDCl_3$) $\delta = 26.1$ (Cy), 26.2 (Cy), 27.2, 32.1, 41.0 (Me), 129.2 (=CH), 153.7 (=CH), 199.5 (C=O) ; IR (liquid film): $\tilde{\nu}_{max} = 2925$ (s, C–H), 2852 (s, C–H), 1697 (s, C=O), 1675 (s, C=C), 1624 (s, C=C), 1449 (m), 1357 (m), 1252 (s), 909 cm^{-1} (s); found (HRMS, EI) = 152.12058 [M^+], $C_{10}H_{16}O$ requires *M* 152.12012. These data are comparable to those for **3f** prepared by a different route.[27]

(*E*)-4-Dec-4-en-3-one (3g): Oil; ^{1}H NMR (500.1 MHz, $CDCl_3$) $\delta = 0.90$ (t, $J = 6.8$, 3H; $(CH_2)_4Me$), 1.10 (t, $J = 7.3$, 3H; $COCH_2Me$), 1.28–1.38 [m, 4H; $(CH_2)_2$Me], 1.47 (quin, $J = 7.3$, 2H; $=CHCH_2CH_2$), 2.12 (dq, $J = 1.3$, 7.3, 2H; CH_2CH=), 2.57 (q, $J = 7.3$, 2H; $COCH_2Me$), 6.10 (dt, $J = 16.0$, 1.3, 1H; =*CH*CO), 6.84 (dt, $J = 16.0$, 6.9, 1H; CH_2CH=); ^{13}C NMR (125.8 MHz, $CDCl_3$) $\delta = 8.2$ (Me), 14.0 (Me), 22.5, 27.9, 31.4, 32.5, 33.2, 130.1 (=CH), 147.3 (=CH), 201.3 (C=O); IR (liquid film): $\tilde{\nu}_{max} = 2958$ (s, C–H), 2931 (s, C–H), 2858 (s, C–H), 1700 (m), 1676 (s, C=O), 1631 (s, C=C), 1459 (m), 1357 (m), 1202 (m), 983 cm^{-1} (m); found (HRMS, EI) = 154.136073 [M^+], $C_{10}H_{18}O$ requires *M* 154.135765. This compound has appeared, but no data were presented.[28]

(*E*)-2-Methylundec-5-en-4-one (3h): Oil; ^{1}H NMR (400.1 MHz, $CDCl_3$) $\delta = 0.89$ (t, $J = 7.0$, 3H; $(CH_2)_4Me$), 0.93 (d, $J = 6.7$, 6H; $CHMe_2$), 1.27–1.34 (m, 4H; $(CH_2)_2$Me), 1.46 (quintet, $J = 7.0$, 2H; CH_2CH_2CH=), 2.16 (m, 1H; CH_2CHMe$_2$) overlapped by 2.21 (dq, $J = 1.5$, 7.0, 2H; CH_2CH=), 2.40 (d, $J = 7.0$, 2H; $COCH_2$), 6.08 (dt, $J = 15.9$, 1.5, 1H; =*CH*CO), 6.81 (1H; dt, $J =$ 15.8, 7.0, CH_2CH=); ^{13}C NMR (100.6 MHz, $CDCl_3$) 14.3 (Me), 22.8, 23.0 ($CHMe_2$), 25.5, 28.1, 31.7, 32.8, 49.5, 131.1 (=CH), 147.8 (=CH), 201.0 (C=O); IR (liquid film): $\tilde{\nu}_{max} = 2965$ (s, C–H), 2930 (m, C–H), 2871 (m, C–H), 1676 (s, C=O), 1626 (C=C), 1360 (s), 1259 (s), 983 cm^{-1} (m); found (HRMS, EI) = 182.16706 [M^+], $C_{12}H_{22}O$ requires *M* 182.16707.

(*E*)-1-Cyclohexyl-5-methyl-hex-1-en-3-one (3j): Oil; ^{1}H NMR (400.1 MHz, $CDCl_3$) $\delta = 0.93$ (d, $J = 6.7$, 6H; $CHMe_2$), 1.08–1.37 (m, 5H; Cy), 1.64–1.80 (2m, 5H; Cy) 2.14 (tsept, $J = 7.0$, 6.6, 2H; $CHMe_2$) 2.27 (m, 1H; $CHCH$=), 2.40 (d, $J = 7.0$, 2H; CH_2*i*Pr) 6.04 (dd, 16.0, 1.2, 1H; =*CH*CO), 6.74 (dd, $J = 16.0$, 6.8, 1H; $CHCH$=); ^{13}C NMR (100.6 MHz, $CDCl_3$); 22.9, 25.3, 25.9, 26.1, 32.0, 40.8, 49.3, 128.4 (=CH), 152.4 (=CH), 201.2 (C=O); IR (liquid film): $\tilde{\nu}_{max} = 2927$ (s, br, C–H), 2853 (s, C–H), 1695 (s, C=O), 1676 (s, C=O), 1626 (s, C=C), 1465 (m), 1449 (m), 1366 (m), 1293 (m), 1196 (m), 981 cm^{-1} (m); found (HRMS, EI) = 194.16679 [M^+], $C_{13}H_{22}O$ requires *M* 194.16707.

General procedure for asymmetric conjugate additions: All conjugate addition preparations were carried out in flame-dried argon-filled glassware.

Cryostat method: A solution of ligand (35.9 mg, 0.10 mmol, 20 mol%) in THF (1 mL) was added to $[Cu(MeCN)_4]BF_4$ (28.3 mg, 0.09 mmol, 18 mol%) and cooled by cryostat (−45 °C to −46 °C). The enone (0.50 mmol) was diluted with THF (0.5 mL). $AlMe_3$ (1.7 eqiuv, ~2.0 M, 0.85 mmol) was diluted to 0.8 mL with THF. An aliquot of the $AlMe_3$ (0.1 mL) solution was added to the ligand–copper solution to form the precatalyst, and the solution was stirred for about 1 min. The remaining reagents were added simultaneously by syringe pump over 20 mins. The solution was stirred for a further 18 h. Undecane (50 μL) was added as internal standard. HCl (2 M, 2 mL) was added to quench the reaction, and the solution was warmed to room temperature with rapid stirring.

Non-cryostat methods: A solution of ligand (35.9 mg, 0.10 mmol, 20 mol%) in THF (1 mL) was added to $[Cu(MeCN)_4]BF_4$ (28.3 mg, 0.09 mmol, 18 mol%), and the resulting mixture was cooled to −20 °C. An aliquot (0.02 mL) of a solution of $AlMe_3$ (2.2 eqiuv, 0.58 mL, 1.91 M, 1.10 mmol in hexanes) was added, forming the precatalyst, and the solution was cooled to −78 °C. The remaining $AlMe_3$ was added, followed by neat nonenone (83 μL, 0.50 mmol), and the mixture was allowed to warm slowly to room temperature overnight. (Alternatively a cyclohexenone/CO_2 bath may be used to maintain approximately −50 °C reaction temperature).

The conjugate addition products were isolated directly from the catalytic reactions by flash chromatography. Compound (*R*)-(+)-**4a** had literature properties.[7, 10] We obtained $[\alpha]_D^{20} = +6.8$ ($c = 1.17$ in $CHCl_3$ for 83% *ee* material). Details of the enantiomer separations are given in Table 7.

Table 7. Chiral GC conditions for the analysis of addition products **4**.[a]

Product	Column	Programme	Elution order [min] (config.)[b]
4a	6-Me-2,3-pe-δ-CD	70 °C isothermal	21.77 (−)-(*S*)
			22.40 (+)-(*R*)
4b	6-Me-2,3-pe-δ-CD	70 °C isothermal	39.39 (−)-(*S*)
			41.35 (+)-(*R*)
4c	6-Me-2,3-pe-δ-CD	75 °C isothermal	6.36 (−)-(*S*)
			6.47 (+)-(*R*)
4d	6-Me-2,3-pe-δ-CD	65 °C isothermal	13.53 (−)-(*S*)
			14.05 (+)-(*R*)
4e	6-Me-2,3-pe-δ-CD	70 °C isothermal	6.10 (+/−)[c]
			6.40 (+/−)
4f	2,6-Me-3-pe-δ-CD	120 °C isothermal	31.81 (−)-(*S*)
			34.40 (+)-(*R*)
4g	6-Me-2,3-pe-δ-CD	75 °C isothermal	29.56 (−)-(*S*)
			31.10 (+)-(*R*)
4h	2,6-Me-3-pe-δ-CD	95 °C isothermal	41.07 (+/−)[c]
			44.83 (+/−)
4i	2,6-Me-3-pe-δ-CD	95 °C isothermal	22.57 (+/−)[c]
			24.90 (+/−)
4j	2,6-Me-3-pe-δ-CD	115 °C isothermal	14.53 (−/+)[c]
			17.00 (−/+)

[a] Carried out on equipment described previously:[10] 6-Me-2,3-pe-δ-CD is 25 m Octakis(6-0-methyl-2,3-di-*O*-pentyl-γ-cyclodextrin 0.25 μm internal diameter (60% in OV1701, w/w)); 2,6-Me-3-pe-δ-CD is 25 m Octakis(2,6-di-*O*-methyl-3–0-pentyl)-γ-cyclodextrin 0.25 μm i.d. (50% in OV1701 *w/w*.[23] [b] Antipode assignment based on largest peak in GC trace corresponding with the sign of the optical rotation of the bulk sample. [c] Value of optical rotation does not allow for confident assignment.

(*R*)-(+)-4-methyldecan-2-one (4b): Isolated yield 58%; oil; $[\alpha]_D^{24} = +9.6$ ($c = 0.98$ in $CHCl_3$, 86% *ee*); ^{1}H NMR (400.1 MHz, $CDCl_3$) $\delta = 0.89$ (t, $J =$ 6.9, 3H; $(CH_2)_5Me$), overlapped by 0.89 (d, $J = 6.6$, 3H; *Me*CH), 1.1–1.35 (m, 10H; $(CH_2)_5$), 1.89 (m, 1H; *n*Hex*CH*Me), 2.13 (s, 3H; *Me*CO), 2.22 (dd, $J = 15.8$, 8.1, 1H; $CH_{2\alpha}$COMe), 2.40 (dd, $J = 15.8$, 5.7, 1H; $CH_{2\beta}$COMe); ^{13}C NMR (100.6 MHz, $CDCl_3$) $\delta = 14.5$, 20.2, 23.0, 27.3, 29.7, 29.8, 30.8, 32.3, 37.3, 51.7, 209.6 (C=O); IR (liquid film): $\tilde{\nu}_{max} = 2956$ (s, C–H), 2926 (s, C–H), 2872 (s, C–H), 2855 (s, C–H), 1717 (s, C=C), 1463 (m), 1364 (m), 1165 cm^{-1} (m); found (HRMS, EI) = 170.16747 [M^+], $C_{11}H_{22}O$ requires *M* 170.16707. Apparently only polarimetry data have been published for (*R*)-**4b**.[16]

(*R*)-(+)-4,6-Dimethylheptan-2-one (4c): Isolated yield 63%; oil; $[\alpha]_D^{24} = +14.4$ ($c = 1.17$ in $CDCl_3$, 87% *ee*); ^{1}H NMR (400.1 MHz, $CDCl_3$); 0.87–0.89 (3 × d, $J = \sim 6.6$, 9H; diastereotopic $CHMe_2$ overlapped by CH*Me*), 1.02–1.13 (m, 2H; *i*PrCH_2CH), 1.62 (apparent dbr nonet, $J = 1.1$, 6.6, 1H; CH_2CHMe$_2$), 2.07 (m, 1H; MeC*H*), 2.13 (s, 3H; CO*Me*), 2.21 (dd, $J = 15.6$, 8.2, 1H; $CH_{2\alpha}$COMe), 2.38 (dd, $J = 15.7$, 5.5, 1H; $CH_{2\beta}$COMe); ^{13}C NMR (100.6 MHz, $CDCl_3$) $\delta = 20.2$ (Me), 22.5 (Me), 23.6, 25.6, 27.4, 29.1, 46.9, 52.0, 228.2 (C=O); IR (liquid film): $\tilde{\nu}_{max} = 2956$ (s, C–H), 2930 (s, C–H), 2871 (s, C–H), 2842 (w), 1717 (s, C=C), 1468 (m), 1421 (w), 1384 (m), 1365 (s), 1169 cm^{-1} (m); found (HRMS, EI) = 142.13560 [M^+], $C_9H_{18}O$ requires *M* 142.13577. Only limited data have appeared for this compound.[29]

(*R*)-(+)-4,6,6-Trimethylheptan-2-one (4d): Isolated yield 46%; oil; $[\alpha]_D^{24} = +6.7$ ($c = 0.99$ in $CHCl_3$, 93% *ee*); ^{1}H NMR (400.1 MHz, $CDCl_3$) $\delta = 0.91$ (s, 9H; *t*Bu), 0.94 (d, $J = 6.6$, 3H; *t*BuCHMe), 1.11 (dd, $J = 13.9$, 6.3, 1H; $CH_{2\alpha}t$Bu), 1.19 (dd, $J = 13.9$, 4.2, 1H; $CH_{2\beta}t$Bu), 2.04–2.14 (m, 1H; CHMe) overlapped by 2.12 (s, 3H; COMe), 2.27 (dd, $J = 15.8$, 8.2, 1H; $CH_{2\alpha}$ COMe), 2.42 (dd, $J = 15.8$, 5.5, 1H; $CH_{2\beta}$COMe); ^{13}C NMR (100.6 MHz, $CDCl_3$) $\delta = 23.1$, 26.3, 30.4 (3C, *t*Bu), 30.8, 31.5 (C), 51.3, 53.9, 209.4 (C=O);

IR (liquid film): $\tilde{\nu}_{max} = 2955$ (s, C–H), 2870 (m, C–H), 1717 (s, C=C), 1364 (s), 1246 (w), 1157 cm^{-1} (m); found (HRMS, EI) = 165.15113 [M^+], $C_{10}H_{20}O$ requires M 165.15141. Only limited data have appeared for this compound.[30]

(−)-4,5-Dimethylhexan-2-one (4e): Isolated yield 55%, 97% conversion (GC); oil; $[\alpha]_D^{24} = -6.6$ ($c = 1.05$ in $CDCl_3$, 90% *ee*); ^{1}H NMR (400.1 MHz, $CDCl_3$) $\delta = 0.83$ (d, $J = 6.8$, 3H; CH$Me_{2\alpha}$), 0.84 (d, $J = 6.8$, 3H; CH$Me_{2\beta}$), 0.85 (d, $J = 6.8$, 3H; *i*PrCH*Me*), 1.50 (dbr septet, $J = 6.8$, 2.1, 1H; C*H*Me_2), 1.93 (m, 1H; C*H*Me), 2.14 (s, 3H; COMe), 2.20 (dd, $J = 15.7$, 9.2, 1H; $CH_{2\alpha}$COMe), 2.44 (dd, $J = 15.7$, 4.7, 1H; $CH_{2\beta}$COMe); ^{13}C NMR (67.8 MHz, $CDCl_3$) $\delta = 15.9$ (Me), 18.3 (Me), 19.8 (Me), 30.4, 32.2, 34.7, 48.4, 209.0 (C=O); IR (liquid film): $\tilde{\nu}_{max} = 2959$ (s, C–H), 2875 (s, C–H), 1717 (s, C=C), 1464 (m), 1368 (m), 1164 cm^{-1} (m); found (HRMS, EI) = 128.12047 [M^+], $C_8H_{16}O$ requires M 128.12012.

***(R)*-(+)-4-Cyclohexyl-4-methylbutan-2-one (4f)**: Isolated yield 58%; oil; $[\alpha]_D^{24} = +5.4$ ($c = 1.03$ in $CHCl_3$, 92% *ee*); ^{1}H NMR (400.1 MHz, $CDCl_3$) $\delta = 0.85$ (d, $J = 6.8$, 3H; CyCH*Me*), 0.94–1.50 (m, 2H; Cy) overlapped by 1.30–1.50 (m, 4H; Cy), 1.60–1.70 (m, 3H; Cy), 1.70–1.79 (m, 2H; Cy), 1.90 (m, 1H; Cy*CH*), 2.13 (s, 3H; *Me*CO), 2.20 (dd, $J = 15.8$, 9.2, 1H; $CH_{2\alpha}$COCy), 2.47 (dd, $J = 15.8$, 4.7, 1H; $CH_{2\beta}$COCy); ^{13}C NMR (100.6 MHz, $CDCl_3$) $\delta = 17.0$, 27.0, 27.1, 29.5, 30.7, 34.6, 43.2, 49.0, 209.9 (C=O), the signals at 27.0, 27.1 and 30.7 show fine structure due to the presence of diastereotopic carbons; IR (liquid film): $\tilde{\nu}_{max} = 2924$ (s, C–H), 2852 (s, C–H), 1717 (s, C=C), 1448 (m), 1357 (m), 1164 (m), 890 cm^{-1} (w); found (HRMS, EI) = 168.150677 [M^+], $C_{11}H_{20}O$ requires M 168.15141.

***(R)*-(+)-5-Methyldecan-3-one (4g)**: Isolated yield 52%; oil; $[\alpha]_D^{24} = +5.6$ ($c = 1.07$, $CDCl_3$, 80% *ee*); ^{1}H NMR (400.1 MHz, $CDCl_3$) $\delta = 0.88$ (d, $J = 6.6$, 3H; *n*PentCH*Me*) overlapped by 0.89 (t, $J = 6.9$, 3H; $(CH_2)_4Me$), 1.05 (t, $J = 7.3$, 3H; *Me*CH_2CO), 1.10–1.36 (m, 8H; $(CH_2)_4$), 1.20–1.35, 1.97–2.05 (m, 1H; C*H*Me), 2.20 (dd, $J = 15.6$, 8.0, 1H; $CH_{2\alpha}$COEt), 2.37 (dd, $J = 15.6$, 5.7, 1H; $CH_{2\beta}$COEt) overlapped by 2.40 (dq, $J = 10.6$, 2.4, 2H; MeCH_2CO); ^{13}C NMR (100.6 MHz, $CDCl_3$) $\delta = 8.2$ (Me), 14.5 (Me), 20.3 (Me), 23.0, 27.0, 29.7, 32.4, 36.9, 37.4, 50.4 216.2 (C=O); IR (liquid film): $\tilde{\nu}_{max} = 2957$ (s, C–H), 2927 (s, C–H), 2872 (s, C–H), 2866 (s), 1716 (s, C=C), 1459 (m), 1412 (w), 1376 (m), 1106 (m), 725 cm^{-1} (w); found (HRMS, EI) = 170.166296 [M^+], $C_{11}H_{22}O$ requires M 170.167066.

(+)-2,6-Dimethylundecan-4-one (4h): Isolated yield 54%; oil; $[\alpha]_D^{24} = +2.8$ ($c = 1.08$ in $CHCl_3$, 79% *ee*); ^{1}H NMR (400.1 MHz, $CDCl_3$) $\delta = 0.88$ (d, $J = 6.6$, 3H; *n*PentCH*Me*) overlapped by 0.88 (t, $J = 6.8$, 3H; $(CH_2)_4Me$), 0.915 (d, $J = 6.7$, 3H; CH$Me_{2\alpha}$) overlapped by 0.92 (d, $J = 6.7$, 3H; CH$Me_{2\beta}$), 1.10–1.35 (m, 8H; $(CH_2)_4$), 2.00 (m, 1H; C*H*Me), 2.14 (m, 1H; CH_2CHMe_2) overlapped by 2.18 (dd, $J = 15.8$, 8.0, 1H; $CH_{2\alpha}$CO*i*Bu), 2.26 (d, $J = 7.1$, 2H; $COCH_2$*i*Pr), 2.35 (dd, $J = 15.8$, 5.6, 1H; $CH_{2\beta}$CO*i*Bu); ^{13}C NMR (100.6 MHz, $CDCl_3$) $\delta = 14.5$ (Me), 20.3 (Me), 23.0 (3C), 24.9, 27.0, 29.6, 32.4, 37.3, 51.2, 52.8; C=O signal not apparent at signal-to-noise level in spectrum; IR (liquid film): $\tilde{\nu}_{max} = 2956$ (s, C–H), 2927 (s, C–H), 2872 (s, C–H), 1712 (s, C=C), 1467 (m), 1366 (m), 1144 (w), 1044 cm^{-1} (w), found (HRMS, EI) = 198.197378 [M^+], $C_{13}H_{26}O$ requires M 198.198366.

(−)-2,5-Dimethyldecan-3-one (4i): Isolated yield 62%; oil; $[\alpha]_D^{24} = -8.9$ ($c = 1.12$ in $CHCl_3$, 68% *ee*); ^{1}H NMR (400.1 MHz, $CDCl_3$) $\delta = 0.87$ (d, $J = 6.7$, 3H; *n*PentCH*Me*) overlapped by 0.88 (t, $J = 6.9$, 3H; $(CH_2)_4Me$), 1.08 (d, $J = 6.9$, 6H; CHMe_2), 1.20–1.35 (m, 8H; $(CH_2)_4$), 2.02 (m, 1H; CH_2CHMe), 2.26 (dd, $J = 16.2$, 8.0, 1H; $CH_{2\alpha}$CO*i*Pr), 2.41 (dd, $J = 16.2$, 5.7, 1H; $CH_{2\beta}$CO*i*Pr), 2.58 (septet, $J = 6.9$, 1H; C*H*Me_2); ^{13}C NMR (100.6 MHz, $CDCl_3$) $\delta = 14.5$ (Me), 18.5 ($CHMe_\alpha$), 18.6 ($CHMe_\beta$), 20.3, 23.0, 27.1, 29.4, 32.4, 37.3, 41.5, 48.4, 216.0 (C=O); IR (liquid film): $\tilde{\nu}_{max} =$ 2961 (s, C–H), 2928 (s, C–H), 2872 (m, C–H), 2857 (m, C–H), 1711 (s, C=C), 1466 (m), 1381 (m), 1032 (w), 725 cm^{-1} (w); found (HRMS, EI) = 184.182085 [M^+], $C_{12}H_{24}O$ requires M 184.182716.

(+)-1-Cyclohexyl-1,5-dimethylhexan-4-one (4j): Isolated yield 59%; oil; $[\alpha]_D^{24} = +1.4$ ($c = 1.06$, $CDCl_3$, 78% *ee*); ^{1}H NMR (500.1 MHz, $CDCl_3$) $\delta =$ 0.83 (d, $J = 6.8$, 3H; CyCH*Me*), 0.91 (d, $J = 6.8$, 3H; CHMe_2) overlapped by 0.92 (d, $J = 6.8$, 3H; CHMe_2), 0.92–1.05 (m, 2H; Cy), 1.06–1.25 (m, 4H; Cy), 1.58 (m, 3H; Cy), 1.70–1.78 (m, 2H; Cy), 1.92 (m, 1H; Cy*CH*Me), 2.14 (septet, $J = 6.8$, 1H; C*H*Me_2) overlapped by 2.16 (dd, $J = 15.7$, 9.1, 1H; $CHCH_{2\alpha}$CO*i*Bu), 2.26 (d, $J = 6.8$, 2H; $COCH_2$*i*Pr), 2.41 (dd, $J = 15.7$, 4.6, 1H; $CHCH_{2\beta}$CO*i*Bu); ^{13}C NMR (100.6 MHz, $CDCl_3$) $\delta = 16.8$ (Me), 22.8 (2Me), 24.7, 26.9, 29.2, 30.6, 34.2, 42.9, 48.3, 52.7, 211.5 (C=O), the signals at 22.8 and 26.9 show fine structure due to the presence of diastereotopic carbons; IR (liquid film): $\tilde{\nu}_{max} = 2955$ (s, C–H), 2925 (s, C–H), 2852 (s, C–H), 1711(s, C=C), 1448 (m), 1366 cm^{-1} (m); found (HRMS, EI) = 198.197378 [M^+], $C_{13}H_{26}O$ requires M 198.198366.

(−)-(*R*)-Muscone: Addition of $AlMe_3$ to enone **7** under standard 5% loading conditions afforded Muscone after flash chromatography (eluent: 2% Et_2O in petrol). Yield 39%; oil; $[\alpha]_D^{20} = -7.6$ ($c = 1.05$ in $CDCl_3$, 77% *ee*); ^{1}H NMR (400.1 MHz, $CDCl_3$) $\delta = 0.94$ (d, $J = 6.7$, 3H; CH*Me*), 1.20–1.38 (m, 20H; $(CH_2)_{10}$), 1.53–1.75 (m, 2H; $(CH_2)_{10}CH_2CHMe$), 2.06 (m, 1H; C*H*Me), 2.19 (dd, $J = 14.9$, 5.0, 1H; $CHCH_{2\alpha}$CO), 2.41 (t, $J = 6.9$, 2H; $(CH_2)_{10}CH_2$CO) overlapped by 2.43 (dd, $J = 14.9$, 8.2, 1H; $CHCH_{2\beta}$CO); ^{13}C NMR (100.6 MHz, $CDCl_3$) $\delta = 21.3$ (Me), 23.2, 25.2, 26.3, 26.4, 26.7, 26.7, 26.8, 26.9, 27.3, 27.7, 29.2, 35.7, 42.2, 50.6, 212.3 (C=O); IR (liquid film): $\tilde{\nu}_{max} = 2928$ (s, C–H), 2857 (s, C–H), 1711 (s, C=C), 1459 cm^{-1} (m); found (HRMS, EI) = 238.22977 [M^+], $C_{16}H_{30}O$ requires M 238.22966. These data were consistent with published values.[31]

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[1] Synthetic reviews: N. Krause, A. Hoffmann-Roder, *Synthesis* **2001**, 171–196, and references therein.
[2] Mechanistic reviews: a) E. Nakamura, S. Mori, *Angew. Chem.* **2000**, *112*, 3902–3924; *Angew. Chem. Int. Ed.* **2000**, *39*, 3750–3771; b) S. Woodward, *Chem. Soc. Rev.* **2000**, *29*, 393–401.
[3] A. Alexakis, J. Vastra, J. Burton, P. Mangeney, *Tetrahedron: Asymmetry* **1997**, *8*, 3193–3196; K. Soai, T. Hayasaka, S. Ugajin, *J. Chem. Soc. Chem. Commun.* **1989**, 516–517.
[4] I. H. Escher, A. Pfaltz, *Tetrahedron* **2000**, *56*, 2879–288; S. J. Degrado, H. Mizutani, A. H. Hoveyda, *J. Am. Chem. Soc.* **2001**, *123*, 755–756.
[5] B. L. Feringa, *Acc. Chem. Res.* **2000**, 33, 346–353.
[6] C. Bolm, M. Ewald, M. Felder, *Chem. Ber.* **1992**, 125, 1205–1215.
[7] H. Mizutani, S. J. Degrado, A. H. Hoveyda, *J. Am. Chem. Soc.* **2002**, *124*, 779–781.
[8] S. Woodward, *Tetrahedron* **2002**, *58*, 1017–1050, especially section 5.3.
[9] S. M. Azad, S. M. W. Bennett, J. Green, E. Sinn, C. M. Topping, S. Woodward, S. M. Brown, *J. Chem. Soc. Perkin Trans. 1* **1997**, 689–694.
[10] S. M. W. Bennett, S. M. Brown, A. Cunningham, M. R. Dennis, J. P. Muxworthy, M. A. Oakley, S. Woodward, *Tetrahedron* **2000**, *56*, 2847–2855.
[11] M. Takahashi, K. Ogasawara, *Tetrahedron: Asymmetry* **1997**, *8*, 3125–3130.
[12] As far as we are aware Corey has been the only one to specifically address this point: E. J. Corey, R. Naef, F. J. Hannon, *J. Am. Chem. Soc.* **1986**, *108*, 7114–7116.
[13] P. L. Bryant, C. R. Harwell, A. A. Mrse, E. F. Emery, Z. Gan, T. Caldwell, A. P. Reyes, P. Kuhns, D. W. Hoyt, L. S. Simeral, R. W. Hall, L. G. Butler, *J. Am. Chem. Soc.* **2001**, *123*, 12009–12017; V. N. Panchenko, V. A. Zakharov, I. G. Danilova, E. A. Paukshtis, I. I. Zakharov, V. G. Goncharov, A. P. Suknev, *J. Mol. Catal. A* **2001**, *174*, 107–117.
[14] L. S. Hegedus, P. M. Kendall, S. M. Lo, J. R. Sheats, *J. Am. Chem. Soc.* **1975**, *97*, 5448–5452.
[15] D. A. Evans, M. D. Ennis, D. J. Mathre, *J. Am. Chem. Soc.* **1982**, *104*, 1737–1739; V. Garcia-Ruiz, S. Woodward, *Tetrahedron: Asymmetry* **2002**, *13*, 2177–2180.
[16] G. Bram, D. Cabaret, N. Maigrot, J.-P. Mazaleyrat, Z. Welvart, *J. Chem. Res.* **1979**, 196–197.
[17] P. K. Fraser, S. Woodward, *Tetrahedron Lett.* **2001**, *42*, 2747–2749.
[18] A. Alexakis, C. Benhaim, S. Rosset, M. Humam, *J. Am. Chem. Soc.* **2002**, *124*, 5262–5263.
[19] A. Alexakis, C. Benhaim, X. Fournioux, A. van den Heuvel, J.-M. Leveque, S. March, S. Rosset, *Synlett* **1999**, 1811–1813.

  0947-6539/03/0903-0782 $ 20.00+.50/0

[20] Up to 68% stereoselectivity was reported by Iwata's group: Y. Takemoto, S. Kuraoka, N. Hamaue, C. Iwata, *Tetrahedron: Asymmetry* **1996**, *7*, 993–996. Typically the selectivities realised in catalytic asymmetric additions of AlR_3 reagents is poor. For example, compare $ZnEt_2$ with $AlEt_3$ in: A. Alexakis, C. Benhaim, *Tetrahedron: Asymmetry* **2001**, *12*, 1151–1157.
[21] G. J. Kubas, *Inorg. Synth.* **1990**, *28*, 68–70.
[22] S. M. W. Bennett, M. R. Dennis, P. K. Fraser, C. M. Topping, S. M. Brown, S. Radojevic, G. Conole, *J. Chem. Soc. Perkin 1 Trans.* **1999**, 3127–3132.
[23] C. Börner, M. R. Dennis, E. Sinn, S. Woodward, *Eur. J. Org. Chem.* **2001**, 2435–2436.
[24] O. De Lucchi, D. Fabri, *Synlett* **1990**, 287–289.
[25] P. Salvadori, C. Rosini, D. Pini, C. Bertucci, P. Altemura, G. Uccello-Barretta, A. Raffaelli, *Tetrahedron* **1987**, *43*, 4969–4978.
[26] A.-M. Loiseau, R. Luft, S. Zunino, *Bull. Soc. Chim. Fr.* **1982**, 144–152.
[27] J. O. Metzger, M. Blumenstein, *Chem. Ber.* **1993**, *126*, 2493–2499.
[28] H. Tokuyama, S. Yokoshima, T. Yamashita, T. Fukuyama, *Tetrahedron Lett.* **1998**, *39*, 3189–3192.
[29] A. Hinnen, J. Dreux, *Bull. Chem. Soc. Fr.* **1964**, 1492–1498.
[30] G. A. Talstikov, F. Kh. Valitov, A. V. Kuchin, *Zh. Obshch. Khim.* **1980**, *50*, 2715–2720 [*Chem. Abs.* **1981**, *94*, 174234].
[31] V. Rautenstrauch, R. L. Snowden, S. M Linder, *Helv. Chim. Acta* **1990**, 73, 896–901.

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