Optimisation, Scope and Limitations of Enantioselective Aldol Reactions of an S-Ketene Silyl Acetal with Aliphatic Aldehydes under (*R*)-BINOL-Titanium(IV) Catalysis Conditions

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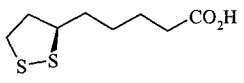
Dedicated to Dr. Maximilian A. Grassberger on the occasion of his 65th birthday

Keywords: Aldehydes / Aldol reaction / Asymmetric catalysis / Ketene silyl acetal / Titanium

The Mukaiyama aldol reaction between the functionalised aldehydes **5** and the S-ketene silyl acetal **2** catalysed by 1,1′-binaphthyl-derived chiral titanium(IV) complex **4** afforded the corresponding aldol products **6** in good yields and with good to excellent enantioselectivities. The chemical yield could further be enhanced, without loss of stereoselection, by addition of phenol and/or molecular sieves. The presented aldol reactions with aluminium, boron and ytterbium-BINOL catalysts demonstrate that only low chiral induction can be achieved. Aldol product **6a** was converted into an α-lipoic acid precursor **8**, thus providing a formal synthesis of this biologically active compound.

Introduction

Because of the recent interest in (*R*)-α-lipoic acid (**1**), a pharmacologically important compound,[1] reliable and efficient methods for its asymmetric synthesis are required. A variety of stereoselective approaches to compound **1** have so far been reported. Enzyme-catalysed reactions of key intermediates[2] have frequently been utilised, but "chemical" routes, such as the iron-mediated method developed by Grée[3] or the Sharpless asymmetric dihydroxylation reaction, have also been employed.[4] We have recently successfully employed asymmetric allylation to prepare enantiopure homoallyl alcohols that can serve as useful intermediates in the synthesis of **1**.[5]



(*R*)-(+)-Lipoic Acid **1**

As part of our research into the preparation of enantiopure *sec*-alcohols, an efficient procedure for enantioselective aldol reactions − in particular with aliphatic functionalised aldehydes − was required. In recent years, considerable success has been achieved in enhancing the yields and stereoselectivities of aldol reactions, ultimately resulting in practical procedures with very useful levels of enantioselectivity.[6] One of the most popular ligands for a variety of metal-mediated enantioselective carbon-carbon bond-forming reactions is C_2-symmetric 1,1′-binaphthyl-2,2′-diol (**4**, abbreviated as BINOL).[7] The use of chiral ligands is not restricted to BINOL **4** and its derivatives: several other highly effective ligands have successfully been employed in enantioselective reactions.[8] We decided to examine BINOL **4** because it is relatively cheap and, more importantly, commercially available in both its *R* and *S* forms. The first BINOL/titanium-catalysed aldol reactions with S-ketene silyl acetal **2** were carried out in the mid-1990s, in particular by Keck[9a] and Mikami.[10a−10c] In general, they obtained the resulting aldol products in reasonable yields and with good enantioselectivities (up to 97% *ee*). Most of these experiments were performed with benzaldehyde or unfunctionalised aldehydes; only a few examples involving functionalised substrates, such as α-benzyloxy- and α-chloro-substituted aldehydes[8d,9,10] and 2,2,2-trifluoroethanal,[11] were reported. We have therefore investigated a broad variety of aliphatic functionalised aldehydes as substrates in a series of BINOL/metal-catalysed aldol reactions. The optimisation and the scope and limitations of the enantioselective aldol reaction with S-ketene silyl acetal **2** as nucleophilic component in the presence of **4** and titanium(IV) are reported here (Scheme 1).

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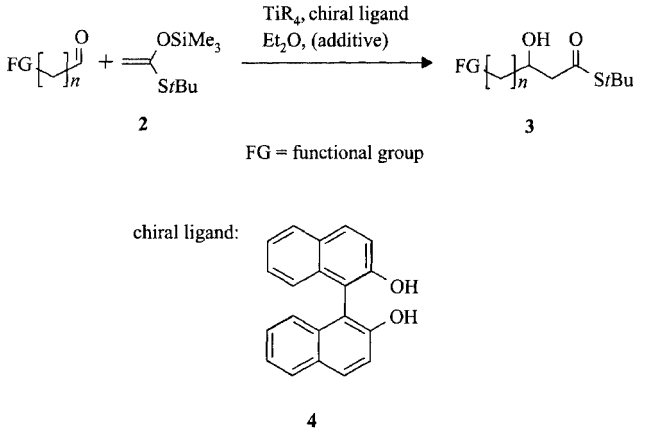
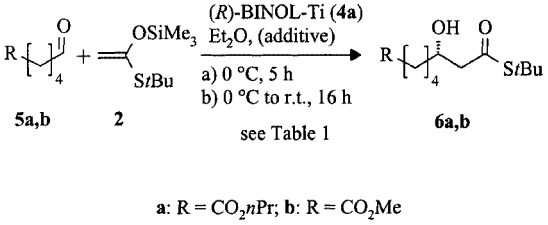


Scheme 1

yield and stereoselectivity (entry 4, Table 1). The reaction mixture was routinely worked up by addition of 2 N HCl solution, although the workups of the initial experiments were done by addition of saturated aqueous NH_4Cl solution instead of acid, resulting in isolation of the corresponding *O*-silylated product **7** as a second component (entries 2, 3 and 6 in Table 1; further examples see Table 2).



a: R = CO_2nPr; **b**: R = CO_2Me

Scheme 2

Results and Discussion

Starting with easily accessible model substrates methoxycarbonyl- and *n*-propoxycarbonyl-substituted aldehydes **5a** and **5b** (which may actually serve as intermediates for the synthesis of **1**), enantioselective aldol reactions were performed with 1.5 equivalents of S-ketene silyl acetal **2** (Scheme 2). Variations of reaction conditions were systematically examined, and typical results are compiled in Table 1. The first experiments were carried out according to a procedure described by Keck and Krishnamurthy.[9] (*R*)-BINOL-Ti catalyst **4a**[12] was generated in situ by mixing (*R*)-BINOL **4** and Ti(O*i*Pr)$_4$ in diethyl ether at room temperature.[13] Our initial efforts focused on reduction of the quantity of premixed catalyst from 10 to 7.5 and 5 mol % (entries 1, 3 and 4, Table 1). It turned out that the enantioselectivity and yield of the aldol reaction were strongly dependent on the amount of catalyst. Use of 10 mol % and also of 7.5 mol % of (*R*)-BINOL-Ti catalyst **4a** provided alcohol **6a** in good yields and with excellent enantioselectivities (93% and > 97% *ee*); however, reduction of the quantity of catalyst **4a** to 5 mol % dramatically decreased both

Combinations of BINOL or its derivatives with achiral and chiral activators were very useful in a variety of asymmetric transformations. These additives may enhance enantioselectivity as well as chemical yield.[14−19] Molecular sieves are a simple and efficient additive for enantioselective C−C bond-forming reactions.[10c] The aldol reaction between model compound **5a** and **2** in the presence of 5 mol % of catalyst **4a** and finely powdered 4 Å molecular sieves (activated by heating to 150 °C, 5 h, 0.15 mbar) afforded **6a** in higher yield and with excellent enantioselectivity (cf. entries 4 and 5, Table 1). Another favourable additive is phenol,[10b][14b,18] which strongly promoted the aldol addition between **5a** and **2** to afford **6a** in better yield and with an enantioselectivity of > 97% *ee* (cf. entries 4 and 8, Table 1). An excellent level of enantioselectivity and the best yield of **6a** could be attained by use of both 4 Å molecular sieves and phenol as additives (entry 11, Table 1). Reduction of the ratio of catalyst **4a**/phenol from 1:5 to 1:1 gave no significant difference in the efficiency of the aldol addition of **5b** and **2** (cf. entries 6 and 7, Table 1).

Table 1. Aldol reactions of aldehydes **5a** and **5b** with S-ketene silyl acetal **2** under conditions of Ti(O*i*Pr)$_4$/(*R*)-BINOL **4a** catalysis (Scheme 2)

Entry	Aldehyde **5**	Amount of catalyst	Additive	Product **6**	Yield of **6**	ee
1	**5a**	10 mol %	−	**6a**	66%	≥ 97%
2	**5b**	10 mol %	−	**6b**	48%[a][b]	96%
3	**5a**	7.5 mol %	−	**6a**	50%[b][c]	93%
4	**5a**	5 mol %	−	**6a**	27%	41%
5	**5a**	5 mol %	mol. sieves (4 Å)	**6a**	64%	≥ 97%
6	**5b**	10 mol %	phenol (50 mol %)	**6b**	39%[b][d]	96%
7	**5b**	10 mol %	phenol (10 mol %)	**6b**	65%	96%
8	**5a**	5 mol %	phenol (50 mol %)	**6a**	70%	≥ 97%
9	**5a**	2.5 mol %	phenol (12.5 mol %)	**6a**	61%	90%
10	**5a**	1.25 mol %	phenol (6.3 mol %)	**6a**	21%	32%
11	**5a**	10 mol %	phenol (50 mol %) mol. sieves (4 Å)	**6a**	76%	≥ 97%
12	**5a**	10 mol %	Me_3SiCl (40 mol %)	**6a**	39%	≥ 97%
13	**5a**	10 mol %	2-*tert*-butylphenol (20 mol %)	**6a**	24%	91%

[a] In addition, *O*-silylated product **7b** was isolated in 20% yield. [b] Workup with sat. aq. NH_4Cl soln. instead of 2 N HCl soln.; see Exp. Sect. [c] In addition, *O*-silylated product **7a** was isolated in 24% yield. [d] In addition, *O*-silylated product **7b** was isolated in 17% yield.

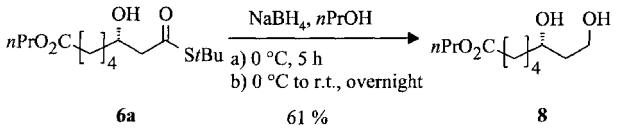
Table 2. Aldol reactions between aldehydes **5c**−**5q** and S-ketene silyl acetal **2** under conditions of Ti(O*i*Pr)$_4$/(*R*)-BINOL **4a** catalysis (Schemes 3−5)

Entry	Aldehyde **5**	Amount of catalyst	Additive	Product **6**	Yield of **6**	ee
1	**5c**	10 mol %	−	**6c**	71%	82%
2	**5c**	10 mol %	phenol (50 mol %)	**6c**	76%	93%
3	**5d**	10 mol %	−	**6d**	52%	38%
4	**5e**	10 mol %	−	**6e**	36%	46%
5	**5e**	10 mol %	phenol (50 mol %)	**6e**	58%	53%
6	**5f**	10 mol %	−	**6f**	65%	95%
7	**5f**	10 mol %	phenol (50 mol %)	**6f**	71%	96%
8	**5g**	10 mol %	−	**6g**	68%	97%
9	**5g**	10 mol %	phenol (50 mol %)	**6g**	73%	96%
10	**5h**	10 mol %	−	**6h**	50%	94%
11	**5h**	10 mol %	phenol (50 mol %)	**6h**	85%	92%
12	**5h**	5 mol %	phenol (25 mol %)	**6h**	56%	92%
13	**5h**	5 mol %	phenol (25 mol %) mol. sieves (4 Å)	**6h**	43%[a][b]	94%
14	**5i**	10 mol %	−	**6i**	23%	90%
15	**5i**	10 mol %	phenol (20 mol %)	**6i**	22%[b][c]	95%
16	**5j**	10 mol %	−	**6j**	26% [b][d]	71%
17	**5j**	10 mol %	phenol (20 mol %)	**6j**	65%	63%
18	**5k**	10 mol %	−	**6k**	23%	62%
19	**5l**	10 mol %	−	**6l**	76%[b][e]	95%
20	**5m**	10 mol %	phenol (50 mol %)	**6m**	31%[f]	[g]
21	**5n**	10 mol %	−	**10**	40%[h]	[g]
22	**5o**	10 mol %	−	**6o**	0%	−
23	**5p**	10 mol %	−	**6p**	0%	−
24	**5q**	10 mol %	−	**6q**	0%	−

[a] In addition, desilylated product **7h** was isolated in 31% yield. [b] Workup with sat. aq. NH_4Cl soln. instead of 2 N HCl soln.; see Exp. Sect. [c] In addition, desilylated product **9** was isolated in 48% yield. [d] In addition, *O*-silylated product **7j** was isolated in 2% yield. [e] In addition, *O*-silylated product **7l** was isolated in 11% yield. [f] Mixture of two diastereomers (64:36). [g] Not determined. [h] Mixture of *cis*/*trans* diastereomers (55:45).

We next studied the effect of reducing the amount of catalyst in the presence of phenol. Interestingly, the catalyst loading could be reduced to 2.5 mol % of **4a** with almost no negative effect, except that the *ee* was decreased slightly (entries 8 and 9, Table 1). On the other hand, use of only 1.25 mol % of catalyst **4a** and 6.3 mol % of phenol resulted in poor selectivity (32% *ee*) and a low yield (21%) of **6a** (entry 10). Aldol reactions in the presence of sterically bulky phenols, such as 2-*tert*-butylphenol (entry 13) and chlorotrimethylsilane (entry 12), furnished **6a** with good to excellent enantioselectivities, but the yields were only moderate.

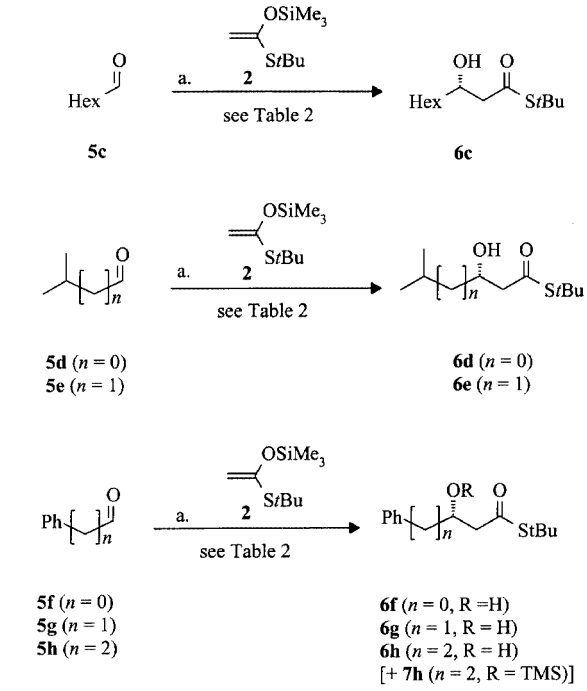
At this point it should be mentioned that reduction of the thioester unit of enantiopure compounds **6a** and **6b** with sodium borohydride directly affords key intermediates for the synthesis of enantiopure (*R*)-α-lipoic acid (**1**). Treatment of aldol product **6a** afforded the 1,3-diol **8** in 61% yield. The conversion of the methyl ester analogue of **8** into (*R*)-α-lipoic acid (**1**) has already been reported.[20] A short and enantioselective formal total synthesis of (*R*)-**1** with an asymmetric aldol reaction as a crucial step has thus been established as shown in Equation (1).



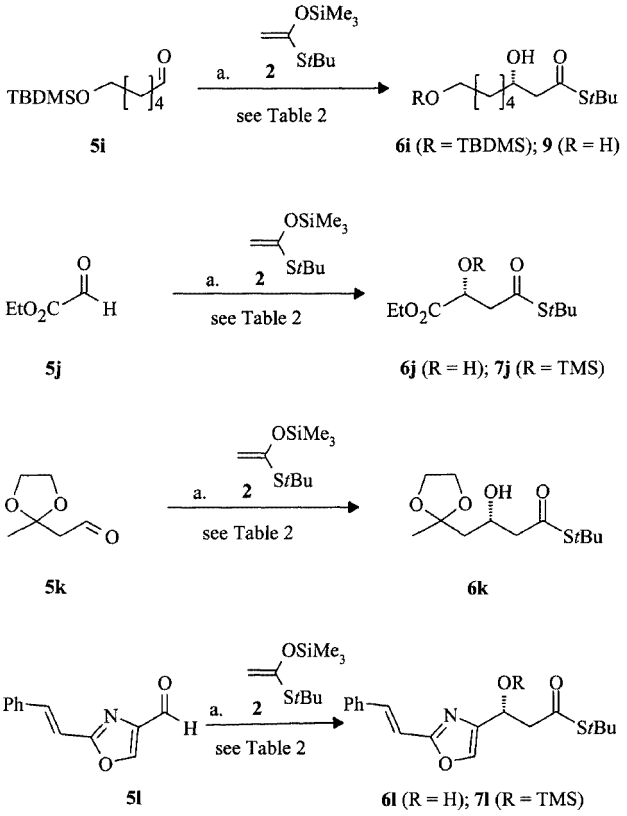
6a 61 % **8** (1)

To demonstrate the scope and limitations of the above optimisation we applied (*R*)-BINOL-Ti catalyst **4a** to a variety of (mostly) aliphatic aldehydes **5c**−**q** (Schemes 3−5). The results are summarised in Table 2. In general, use of phenol as additive has effects similar to those found for the corresponding reactions of **5a** and **5b**. Addition of phenol increased the yields of aldol products **6**, while enantioselectivities were similar or even slightly higher. Good to excellent results could be obtained with most of the aldehydes employed (e.g., **5c**, **5f**−**i**, **5l**, see Table 2). On the other hand, only moderate enantioselectivities were observed with aldehydes **5d** (38% *ee*), **5e** (53% *ee*) and functionalised precursors **5j** (71% *ee*) and **5k** (62% *ee*).

Remarkably, the steric hindrance of an isopropyl group seems to have less influence on the stereoselectivity under the reaction conditions applied. With elongation of the chain from $n = 0$ to $n = 1$, the enantioselectivity of aldol products increased slightly from 38% to 46% *ee* (cf. entries 3 and 4, Table 2). Nitro-substituted and methoxycarbonyl-substituted aldehydes **5m** and **5n**[21] gave the expected aldol products only in moderate yields (entries 20 and 21, Table 2). In the latter aldol reaction, the intermediate **6n** could only be obtained as crude product, since it completely cyclised to the γ-lactone **10** during purification by chromatography.[22] Chiral aldehydes **5m** and **5n** were used in racemic form, and mixtures of diastereomers with ratios of 64:36 and 55:45, respectively, were therefore obtained. De-

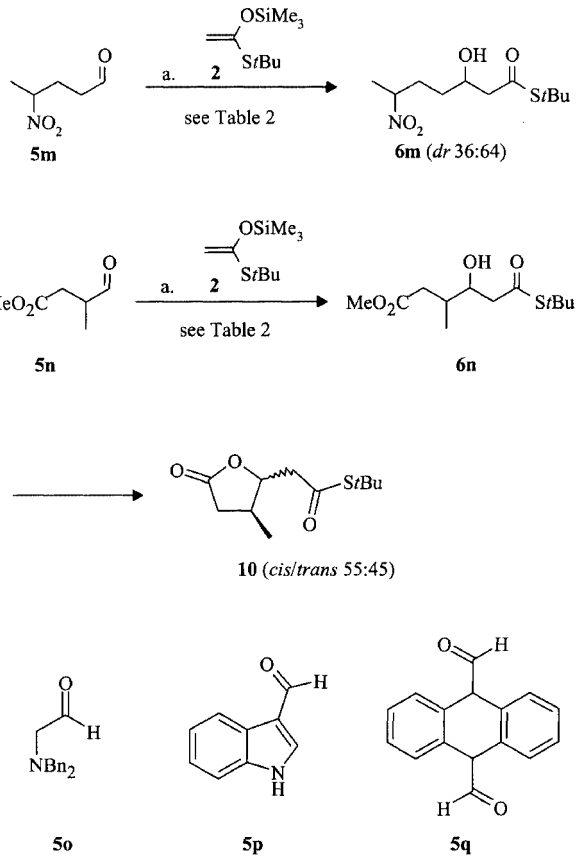


Scheme 3. a) (*R*)-BINOL-Ti **4a**, Et_2O, (phenol), 0 °C, 5 h, then 0 °C to room temp., 16 h



Scheme 4. a) (*R*)-BINOL-Ti **4a**, Et_2O, (phenol), 0 °C, 5 h, then 0 °C to room temp., 16 h

termination of the *ee* values of products **6m** and **10** was not possible, because the diastereomers could not be completely separated by column chromatography or by HPLC. No al-



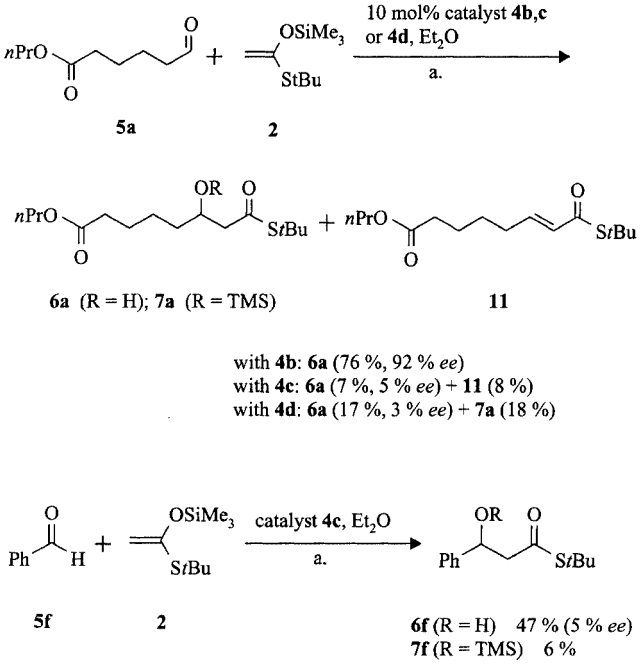
Scheme 5. a) (*R*)-BINOL-Ti **4a**, Et_2O, (phenol), 0 °C, 5 h, then 0 °C to room temp., 16 h

dol reactions were observed with aldehydes **5o−q** as precursors under the conditions developed above for catalyst **4a** (entries 22−24, Table 2, Scheme 5). In these cases only starting material was recovered.

The enantiomeric purities of the resulting aldol products **6** were unambiguously established by ^1H and ^{13}C NMR spectroscopy on the corresponding MPTA esters prepared with (*S*)-configured Mosher's acid chloride.[23] The assignment of the predominating configuration at the newly generated stereocentre of compounds **6** as depicted in the Schemes is based on comparison with the signs of specific rotation of known compounds (**6d**, **6f**, **6h** and **6l**) or by analogy if closely related products had been described in the literature (**6a**, **6b**, **6c**, **6i**, **6j** and **6k**). In good accordance with Keck's and Mikami's results, (*R*)-BINOL-titanium catalyst **4a** promotes the preferential attack of **2** to the *Re* face of the aldehydes investigated. A mechanistic interpretation will be provided in connection with quantum mechanical calculations performed for the asymmetric aldol addition.[24]

Not only the isopropoxy-substituted (*R*)-BINOL-Ti catalyst **4a**, but also the ethoxy-substituted (*R*)-BINOL-Ti catalyst **4b** may efficiently be used. Catalyst **4b** gave a comparably good result with model compound **5a** (Scheme 6), as observed with the use of catalyst **4a**. The *tert*-butoxy ligand (catalyst **4c**) is apparently not suitable for the carbon−carbon bond formation, due to a dramatic de-

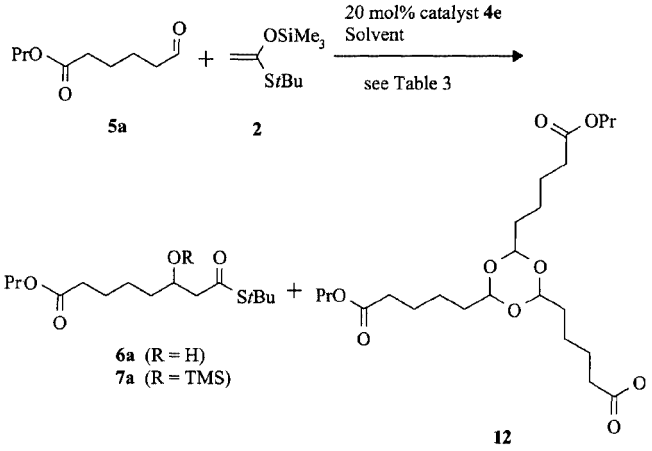
crease of the Lewis acidity of the titanium species.[25] Aldol reactions of **5a** and **5f** with **2** in the presence of catalyst **4c** afforded the desired alcohols **6a** and **6f**, respectively, with negligible enantioselectivities and in low yields (Scheme 6). Furthermore, the reaction between **2** and **5a** resulted in the formation of α,β-unsaturated thioester **11** as a by-product.



Scheme 6. a) Et_2O, 0 °C, 5 h, then 0 °C to room temp., 16 h

In analogy with the preparation of a tosylated titanium-TADDOLate catalyst by mixing of (*R*,*R*)-TADDOL and $Ti(OiPr)_2(OTs)_2$, generated in situ,[26] we applied this procedure to the generation of tosyl-substituted catalyst **4d** by mixing of (*R*)-BINOL **4** with $Ti(OiPr)_2(OTs)_2$ (reaction time 30 min at room temp.). Application of this new catalyst **4d** to the model addition between **2** and **5a** under standard conditions (Scheme 6) provided the aldol products **6a** and **7a** in 17% and 18% yields, respectively. However, the resulting *ee* value of **6a** was disappointingly low (3% *ee*).

We also investigated aldol reactions with catalyst **4e**, prepared from (*R*)-BINOL **4** and TiF_4 according to a procedure described by Carreira et al. (Scheme 7).[27] The results of these additions are compiled in Table 3. Unfortunately, the chemical yields for alcohol **6a** and its silylated derivative **7a** were generally low, independently of the solvent used. When the reaction was performed in diethyl ether (entry 3, Table 3) the best result in terms of the enantiomeric excess (24% *ee*) was obtained. However, aldol products **6a**/**7a** were inevitably accompanied in all cases by 1,3,5-trioxane derivative **12** as the major component. This main component arises from Lewis acid-catalysed cyclotrimerisation of aldehyde **5a**.[28]



Scheme 7

Finally, the use of aluminium, boron and ytterbium as central atoms in BINOL complexes should briefly be discussed. On treatment of (*R*)-BINOL **4** with $AlMe_3$ at room temperature for 0.5 h (*R*)-BINOL-Al catalyst **4f** was obtained.[29] This catalyst was used for the aldol reaction between **5a** and **2**. With dichloromethane as solvent and (*R*)-BINOL-Al catalyst **4f** (reaction conditions: −20 or −78 °C; 2−18 h; 0.20:0.10 equiv. of $AlMe_3$/(*R*)-**4**), aldol products **6a**/**7a** were observed in 38% yield and with *ee* values only of up to 18%. A change of solvent from dichloromethane to hexane or toluene resulted in strong decreases in the yield and enantioselectivity of **6a** (11−14% yield, 2−4% *ee*). Notably, addition of 4-Å molecular sieves did not affect the *ee* value (38% yield of **6a**, 16% *ee*).

Furthermore, the known boron catalysts [(*R*)-BINOL]$_2$BH **4g**[30] and (*R*)-BINOL-BOPh **4h**[31] were used in the aldol addition between **2** and **5a** under standard reaction conditions (see Scheme 2). The reaction promoted by

Table 3. Aldol addition between **5a** and **2** in the presence of (*R*)-BINOL/TiF_4 (**4e**)

Entry	Solvent	Temperature	Time	Yield of **6a**, **7a** and **12**	*ee*[a]
1	CH_2Cl_2	−78 °C to room temp.	14 h	4, 0 and 72%	14% (+)
2	MeCN	−40 °C to room temp.	12 h	16, 17 and 34%	7% (−)
3	Et_2O	a) −78 °C to room temp. b) room temp.	a) 16 h b) 24 h	11, 0 and 41%	24% (+)
4	Toluene/MeCN	a) −78 °C to room temp. b) room temp.	a) 16 h b) 24 h	0, 8 and 11%	10% (+)
5	Benzotrifluoride	a) −20 °C to room temp. b) room temp.	a) 10 h b) 24 h	8, 13 and 77%	16% (+)

[a] The sense of the optical rotation of the product is given in parentheses.

catalyst **4g** furnished aldol products **6a** and **7a** in 20% and 7% yields, respectively, product **6a** being formed with an enantioselectivity of only 30%. Catalyst **4h** did not afford the desired aldol product **6a** (or **7a**) under the reaction conditions applied. The catalyst (*R*)-BINOL-Yb **4i** was generated by mixing of (*R*)-BINOL **4** with $Yb(OTf)_3$ in a 1:1 stoichiometry, similarly to the generation of **4a** described above. This catalyst promoted the formation of alcohol **6a** in 47% yield, but unfortunately with very low enantioselectivity (9% *ee*).

Conclusions

The results reported here highlight the use of functionalised aliphatic aldehydes as substrates in enantioselective aldol reactions with S-ketene silyl acetal **2** to obtain chiral aliphatic *sec*-alcohols in good yields and with high to excellent enantioselectivities. In particular, catalysts **4a** and **4b** are highly efficient for the preparation of the key compounds **6a** and **6b**, which are key intermediates in the synthesis of (*R*)-α-lipoic acid (**1**). For the first time, the crucial stereogenic centre of a precursor of this biological active compound has been generated simply by an asymmetric catalysed aldol reaction.[5] Preliminary experiments with aluminium, boron and ytterbium-BINOL catalysts demonstrated that only inferior chiral induction could be achieved under the reaction conditions employed. Related aldol reactions employing substituted BINOL derivatives will be reported in a forthcoming paper.[32]

Experimental Section

General Remarks: All reactions were performed under argon atmosphere in flame-dried flasks, and the components were added by syringe. All solvents were dried by standard methods. IR spectra were measured with Beckman IR Acculab 4, Beckman IR 5A, Perkin−Elmer IR 1420 or Perkin−Elmer FT-IR spectrometer Nicolet 5 SXC. Mass spectra were recorded with a Varian MAT 711 spectrometer. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution on Bruker instruments (AC 500, WM 300, WH 270, AC 250). The chemical shifts are relative to TMS or to the $CDCl_3$ signal (δ_H = 7.27 ppm, δ_C = 77.0 ppm). Higher order NMR spectra were approximately interpreted as first-order spectra if possible. Missing signals of minor isomers are hidden by signals of major isomers, or they could not be unambiguously identified due to low intensity. Neutral alumina (activity III, Fa. Merck) was used for column chromatography. Melting points (uncorrected) were measured with an apparatus from Büchi (SMP-20). Optical rotations were determined in a 1 mL cell with a path length of 10 cm on a Perkin−Elmer 241 polarimeter (Na_D line). The $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1} and the concentrations are given in g/100 cm^3.

Starting materials **2**,[33] **5a** and **5b**[34] **5i**,[35] **5k**,[36] **5l**,[37] **5m**,[38] **5n**,[21] **5o**[39] and **5p**[40] were prepared by literature procedures. All other chemicals were commercially available and were used as received.

Typical Procedure for Enantioselective Aldol Reaction with (*R*)-BINOL-Ti Catalyst: The (*R*)-BINOL-Ti catalyst was prepared by a procedure described by Keck (method D).[9b] A mixture of $Ti(OR)_4$ (R = *i*Pr, *t*Bu, Et or Ts) and (*R*)-BINOL **4** in diethyl ether (5 mL/mmol of **5**) was stirred for 1.5 h at room temp. The solution was cooled to 0 °C, the corresponding aldehyde **5** (1.0 equiv.) was added, and the mixture was stirred for 10 min. A solution of S-ketene silyl acetal **2** (1.5 equiv.) in diethyl ether (5 mL/mmol of **5**) was then added. The reaction mixture was stirred for 5 h at 0 °C and was then allowed to warm up to room temp. over 16 h. The reaction was quenched by addition of 2 N HCl solution (5 mL/mmol of **5**) and the mixture was stirred for 30 min at room temp. The aqueous layer was extracted three times with diethyl ether (5 mL/mmol of **5**), and the combined organic phases were dried over Na_2SO_4 and concentrated. The crude product was purified by column chromatography (neutral alumina, *n*-hexane/EtOAc, 3:1 or 4:1). Amounts of catalyst and additives, yields and enantioselectivities are given in Table 1 and 2.

In a few experiments the workup was performed by addition of satd. aqueous NH_4Cl (5 mL/mmol of **5**) instead of 2 N HCl (entries 2, 3 and 6 in Table 1; entries 13, 16 and 19 in Table 2; entries 2, 4 and 5 in Table 3).

In cases in which molecular sieves were used, these (4 Å, 600 mg/mmol of **5**) were added during the generation of the catalyst.

Reactions with (*R*)-BINOL-Met (Met = B, Yb) were also performed according to the typical procedure.

Typical Procedure for Desilylation of Aldol Derivatives 7: A mixture of the corresponding silylated thioester **7** and HCl solution (2 N, 1 mL/mmol of **7**) in THF (10 mL/mmol of **7**) was stirred for 3 h at room temp. The reaction was then quenched by addition of satd. aqueous $NaHCO_3$ solution (2 mL/mmol of **7**). The aqueous layer was extracted with diethyl ether (3 × 5 mL/mmol of **7**), and the combined organic phases were dried over Na_2SO_4 and concentrated. The crude product **6** was purified by column chromatography (neutral alumina, *n*-hexane/EtOAc, 4:1 or 3:1).

Analytical and Spectroscopic Data of Compounds Prepared

***n*-Propyl (6*S*)-7-(*tert*-Butylsulfanylcarbonyl)-6-hydroxyheptanoate (6a):** Colourless oil, $[\alpha]_D^{23}$ = +14.5 (*c* = 1.1, $CHCl_3$) (> 97% *ee*). ^1H NMR ($CDCl_3$, 300 MHz): δ = 4.03 (m_c, 3 H, 6-H, OCH_2), 2.64 (dd, *J* = 3.4, 15.7 Hz, 1 H, 7-H), 2.56 (dd, *J* = 8.4, 15.7 Hz, 1 H, 7-H), 2.32 (t, *J* = 7.5 Hz, 2 H, 2-H), 1.68−1.38 (m, 9 H, 3-H, 4-H, 5-H, CH_2, OH), 1.47 (s, 9 H, S−*t*Bu), 0.94 (t, *J* = 7.5 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 200.1 (s, COS), 173.6 (s, C-1), 68.3 (d, C-6), 65.7 (t, OCH_2), 50.9 (t, C-7), 48.3, 29.6 (s, q, *t*Bu), 36.0, 34.1, 24.8, 24.6, 21.9 (5 t, C-2, C-3, C-4, C-5, CH_2), 10.3 (q, CH_3) ppm. IR (neat): $\tilde{\nu}$ = 3600−3180 cm^{-1} (O−H), 3020−2800 (C−H), 1735, 1680 (C=O). $C_{15}H_{28}O_4S$ (304.5): calcd. C 59.18, H 9.27, S 10.53; found C 58.87, H 9.42, S 10.59.

***n*-Propyl (6*S*)-7-(*tert*-Butylsulfanylcarbonyl)-6-(trimethylsiloxy)heptanoate (7a):** Colourless oil. ^1H NMR ($CDCl_3$, 200 MHz): δ = 4.11 (m_c, 1 H, 6-H), 4.02 (t, *J* = 7 Hz, 2 H, OCH_2), 2.62 (dd, *J* = 7, 14.5 Hz, 1 H, 7-H), 2.49 (dd, *J* = 5.5, 14.5 Hz, 1 H, 7-H), 2.30 (t, *J* = 7 Hz, 2 H, 2-H), 1.76−1.48 (m, 8 H, 3-H, 4-H, 5-H, CH_2), 1.45 (s, 9 H, S−*t*Bu), 0.93 (t, *J* = 7.5 Hz, 3 H, CH_3), 0.10 (s, 9 H, $OSiMe_3$) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 200.0 (s, COS), 174.1 (s, C-1), 69.9 (d, C-6), 65.6 (t, OCH_2), 52.5 (t, C-7), 48.3, 29.6 (s, q, *t*Bu), 36.1, 33.5, 24.7, 24.6, 21.4 (5 t, C-2, C-3, C-4, C-5, CH_2), 10.3 (q, CH_3), 0.05 (q, $SiMe_3$) ppm. IR (neat): $\tilde{\nu}$ = 2950−2820 cm^{-1} (C−H), 1745, 1735 (C=O). MS (EI, 80 eV): *m*/*z* (%) = 376 (1) [M$^+$], 361 (2) [M$^+$ − Me], 317 (5) [M$^+$ − *n*PrO], 287 (30) [M$^+$ − S−*t*Bu], 215 (23), 186 (16), 173 (27), 155 (33), 137

(59), 113 (62), 85 (11), 73 (40), 57 (tBu$^+$, 100), 43 (29), 41 (33), 39 (19). HRMS (80 eV): calcd. for $C_{18}H_{36}O_4SSi$ 376.2104; found 376.2136.

Methyl (6*S*)-7-(*tert*-Butylsulfanylcarbonyl)-6-hydroxyheptanoate (6b): Colourless oil, $[\alpha]_D^{23}$ = +13.7 (c = 1.0, $CHCl_3$) (96% *ee*). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.92 (m_c, 1 H, 6-H), 3.56 (s, 3 H, OMe), 2.80 (br. d, J = 4 Hz, 1 H, OH), 2.53 (dd, J = 3.7, 15.7 Hz, 1 H, 7-H), 2.46 (dd, J = 5.4, 15.7 Hz, 1 H, 7-H), 2.24−2.17, 1.57−1.14 (2 m, 2 H, 6 H, 2-H, 3-H, 4-H, 5-H), 1.36 (s, 9 H, S−tBu) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 200.2 (s, COS), 173.4 (s, C-1), 68.0 (d, C-6), 51.5 (q, OMe), 50.7 (t, C-7), 48.2, 29.6 (s, q, tBu), 36.3, 34.1, 24.7, 24.6 (4 t, C-2, C-3, C-4, C-5) ppm. IR (neat): $\tilde{\nu}$ = 3550−3400 cm^{-1} (O−H), 2980−2850 (C−H), 1745, 1735 (C=O). $C_{13}H_{24}O_4S$ (276.4): calcd. C 56.49, H 8.75, S 11.60; found C 56.27, H 8.70, S 11.20.

Methyl (6*S*)-7-(*tert*-Butylsulfanylcarbonyl)-6-(trimethylsiloxy)heptanoate (7b): Colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.10 (m_c, 1 H, 6-H), 3.64 (s, 3 H, OMe), 2.50 (dd, J = 5.4, 14.5 Hz, 1 H, 7-H), 2.49 (dd, J = 7.2, 14.5 Hz, 1 H, 7-H), 2.30 (t, J = 7.5 Hz, 2 H, 2-H), 1.65−1.15 (m, 6 H, 3-H, 4-H, 5-H), 1.44 (s, 9 H, S−tBu), 0.09 (s, 9 H, $OSiMe_3$) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 198.1 (s, COS), 173.8 (s, C-1), 69.1 (d, C-6), 52.3 (t, C-7), 51.2 (q, OMe), 48.0, 29.4 (s, q, tBu), 36.9, 33.8, 24.7, 24.6 (4 t, C-2, C-3, C-4, C-5), 0.03 (q, $SiMe_3$) ppm. IR (neat): $\tilde{\nu}$ = 2970−2870 cm^{-1} (C−H), 1740, 1735 (C=O).

***S*-*tert*-Butyl (3*S*)-3-Hydroxynonanethioate (6c):** Colourless oil, $[\alpha]_D^{23}$ = +20.8 (c = 1.15, $CHCl_3$) (93% *ee*). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.01 (m_c, 1 H, 3-H), 2.77 (br. s, 1 H, OH), 2.66 (dd, J = 3.3, 15.8 Hz, 1 H, 2-H), 2.55 (dd, J = 8.5, 15.8 Hz, 1 H, 2-H), 1.68−1.24 (m, 10 H, 4-H to 8-H), 1.47 (s, 9 H, S−tBu), 0.88 (t, J = 7 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 200.6 (s, C-1), 68.7 (d, C-3), 50.9 (t, C-2), 48.4, 29.7 (s, q, tBu), 36.5, 31.7, 29.1, 25.3, 22.6 (5 t, C-4, C-5, C-6, C-7, C-8), 14.0 (q, C-9) ppm. IR (neat): $\tilde{\nu}$ = 3650−3180 cm^{-1} (O−H), 2960−2860 (C−H), 1680 (C=O). $C_{13}H_{25}O_2S$ (245.4): calcd. C 63.63, H 10.27, S 13.06; found C 63.28, H 10.01, S 13.80.

***S*-*tert*-Butyl (3*R*)-3-Hydroxy-4-methylpentanethioate (6d):**[41] Colourless oil that slowly crystallised during storage (mp, 34−37 °C), $[\alpha]_D^{23}$ = +12.4 (c = 1.24, $CHCl_3$) (38% *ee*). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.80 (m_c, 1 H, 3-H), 2.74 (br. s, 1 H, OH), 2.64 (dd, J = 3, 15.5 Hz, 1 H, 2-H), 2.53 (dd, J = 9, 15.5 Hz, 1 H, 2-H), 1.74−1.64 (m, 1 H, 4-H), 1.47 (s, 9 H, S−tBu), 0.93, 091 (2 d, J = 6.8 Hz, 3 H each, 5-H, 4-CH_3) ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 198.0 (s, C-1), 73.3 (d, C-3), 48.3, 29.7 (s, q, tBu), 48.1 (t, C-2), 33.2 (d, C-4), 18.3, 17.5 (2 q, C-5, 4-CH_3) ppm.

***S*-*tert*-Butyl (3*S*)-3-Hydroxy-5-methylhexanethioate (6e):** Colourless oil, $[\alpha]_D^{23}$ = +8.2 (c = 0.92, $CHCl_3$) (53% *ee*). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.10 (m_c, 1 H, 3-H), 2.75 (br. s, 1 H, OH), 2.64 (dd, J = 3.3, 15.8 Hz, 1 H, 2-H), 2.54 (dd, J = 8.3, 15.8 Hz, 1 H, 2-H), 1.84−1.60, 1.46−1.12 (2 m, 1 H, 2 H, 4-H, 5-H), 1.47 (s, 9 H, S−tBu), 0.91 (t, J = 6.5 Hz, 6 H, 6-H, 5-CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 198.5 (s, C-1), 67.0 (d, C-3), 51.4 (t, C-2), 48.5, 29.8 (s, q, tBu), 45.7 (t, C-4), 24.5 (d, C-5), 23.2, 22.0 (2 q, C-6, 5-CH_3) ppm. IR (neat): $\tilde{\nu}$ = 3650−3100 cm^{-1} (O−H), 2995−2870 (C−H), 1680 (C=O). $C_{11}H_{23}O_2S$ (218.4): calcd. C 60.50, H 10.15, S 14.69; found C 60.70, H 10.58, S 15.12.

***S*-*tert*-Butyl (3*R*)-3-Hydroxy-3-phenylpropanethioate (6f):**[41] Colourless solid, m.p. 41−43 °C, $[\alpha]_D^{23}$ = +35.3 (c = 1.23, $CHCl_3$) (96% *ee*). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.37−7.26 (m, 5 H, Ph), 5.15 (dd, J = 3.9, 8.7 Hz, 1 H, 3-H), 3.18 (br. s, 1 H, OH), 2.89 (dd, J = 8.7, 15.8 Hz, 1 H, 2-H), 2.82 (dd, J = 3.9, 15.8 Hz, 1 H, 2-H), 1.47 (s, 9 H, S−tBu) ppm.

***S*-*tert*-Butyl (3*R*)-3-Phenyl-3-(trimethylsiloxy)propanethioate (7f):**[42] Colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.36−7.19 (m, 5 H, Ph), 5.14 (dd, J = 3.8, 9.3 Hz, 1 H, 3-H), 2.84 (dd, J = 9.3, 14.4 Hz, 1 H, 2-H), 2.61 (dd, J = 3.8, 14.4 Hz, 1 H, 2-H), 1.44 (s, 9 H, S−tBu), 0.03 (s, 9 H, $SiMe_3$) ppm.

***S*-*tert*-Butyl (3*S*)-3-Hydroxy-4-phenylbutanethioate (6g):** Pale yellow oil, $[\alpha]_D^{23}$ = +15.9 (c = 1.15, $CHCl_3$) (97% *ee*). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.34−7.18 (m, 5 H, Ph), 4.27 (m_c, 1 H, 3-H), 2.86−2.55 (m, 5 H, 2-H, 4-H, OH), 1.46 (s, 9 H, S−tBu) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 198.8 (s, C-1), 141.7, 128.4, 128.1, 126.0 (s, 3 d, Ph), 69.7 (d, C-3), 51.6 (t, C-2), 48.0, 29.8 (s, q, tBu), 40.5 (t, C-4) ppm. IR (neat): $\tilde{\nu}$ = 3600−3150 cm^{-1} (O−H), 3085−2865 (=CH, C−H), 1680 (C=O). $C_{14}H_{20}O_2S$ (252.4): calcd. C 66.63, H 7.99, S 12.71; found C 66.84, H 8.20, S 12.37.

***S*-*tert*-Butyl (3*S*)-3-Hydroxy-5-phenylpentanethioate (6h):**[9,43] Colourless oil, $[\alpha]_D^{23}$ = −4.3 (c = 1.85, $CHCl_3$) (94% *ee*). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.32−7.16 (m, 5 H, Ph), 4.04 (m_c, 1 H, 3-H), 2.85−2.56, 1.88−1.67 (2 m, 5 H, 2 H, 2-H, 4-H, 5-H, OH), 1.46 (s, 9 H, S−tBu) ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 198.3 (s, C-1), 141.7, 128.4, 128.3, 125.8 (s, 3 d, Ph), 67.9 (d, C-3), 50.9 (t, C-2), 48.5, 29.7 (s, q, tBu), 38.0, 31.6 (2 t, C-4, C-5) ppm.

***S*-*tert*-Butyl (3*S*)-5-Phenyl-3-(trimethylsiloxy)pentanethioate (7h):** Colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.17−7.02 (m, 5 H, Ph), 4.07 (m_c, 1 H, 3-H), 2.63−2.41, 1.79−1.52 (2 m, 4 H, 2 H, 2-H, 4-H, 5-H), 1.33 (s, 9 H, S−tBu), 0.01 (s, 9 H, $OSiMe_3$) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 198.2 (s, C-1), 141.9, 128.4, 128.3, 125.8 (s, 3 d, Ph), 69.1 (d, C-3), 52.3 (t, C-2), 48.1, 29.8 (s, q, tBu), 39.2, 31.7 (2 t, C-4, C-5), 0.3 (q, $OSiMe_3$) ppm. IR (neat): $\tilde{\nu}$ = 3090−2870 cm^{-1} (=CH, C−H), 1685 (C=O). $C_{18}H_{30}O_2SSi$ (338.6): calcd. C 63.85, H 8.93, S 9.47; found C 63.49, H 9.17, S 9.25.

***S*-*tert*-Butyl (3*S*)-8-[*tert*-Butyl(dimethyl)siloxy]-3-hydroxyoctanethioate (6i):** Pale yellow oil, $[\alpha]_D^{23}$ = +11.9 (c = 1.2, $CHCl_3$) (95% *ee*). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.02 (m_c, 1 H, 3-H), 3.59 (t, J = 6.5 Hz, 2 H, 8-H), 2.77 (d, J = 4 Hz, 1 H, OH), 2.68 (dd, J = 3.3, 15.6 Hz, 1 H, 2-H), 2.52 (dd, J = 8.5, 15.6 Hz, 1 H, 2-H), 1.63−1.25 (m, 8 H, 4-H, 5-H, 6-H, 7-H), 1.47 (s, 9 H, S−tBu), 0.89 (s, 9 H, Si−tBu), 0.04 (s, 6 H, $SiMe_2$) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 199.6 (s, C-1), 68.6 (d, C-3), 63.1 (t, C-8), 50.9 (t, C-2), 48.4, 29.7 (s, q, tBu), 36.5, 32.7, 25.7, 25.2 (4 t, C-4, C-5, C-6, C-7), 25.9, 18.3 (s, q, Si−tBu), −3.6 (q, $SiMe_2$) ppm. IR (neat): $\tilde{\nu}$ = 3600−3200 cm^{-1} (O−H), 2995−2850 (C−H), 1680 (C=O). MS (EI, 80 eV): m/z (%) = 347 (1) [M$^+$], 305 (17) [M$^+$ − tBu], 249 (14), 231 (17), 215 (26), 197 (22), 173 (55), 171 (42), 131 (OSi−tBuMe$_2^+$, 24), 123 (26), 115 (11) [Si−tBuMe$_2^+$], 99 (26), 95 (31), 81 (33), 75 (83), 57 (100) [tBu$^+$], 41 (23), 29 (13). $C_{18}H_{38}O_3SSi$ (362.6): calcd. C 59.62, H 10.56, S 8.85; found C 59.85, H 10.91, S 8.87.

***S*-*tert*-Butyl (3*S*)-3,8-Dihydroxyoctanethioate (9):** Colourless oil, $[\alpha]_D^{23}$ = +17.5 (c = 0.04, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.03 (m_c, 1 H, 3-H), 3.62 (t, J = 6.5 Hz, 2 H, 8-H), 2.63 (dd, J = 3.6, 15.6 Hz, 1 H, 2-H), 2.55 (dd, J = 8.2, 15.6 Hz, 1 H, 2-H), 1.62−1.36 (m, 10 H, 4-H, 5-H, 6-H, 7-H, OH), 1.47 (s, 9 H, S−tBu) ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 200.4 (s, C-1), 68.5 (d, C-3), 62.6 (t, C-8), 51.0 (t, C-2), 48.4, 29.7 (s, q, tBu), 36.4, 32.5, 25.5, 25.1 (4 t, C-4, C-5, C-6, C-7) ppm. IR (neat): $\tilde{\nu}$ = 3600−3100 cm^{-1} (O−H), 3070−2890 (C−H), 1690 (C=O). $C_{12}H_{24}O_3S$ (248.4): calcd. C 58.02, H 9.74; found C 57.69, H 9.37.

Ethyl (3*R*)-3-(*tert*-Butylsulfanylcarbonyl)-2-hydroxypropanoate (6j): Pale yellow oil (b.p., 100 °C/0.01 mbar), $[\alpha]_D^{23} = +14.9$ (c = 1.1, $CHCl_3$) (71% *ee*). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.46 (m_c, 1 H, 2-H), 4.31−4.21 (m, 2 H, OCH_2), 3.15 (br. s, 1 H, OH), 2.97 (dd, J = 4.4, 15.9 Hz, 1 H, 3-H), 2.89 (dd, J = 6.3, 15.9 Hz, 1 H, 3-H), 1.46 (s, 9 H, S−*t*Bu), 1.19 (t, J = 7 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 197.0 (s, COS), 173.3 (s, C-1), 67.4 (d, C-2), 61.9, 14.0 (t, q, OCH_2CH_3), 48.6 (t, C-3), 48.6, 29.6 (s, q, *t*Bu) ppm. IR (neat): $\tilde{\nu}$ = 3650−3100 cm^{-1} (O−H), 3000−2870 (C−H), 1740, 1685 (C=O). MS (EI, 80 eV): m/z (%) = 234 (5) [M^+], 161 (4) [$M^+ - CO_2Et$], 145 (43) [$M^+ - S{-}t$Bu], 117 (37), 89 (17) [S−*t*Bu$^+$], 71 (35), 57 (100) [*t*Bu$^+$], 41 (19), 29 (30). HRMS (80 eV): calcd. for $C_{10}H_{18}O_4S$ 234.0926; found 234.0943.

Ethyl (3*R*)-3-(*tert*-Butylsulfanylcarbonyl)-2-(trimethylsiloxy)propanoate (7j): Pale yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.64 (dd, J = 4.4, 8.4 Hz, 1 H, 2-H), 4.23−4.10 (m, 2 H, OCH_2), 2.67 (dd, J = 4.4, 15.1 Hz, 1 H, 3-H), 2.82 (dd, J = 8.4, 15.1 Hz, 1 H, 3-H), 1.46 (s, 9 H, S−*t*Bu), 1.27 (t, J = 7 Hz, 3 H, CH_3), 0.13 (s, 9 H, $SiMe_3$) ppm.

***S*-*tert*-Butyl (3*S*)-3-Hydroxy-4-(2-methyl-1,3-dioxolan-2-yl)butanethioate (6k):** Yellow oil, $[\alpha]_D^{23} = -3.8$ (c = 1.28, $CHCl_3$) (62% *ee*). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.36 (m_c, 1 H, 3-H), 4.04−3.98 (m, 4 H, OCH_2CH_2O), 2.73 (br. s, 1 H, OH), 2.69 (dd, J = 7.7, 14.9 Hz, 1 H, 2-H), 2.56 (dd, J = 5.1, 14.9 Hz, 1 H, 2-H), 1.96−1.85 (m, 2 H, 4-H), 1.52 (s, 3 H, Me), 1.47 (s, 9 H, S−*t*Bu) ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 199.1 (s, C-1), 107.5 (s, O−C−O), 65.4 (d, C-3), 64.8, 63.7 (2 t, 2 OCH_2), 50.1, 49.0 (2 t, C-2, C-4), 48.6, 29.8 (s, q, *t*Bu), 24.2 (q, CH_3) ppm. IR (neat): $\tilde{\nu}$ = 3600−3050 cm^{-1} (O−H), 2950−2860 (C−H), 1680 (C=O). MS (EI, 80 eV): m/z (%) = 247 (1) [$M^+ - CH_3$], 229 (1) [$M^+ - CH_3 - H_2O$], 175 (3) [$M^+ - C_4H_7O_2$], 173 (5) [$M^+ - S{-}t$Bu], 131 (22), 129 (37), 115 (16), 111 (44), 87 (95), 57 (48) [*t*Bu$^+$], 43 (100) [CH_3CO^+], 41 (16), 29 (11). HRMS (80 eV): calcd. for $C_{11}H_{19}O_4S$ ($M^+ - CH_3$) 247.1004; found 247.1033.

***S*-*tert*-Butyl (3*R*)-3-Hydroxy-3-(2-styryloxazol-4-yl)propanethioate (6l):**[44] Colourless crystals, m.p. 105−107 °C, $[\alpha]_D^{23} = +38.1$ (c = 1.1, C_6H_6) (95% *ee*). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 7.55 (d, J = 1 Hz, 1 H, =CH), 7.55−7.30 (m, 6 H, =CH, Ph), 6.90 (d, J = 16.5 Hz, 1 H, =CH), 5.20 (dddd, J = 1, 4, 5, 8.5 Hz, 1 H, 3-H), 3.55 (d, J = 5 Hz, 1 H, OH), 3.05 (dd, J = 4, 16 Hz, 1 H, 2-H), 2.95 (d, J = 8.5, 16 Hz, 1 H, 2-H), 1.46 (s, 9 H, S−*t*Bu) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 199.2 (s, C-1), 161.6, 153.5 (2 s, =CN, *C*=CH), 136.5, 135.3, 134.2, 129.1, 128.8, 127.2 (d, s, 4 d, 2 =CH, Ph), 113.6 (d, =CH), 64.3 (d, C-3), 50.0 (t, C-2), 48.5, 29.7 (s, q, *t*Bu) ppm. MS (EI, 80 eV): m/z (%) = 331 (22) [M^+], 274 (13) [$M^+ - t$Bu], 242 (47) [$M^+ - S{-}t$Bu], 224 (27), 214 (48) [$M^+ - COS{-}t$Bu], 200 (100) [$M^+ - CH_2COS{-}t$Bu], 198 (30), 147 (11), 146 (11), 131 (24) [$CH_2COS{-}t$Bu$^+$], 130 (15), 115 (25), 103 (21), 77 (14), 57 (53) [*t*Bu$^+$], 41 (19), 29 (16).

***S*-*tert*-Butyl (3*R*)-3-(2-Styryloxazol-4-yl)-3-(trimethylsiloxy)propanethioate (7l):** Pale yellow crystals, m.p. 77−79 °C. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 7.55−7.30 (m, 7 H, 2 =CH, Ph), 6.89 (d, J = 16 Hz, 1 H, =CH), 5.24 (dd, J = 4.5, 8 Hz, 1 H, 3-H), 2.94 (dd, J = 4.5, 16 Hz, 1 H, 2-H), 2.88 (dd, J = 8, 16 Hz, 1 H, 2-H), 1.45 (s, 9 H, S−*t*Bu), 0.21 (s, 9 H, $SiMe_3$) ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 197.3 (s, C-1), 161.5, 145.1 (2 s, =CN, *C*=CH), 136.2, 135.5, 134.3, 129.2, 128.9, 127.2 (d, s, 4 d, =CH, Ph), 113.9 (d, =CH), 65.5 (d, C-3), 52.1 (t, C-2), 48.1, 29.8 (s, q, *t*Bu), 0.1 (q, $SiMe_3$).

***S*-*tert*-Butyl 3-Hydroxy-6-nitroheptanethioate (6m):** Pale yellow oil, mixture of two diastereomers = 64:36. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.66−4.55 (m, 1 H, 3-H), 4.12−3.95, 3.10−2.95 (2 m, 1 H each, 6-H, OH), 2.68−2.52 (m, 2 H, 2-H), 2.20−1.58 (m, 4 H, 4-H, 5-H), 1.54 (d, J = 6.7 Hz, 3 H, 7-H), 1.47 (s, 9 H, S−*t*Bu) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 200.5 (s, C-1), 83.6, 82.9* (2 d, C-6), 68.1, 67.4* (2 d, C-3), 48.7, 30.0 (s, q, *t*Bu), 50.6, 50.5*, 32.5, 31.9*, 31.4, 30.7* (6 t, C-2, C-4, C-5), 19.5, 19.2* (2 q, CH_3) ppm; * signals of the minor isomer. IR (neat): $\tilde{\nu}$ = 3430−3500 cm^{-1} (O−H), 2995−2920 (C−H), 1720 (C=O), 1675 (NO_2). $C_{11}H_{21}NO_4S$ (263.4): calcd. C 50.17, H 8.04, N 5.32; found C 50.38, H 8.17, N 5.51.

5-[(*tert*-Butylsulfanylcarbonyl)methyl]-4,5-dihydro-4-methyl-2(3*H*)-furanone (10): Colourless oil, *cis*-**10**:*trans*-**10** = 55:45. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 5.03 (td, J = 6, 7.5 Hz, 0.55 H, *cis*-5-H), 4.57 (td, J = 5.5, 7 Hz, 0.45 H, *trans*-5-H), 3.05−2.75, 2.46−2.27 (2 m, 4 H, 1 H, 3-H, 4-H, 5-CH_2), 1.58 (s, 9 H, S−*t*Bu), 1.26 (d, J = 6.5 Hz, 1.65 H, *cis*-4-CH_3), 1.12 (d, J = 7.2 Hz, 1.35 H, *trans*-4-CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz): Major diastereomer: δ = 196.2 (s, *C*OS−*t*Bu), 175.9 (s, C=O), 78.8 (d, C-5), 48.7, 29.7 (s, q, *t*Bu), 48.0, 37.0 (2 t, 2 CH_2), 32.7 (d, C-4), 14.2 (q, 4-CH_3) ppm. Minor diastereomer: δ = 196.0 (s, *C*OS−*t*Bu), 175.6 (s, C=O), 82.4 (d, C-5), 48.8, 29.6 (s, q, *t*Bu), 44.3, 36.5 (2 t, 2 CH_2), 35.7 (d, C-4), 17.3 (q, 4-CH_3) ppm. IR (neat): $\tilde{\nu}$ = 2990−2850 cm^{-1} (C−H), 1780, 1720 (C=O). $C_{11}H_{18}O_3S$ (230.3): calcd. C 57.36, H 7.88; found C 56.98, H 8.27.

***n*-Propyl 7-(*tert*-Butylsulfanylcarbonyl)hept-6-enoate (11):** Pale yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.94 (td, J = 7, 15.5 Hz, 1 H, 6-H), 6.16 (td, J = 1.5, 15.5 Hz, 1 H, 7-H), 4.18 (t, J = 6.8 Hz, 2 H, OCH_2), 2.46 (t, J = 7.2 Hz, 2 H, 2-H), 2.33 (dq, J = 1.5, 7 Hz, 2 H, 5-H), 1.85−1.68 (m, 6 H, 3-H, 4-H, CH_2), 1.64 (s, 9 H, S−*t*Bu), 1.09 (t, J = 7.4 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 192.5 (s, COS), 173.4 (s, C-1), 143.3, 129.6 (2 d, C-6, C-7), 65.9 (t, OCH_2), 48.2, 29.9 (s, q, S−*t*Bu), 34.0, 31.8, 27.5, 24.4, 21.9 (5 t, C-2, C-3, C-4, C-5, CH_2), 10.3 (q, CH_3) ppm. IR (neat): $\tilde{\nu}$ = 3050−2800 cm^{-1} (=CH, C−H), 1735, 1660 (C=O). MS (EI, 80 eV): m/z (%) = 286 (3) [M^+], 197 (11) [$M^+ - S{-}t$Bu], 171 (10), 170 (17), 137 (15), 127 (16), 110 (17), 81 (10), 57 (100) [*t*Bu$^+$], 41 (21), 29 (10). HRMS (80 eV): calcd. for $C_{15}H_{26}O_3S$ 286.1603; found 286.1635.

2,4,6-Tris(4-*n*-propoxycarbonylbutyl)-1,3,5-trioxane (12): Colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.84 (t, J = 5.2 Hz, 3 H, OCHO), 4.03 (t, J = 7.3 Hz, 6 H, OCH_2), 2.31 (t, J = 7.4 Hz, 6 H, CH_2C=O), 1.71−1.59, 1.49−1.39 (2 m, 18 H, 6 H, CH_2), 0.94 (t, J = 7.3 Hz, 9 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 173.6 (s, C=O), 101.2 (d, OCH), 65.8 (t, OCH_2), 34.1, 33.9, 24.7, 23.0, 21.9 (5 t, CH_2), 10.3 (q, CH_3) ppm. IR (neat): $\tilde{\nu}$ = 2920−2810 cm^{-1} (C−H), 1730 (C=O). MS (FD, 70 eV): m/z (%) = 517 (4) [M^+], 406 (38) [$M^+ - 2$ O−*n*Pr], 189 (62), 145 (79), 144 (75), 42 (100). $C_{27}H_{48}O_9$ (516.7): calcd. C 62.77, H 9.36; found C 62.91, H 9.43.

***n*-Propyl (6*S*)-6,8-Dihydroxyoctanoate (8):** Sodium borohydride (0.085 g, 2.24 mmol) was added in portions at 0 °C to a solution of **6a** (0.173 g, 0.569 mmol; > 97% *ee*) in 1-propanol (5 mL). After 5 h at 0 °C the solution was allowed to warm up to room temp. overnight. The solution was then concentrated in vacuo and the residue was dissolved in ethyl acetate (20 mL). The organic phase was washed with sat. aqueous NH_4Cl solution (5 mL), the aqueous layer was extracted with ethyl acetate (3 × 5 mL), and the combined organic phases were dried over Na_2SO_4. Purification of the crude product by column chromatography (EtOAc/*n*-hexane = 1:1 to 1:0) afforded the 1,3-diol **8** (0.075 g, 61%) as a slightly yellow oil. $[\alpha]_D^{25} = -2.5$ (c = 0.9, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz):

δ = 4.00 (t, *J* = 6.8 Hz, 2 H, OCH_2), 3.94−3.59 (m, 3 H, 6-H, 8-H), 2.85 (br. s, 2 H, OH), 2.30 (t, *J* = 7.3 Hz, 2 H, 2-H), 1.70−1.25 (m, 10 H, 3-H, 4-H, 5-H, 7-H, CH_2), 0.91 (t, *J* = 7.5 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 173.8 (s, C-1), 71.7 (d, C-6), 65.9 (t, OCH_2), 61.6 (t, C-8), 38.3, 37.3, 34.2, 25.0, 24.8, 22.0 (6 t, C-2, C-3, C-4, C-5, C-7, CH_2), 10.3 (q, CH_3) ppm. IR (neat): $\tilde{\nu}$ = 3620−3150 cm^{-1} (O−H), 3040−2840 (C−H), 1730 (C=O). $C_{11}H_{22}O_4$ (218.3): calcd. C 60.52, H 10.16; found C 59.99, H 10.03. Because of the sensitivity of this compound, no better elemental analysis could be obtained.

General Procedure for the Transformation of Alcohols 6 into the Corresponding Mosher's Esters by Treatment with Mosher's Acyl Chloride: (*S*)-Mosher's acyl chloride (1.4 equiv.) was added to a solution of the corresponding alcohol **6** (1.0 equiv.) in CH_2Cl_2 and dry pyridine (each 5.5 mL/mmol of **6**) and the reaction mixture was stirred for 40 h at room temp. The mixture was then diluted with CH_2Cl_2 (50 mL/mmol of **6**) and washed successively with 2 N HCl solution, satd. aqueous $NaHCO_3$ solution and H_2O (each 15 mL/mmol of **6**). The organic layer was dried (Na_2SO_4) and the solvent was evaporated to afford the crude product, which was pure by TLC analysis. The *de* value of the resulting ester was determined by ^1H and ^{13}C NMR.

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