Intramolecular Michael-Type Additions to Vinyl Bissulfoxides: Enantioselective Synthesis of Chiral Aldehydes

Timo Gehring,[a] Joachim Podlech,*[a] Alexander Rothenberger[b]

[a] Institut für Organische Chemie, Universität Karlsruhe (TH), Fritz-Haber-Weg 6, 76131 Karlsruhe, Germany
Fax +49(721)6087652; E-mail: joachim.podlech@ioc.uka.de

[b] Institut für Anorganische Chemie, Universität Karlsruhe (TH), Engesserstraße 15, 76131 Karlsruhe, Germany

Received 5 May 2008

Dedicated to Volker Jäger on the occasion of his 65th birthday

Abstract: The diastereoselective auxiliary-based intramolecular Michael-type additions to alkylidene bissulfoxides derived from dithiane and dithiolane were investigated. Utilization of substrates bearing N- and O-nucleophilic functions led to the formation of the respective cyclic substrates with selectivities ranging from 51:49 to 85:15. Cleavage of the bissulfoxide moiety by a two-step sequence yielded chiral carbaldehydes. The enantiomerically pure compounds obtained by this procedure, for example, tetrahydropyran-2-carbaldehyde and homopipecolic aldehyde, are hardly accessible by other routes. Both enantiomers of the target molecules are available since the stereochemical information is introduced with the readily available diethyl D- and L-tartrates.

Key words: nucleophilic additions, sulfoxides, thioacetals, umpolung, stereoelectronic effects

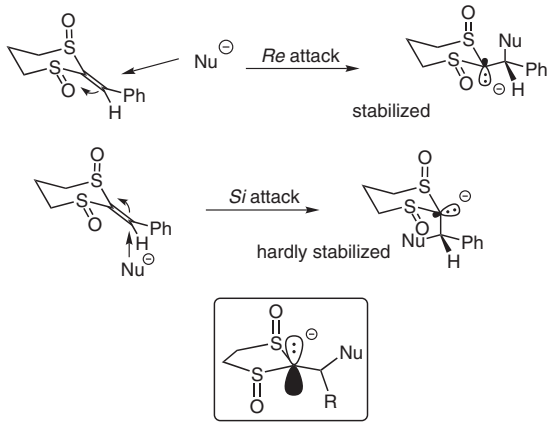
Introduction

Inter- and intramolecular Michael additions to α,β-unsaturated carbonyl compounds are well known to every chemist.[1] The installation of one or two stereogenic centers during these additions leads to widely used chiral substrates, and the configuration of a newly defined stereogenic center can be controlled during the reaction.[1]

Although vinyl sulfoxides show a similar reactivity as α,β-unsaturated carbonyl compounds, much less is known about additions of C-, N- or O-nucleophiles to vinyl sulfoxides.[2] Unsymmetrically substituted sulfoxides are chiral and are easily prepared as enantiopure compounds by asymmetric oxidation of the parent sulfides.[3] During our studies on intermolecular Michael-type additions to chiral dioxygenated ketene *S*,*S*-acetals (alkylidene bissulfoxides[4,5]) we found good selectivities in the additions of C- and N-nucleophiles.[6] Formal hydrolysis of the bissulfoxide moiety yielded 1,4-dicarbonyl compounds with a defined stereogenic center in the α-position.[6a] While we investigated the utilization of 1,3-dithiane- and 1,3-dithiolane-derived alkylidene bissulfoxides, Malacria, Fensterbank et al. used bis(tolylsulfinyl)alkenes in their studies.[7]

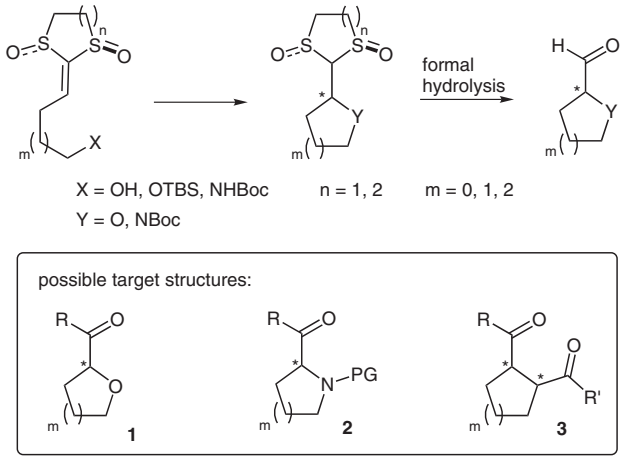
SYNTHESIS 2008, No. 15, pp 2476–2487
Advanced online publication: 08.07.2008
DOI: 10.1055/s-2008-1067176; Art ID: E22108SS

In our previous work, we found that the addition to vinyl bissulfoxides is strongly, albeit not exclusively ruled by stereoelectronic effects.[6d] The primarily formed carbanionic center is preferentially configured in a way allowing an antiperiplanar orientation of the lone pair and an axial S=O double bond. This has a strong influence on the trajectory of a nucleophilic attack (Scheme 1). Other stereoelectronic effects including S–C bonds contribute significantly less.[6d] Dithiolane-derived alkylidene bissulfoxides proved to be significantly better acceptors than the respective dithiane-derived substrates.[6b,d] This might be due to the presence of two stabilizing S=O double bonds in the intermediate carbanion, interacting with the p-lone pair (Scheme 1, bottom). We assumed that similar effects are working – if not exceeded by, for example, steric effects – during intramolecular nucleophilic additions to an alkylidene bissulfoxide moiety.



Scheme 1 Carbanion formation through nucleophilic attack to alkylidene bissulfoxides

To the best of our knowledge, intramolecular additions to alkylidene bissulfoxides have not been investigated yet. Aggarwal et al. reported on intramolecular [3+2] cycloadditions of nitrone moieties in bissulfoxide systems yielding five- and six-membered rings.[5d,e] Intramolecular additions of O- and N-nucleophiles to *p*-tolyl-derived vinyl sulfoxides have occasionally been reported and used for the synthesis of optical active natural compounds.[2d,e,i] The selectivities in these asymmetric intramolecular Michael-type additions were strongly dependent on the utilized solvents and bases, and ranged from 58:42 to



Scheme 2 General scheme for the intramolecular nucleophilic additions to vinyl bissulfoxides and possible target molecules

93:7.[2i] Intramolecular Michael-type additions of C-, N-, or O-nucleophiles to vinyl bissulfoxides should give rise to useful chiral scaffolds hardly accessible by other routes (Scheme 2).

Structures **1**, **2**, and **3** are α-functionalized carbonyl compounds or 1,4-dicarbonyl compounds usually accessible only by umpoled reactions. To study the scope of intramolecular Michael-type additions of different nucleophiles in the synthesis of these and similar compounds, the underlying bissulfoxides were synthesized and conditions for the addition were optimized.

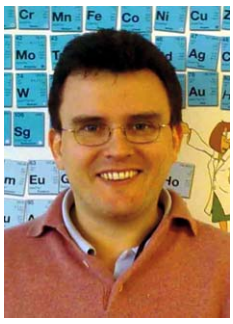
Synthesis of Oxidized Ketene *S*,*S*-Acetals

Stereochemically uniform oxidized cyclic ketene *S*,*S*-acetals are easily obtained by diastereoselective and enantioselective oxidation of ketene *S*,*S*-acetals (vide infra). The

Biographical Sketches

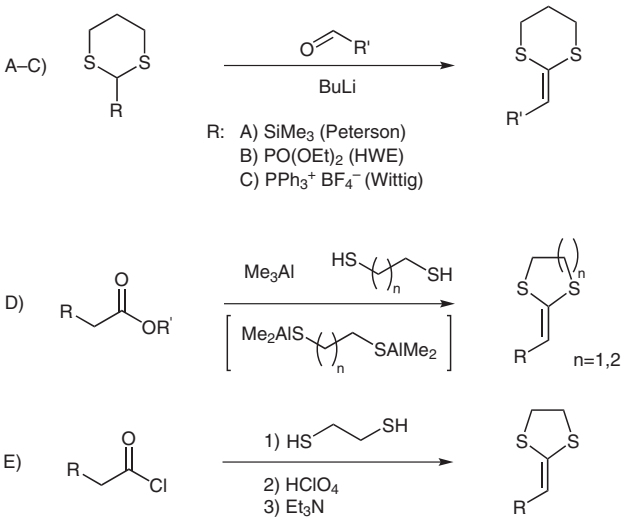
Timo Gehring was born in Heilbronn in 1979. He studied chemistry and mathematics at the University of Karlsruhe (TH) and obtained his Diplomas in 2005 (Chemistry) and 2006 (Mathematics). Since 2006, he is a Ph.D. student in Prof. Podlech's group in Karlsruhe. In 2008, he started a Feasibility Study for Young Scientists (FYS) about the Soai reaction. His scholarships include those from Fonds der chemischen Industrie, Studienstiftung des deutschen Volkes, and Stiftung der deutschen Wirtschaft. His research focuses on the application of chiral bissulfoxide auxiliaries for asymmetric intramolecular Michael-type additions, Morita–Baylis–Hillman reactions, and asymmetric autocatalysis.

Joachim Podlech is Professor of Organic Chemistry at the Universität Karlsruhe (TH). He studied chemistry in his native city at the Ludwig-Maximilians-Universität in Munich, Germany, where he received his Dr. rer. nat. (1993) in organic chemistry under the supervision of G. Szeimies. He joined the group of D. Seebach at the ETH in Zürich for a postdoctoral stay (1993–1995) and completed his Habilitation at the University of Stuttgart (1999) in the group of V. Jäger. He became Professor at the University of Karlsruhe in 2003. He was, *inter alia*, a Liebig Fellow (1995–1997) of the Fonds der Chemischen Industrie and held a Habilitandenstipendium of the Deutsche Forschungsgemeinschaft (1998–1999). His research interests focus on the development of organic synthetic methods starting from amino acids, on the synthesis of peptidomimetics, natural product synthesis (especially on the synthesis of mycotoxins), syntheses involving sulfoxides, and on the elucidation of stereoelectronic effects of sulfur-containing functional groups.



Alexander Rothenberger was born in Stuttgart in 1972 and is Privatdozent in the Institute of Inorganic Chemistry at the University of Karlsruhe (TH). He studied chemistry in Würzburg and completed his diploma thesis in the group of Prof. Stalke in 1998. He received his Ph.D. from Gonville & Caius College at the University of Cambridge in 2002 under the guidance of Dr. Ron Snaith and Dominic S. Wright. In 2002 he joined the group of Prof. Dieter Fenske at the University of Karlsruhe (TH) and completed his habilitation in 2007. His scholarships include a Gottlieb-Daimler- and Karl-Benz-Stipendium, an EPSRC quota award, a Cambridge European Trust Bursary, and a DFG-Forschungsstipendium. In 2008, he will join the group of Prof. Kanatzidis at Nortwestern University, Evanston. His research interests include the development of novel synthetic routes, cluster chemistry, and materials chemistry of Group 15/16 systems.

latter compounds have frequently been used in organic synthesis[8] and can be obtained by various methods (Scheme 3).



Scheme 3 Methods for the preparation of ketene *S*,*S*-acetals

These include Peterson olefination (A, Scheme 3),[9] Horner–Wadsworth–Emmons (HWE) reaction (B),[5c,10] Wittig reaction (C),[11] reaction of esters or lactones with trimethylaluminum and dithiols (D),[12,13] or elimination in pre-formed dithiolanium salts (E).[14]

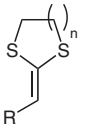
Ketene *S*,*S*-acetals synthesized in the present work are summarized in Table 1. We obtained *tert*-butyldimethylsilyl (TBS)-protected ketene *S*,*S*-acetal **10** (entry 7) in good yields by Peterson olefination starting from TBS-protected 5-hydroxypentanal.

For the preparation of dithiolane-derived ketene *S*,*S*-acetals, Peterson olefination or HWE reaction are not suitable since deprotonation of dithiolane would induce a cycloreversion leading to the formation of ethene and dithioformate.[1,7] In our previous work,[6b] we utilized method E starting from ethane-1,2-dithiol and an acyl chloride.[14] Due to the higher functionalized substrates needed in the present work, we decided to use a method developed by Corey et al. who synthesized ketene *S*,*S*-acetals containing unprotected hydroxy groups by reaction of carboxylic esters or lactones with trimethylaluminum and dithiols (route D in Scheme 3).[12] This route was successfully followed in the synthesis of the previously unknown substrates **4** and **6**.

Most hydroxy-substituted *S*,*S*-acetals are not stable under acidic conditions due to a fast nucleophilic addition of a free hydroxy group. This side reaction, which is observed within minutes even during the acquisition of NMR spectra, is usually prevented by the addition of a small amount of triethylamine. The *S*,*S*-acetals thus prepared are either directly used for the subsequent oxidation or are purified by chromatography.

We were able to advance method D for the synthesis of *N*-*tert*-butyloxycarbonyl (Boc)-protected amino-substituted

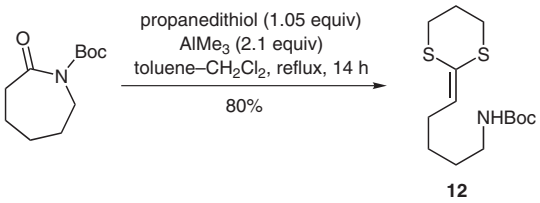
Table 1 Ketene *S*,*S*-Acetals **4**–**12** Prepared



Entry	R	n + 4 (ring size)	Method[a]	Product	Yield (%)
1	$(CH_2)_2OH$	5	D[b]	**4**	–[c]
2	$(CH_2)_3OH$	5	D[b]	**5**[15]	–[c]
3	$(CH_2)_4OH$	5	D[b]	**6**	–[c]
4	$(CH_2)_2OH$	6	D[b]	**7**[16]	–[c]
5	$(CH_2)_3OH$	6	D[b]	**8**[13a]	64
6	$(CH_2)_4OH$	6	D[b]	**9**[13a]	quant[c,d]
7	$(CH_2)_4OTBS$	6	A	**10**	75
8	$(CH_2)_4NHBoc$	5	D	**11**	61[e]
9	$(CH_2)_4NHBoc$	6	D	**12**	80[d,f]
10	$(CH_2)_4NHBoc$	6	B	**12**	73

[a] Method as specified in Scheme 3.
[b] Starting from the respective lactone.
[c] Immediately oxidized without purification.
[d] Crude product.
[e] Starting from methyl *N*-*tert*-butyloxycarbonyl-6-aminohexanoate, r.t., 14 h.
[f] Starting from *N*-*tert*-butyloxycarbonyl-ε-caprolactam.

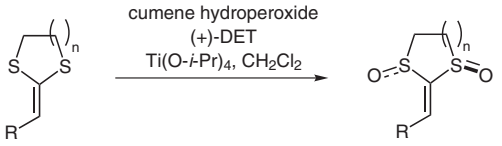
ketene *S*,*S*-acetals of type **12**. Compound **12** is also accessible via HWE reaction in 73% yield starting from *tert*-butyl 5-oxopentylcarbamate (Table 1, entry 10). It is known that *N*-acyl derivatives of lactams can be ring-opened by nucleophiles like alcoholates or Grignard reagents.[18] So we tried a direct synthesis of ketene *S*,*S*-acetal **12** starting from *tert*-butyl 2-oxoazepane-1-carboxylate (*N*-Boc-ε-caprolactam) by reacting with trimethylaluminum and propane-1,3-dithiol (Scheme 4). Under the same conditions, a synthesis of **11** with ethane-1,2-dithiol failed. To the best of our knowledge, this synthesis of ketene *S*,*S*-acetals starting from protected lactams has not been published previously. The scope of this reaction is currently under investigation in our laboratories.



Scheme 4 Synthesis of *N*-Boc-protected amino-substituted ketene *S*,*S*-acetals

A well-established oxidation protocol developed by Kagan[19] and co-workers and optimized by Modena et

al.[3,20] was first used by Aggarwal et al.[9b] for the enantio- and diastereoselective oxidation of ketene *S*,*S*-acetals, and has been slightly modified by us to improve the workup process.[6] With these conditions, generally good yields up to 87% were obtained (Scheme 5, Table 2), though in some cases already addition occurred. Purification by chromatography gave enantiomerically and diastereomerically uniform product.



Scheme 5 Asymmetric oxidation of ketene *S*,*S*-acetals

Table 2 Oxidation of Ketene *S*,*S*-Acetals (Scheme 5)

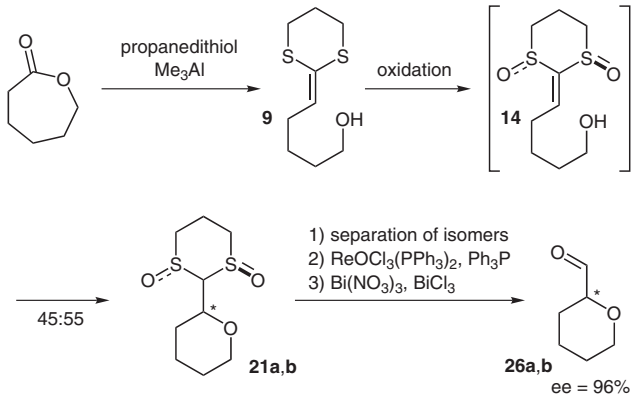
Entry	R	n + 4 (ring size)	Starting material	Product	Yield (%)
1	$(CH_2)_2OH$	5	**4**	–	–[a]
2	$(CH_2)_3OH$	5	**5**	**18a**,**b**[b]	56[c]
3	$(CH_2)_4OH$	5	**6**	**19a**,**b**[b]	74[d]
4	$(CH_2)_2OH$	6	**7**	**13**[a,e]	–[a]
5	$(CH_2)_3OH$	6	**8**	–[b]	50
6	$(CH_2)_4OH$	6	**9**	**14/21a**,**b**	87[f]
7	$(CH_2)_4OTBS$	6	**10**	**15**	50[g]
8	$(CH_2)_4NHBoc$	5	**11**	**16**	57
9	$(CH_2)_4NHBoc$	6	**12**	**17**	80[d]
10	$(CH_2)_4OH$	6	**9**	*ent*-**14/21a**,**b**	~80[f,h]

[a] Presumably polymerization had occurred.
[b] Addition occurred during oxidation, see Table 3.
[c] Over 2 steps starting from δ-valerolactone.
[d] Over 2 steps starting from *tert*-butyl 2-oxoazepane-1-carboxylate.
[e] Impure product.
[f] Partial addition occurred; yield given over 2 steps starting from ε-caprolactone.
[g] Slightly impure material due to partial deprotection and subsequent addition.
[h] Oxidation with (–)-D-DET.

Intramolecular Additions of O-Nucleophiles

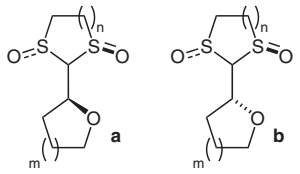
Intramolecular addition of a hydroxy function to the alkylidene bissulfoxide moiety should lead to tetrahydrofuran or tetrahydropyran derivatives and their homologues. The thus obtained enantiomerically pure carbaldehydes were hardly accessible before. Whenever used (in different oxidation states) they were obtained by resolution of racemic materials.[21]

Alkylidene bissulfoxide **15** bearing a TBS-protected alcohol was obtained by Peterson olefination and subsequent oxidation. Liberation of the hydroxy function by treatment with tetrabutylammonium fluoride led within 45 minutes to intramolecular addition with formation of the tetrahydropyran derivatives **21a** and **21b** with a 45:55 selectivity (Scheme 6, Table 3). Bissulfoxide **15** was not stable over a longer period since deprotection and addition occurred upon allowing to stand on the bench for several days to weeks. To avoid a TBS-protection during the preparation of the bissulfoxide, a domino sequence consisting of asymmetric oxidation und Michael-type addition of an unprotected substrate was tested. It turned out that oxidation of dithiane-derived ketene *S*,*S*-acetal **9** delivered a substrate **14** reactive enough for a partial immediate intermolecular addition of the hydroxy group. Complete addition was observed upon standing on the bench or after treatment with triethylamine or lithium hydroxide even at room temperature. Tetrahydropyrans **21a**,**b** were obtained with this variation in 80% yield and with 45:55 (**21a**:**21b**) selectivity.



Scheme 6 Intramolecular additions of O-nucleophiles

Table 3 Intramolecular Additions of O-Nucleophiles (cf. Scheme 6)



Entry	m + 4 (ring size)	n + 4 (ring size)	Starting material	Product	dr (*R*/*S*)	Yield (%)
1	5	5	**5**	**18a**,**b**	49:51[a–c]	56[d]
2	6	5	**6**	**19a**,**b**	85:15[a–c]	74[d]
3	5	6	**8**	**20a**,**b**	46:54[b]	45
4	6	6	**15**	**21a**,**b**	45:55	64
5	6	6	**14**[e]	**21a**,**b**	45:55	80[f]
6	6	6	*ent*-**14**[g]	*ent*-**21a**,**b**	55:45	~80[f]

[a] Not separable by conventional chromatography.
[b] Cyclization occurred during asymmetric oxidation.
[c] Assignment of isomers was not possible.
[d] Over 2 steps.
[e] Contained already traces of **21a**,**b**.
[f] Cyclization with LiOH.
[g] *ent*-**14** contained already traces of *ent*-**21a**,**b**.

As observed previously,[6b,d] dithiolane-derived bissulfoxides proved to be even more reactive: During the oxidation of **6** to the corresponding unprotected bissulfoxide a complete concomitant cyclization occurs in good yield (74% over 2 steps) leading to **19a** and **19b** with 85:15 selectivity (Table 3, entry 2). Though significantly better selectivities were obtained in this case, these isomers could not be separated by conventional chromatography at this stage.

Not astonishingly, immediate cyclization was observed during the oxidation of dithiolane species **5** leading to the tetrahydrofuran derivatives **18a** and **18b** with 51:49 selectivity. Similarly, poor selectivities have been observed for the intermolecular additions of O-nucleophiles.[22] The structures of isomers **19b**, **20b** and **21b** were unambiguously determined by X-ray crystallographic analysis (Figure 1).[27]

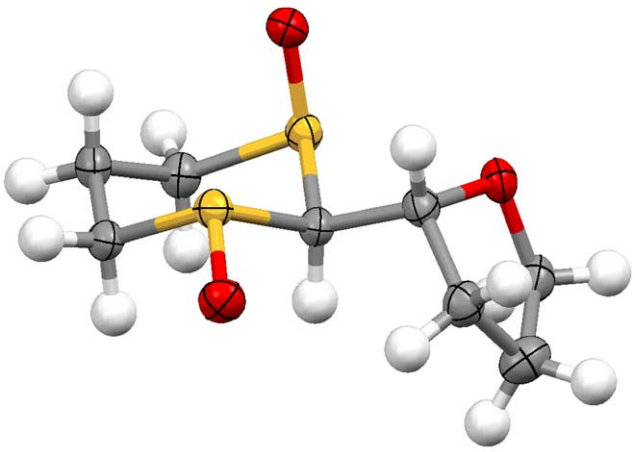
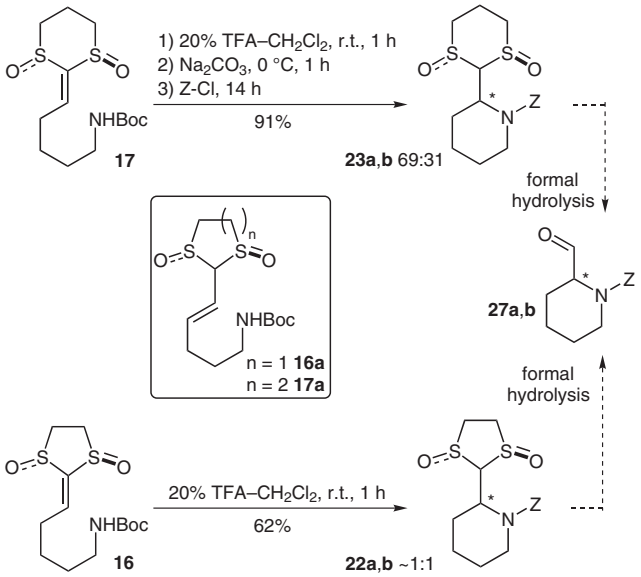


Figure 1 Structure of tetrahydropyran **20b** in the crystal.[23]

The intramolecular reaction of the bissulfoxides derived from substrates **4** and **7** should lead to four-membered rings, where the ring closure should be favored according to Baldwin's rules.[24] Nevertheless this type of reaction was not observed; presumably the intermolecular reactions resulted in the formation of unspecified oligomers.

Intramolecular Additions of N-Nucleophiles

Deprotection of the *N*-Boc-protected derivatives **16** and **17** was achieved with 20% trifluoroacetic acid in dichloromethane at room temperature for one hour. In the highly reactive dithiolane dioxide **16** addition occurred even under acidic conditions with ~1:1 selectivity and 62% yield. The resulting secondary amine was precipitated as trifluoroacetate salt from tetrahydrofuran–diethyl ether as a mixture of diastereomers. Separation of the diastereomers via column chromatography was achieved after protection of the amine moiety with the benzyloxycarbonyl (Z) group. It should be noted that to some extent a shift of the double bond of Boc-protected amine **16** was observed in the presence of triethylamine even at –78 °C (**16a** in Scheme 7).



Scheme 7 Intramolecular additions of N-nucleophiles to dithiane- and dithiolane-derived bissulfoxides

In the deprotected amine **17** cyclization was achieved by treatment with excess base (Na_2CO_3 or $BaCO_3$) for one hour at 0 °C in water, and the adducts were trapped as the Z-protected derivatives **23a**,**b**. The initially formed addition products (secondary amines) were quite polar. While they could be purified, the different diastereomers could not be separated. After Z-protection, the obtained diastereomers could be separated by column chromatography. This three-step deprotection–cyclization–protection sequence proceeded in the case of substrate **17** in excellent yield (91%) (Scheme 7). Diastereoselectivity was 69:31 (**23a**:**23b**) when the cyclization was performed at 0 °C. Assignment of the absolute configuration in **17** was not possible. Aldehyde **27a** obtained at the end of the sequence was known and comparison with the published specific optical rotation[25] gave evidence for a preferential *Si* attack at this stage of the synthesis. The newly formed stereogenic center in the major isomers **a** is *S*-configured, the minor isomer **b** has an *R*-configuration. No improvement of selectivities could be achieved by variation of reaction conditions like solvent, base, or temperature (Table 4).

These intramolecular additions of N-nucleophiles turned out to be significantly faster than the respective intermolecular reactions. While the intermolecular reaction of a similar alkylidene sulfoxide with piperidine as solvent led to a 20% conversion within 48 hours at room temperature, the here presented intramolecular additions were completed in less than one hour at 0 °C.[6d] Cleavage of the bissulfoxide auxiliaries with liberation of a carbonyl group (e.g., an aldehyde function) led to compounds which are difficult to access by other methods in enantiomerically pure form. While the 5-membered rings are proline derivatives,

Table 4 Intramolecular Additions of N-Nucleophiles (Scheme 7)

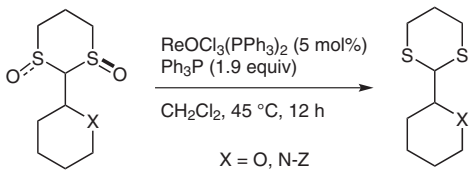
Entry	Starting material	Conditions		Product (dr) (*S*,*R*)	Yield (%)
		Deprotection	Cyclization		
1	**17**	20% TFA in CH_2Cl_2, r.t., 1 h	Na_2CO_3 or $BaCO_3$ (20 equiv) H_2O, 0 °C, 1 h	**23a**,**b** (69:31)[a]	91[b]
2	**17**	20% TFA in CH_2Cl_2, r.t. 1 h	LiOH, MeOH, –40 °C, 40 h	**23a**,**b** (47:53)[a]	–[c]
3	**17**	20% TFA in CH_2Cl_2, r.t., 1 h	$BnNMe_3OH$, MeOH, –40 °C, 40 h	mixture of **23a**,**b** and **17a**	–[c]
4	**17**	20% TFA in CH_2Cl_2, r.t., 1 h	$BnNMe_3OH$, CH_2Cl_2, –40 °C, 40 h	**23a**,**b** (47:53)[a]	–[c]
5	**16**	10% TFA in CH_2Cl_2, r.t., 1 h	–[d]	**22a**,**b** (~1:1)	62
6	**16**	none	Et_3N, r.t., 1 h	**16a**	–[c]

[a] Concomitant protection with Z-Cl in the presence of Na_2CO_3 and H_2O; dr was determined as Z-protected derivative (^{1}H NMR).
[b] Yield over 3 steps from **17** (deprotection-cyclization-protection sequence).
[c] Not determined.
[d] Cyclization occurred during deprotection.

which are simply obtained in any enantiomeric form and oxidation state, the higher homologue pipecolic acid is very expensive in enantiomerically pure form. Though its derivatives were frequently used especially in medicinal chemistry,[26] it was mandatory either to resolve the racemic material[27] or to apply enantioselective multistep reactions like Seebach's Boc-BMI method.[28]

Cleavage of the Auxiliary

Cleavage of the auxiliary liberating a carbonyl compound has been performed by Aggarwal et al. using a Pummerer reaction yielding the respective carbothioate. Substrates used by them were – due to the substitution pattern – not prone to racemization or epimerization.[5b,29] We tested a Pummerer reaction with substrate **19** (dr = 85:15) leading to *S*-ethyl tetrahydro-2*H*-pyran-2-carbothioate in 59% yield but poor enantioselectivity (31% ee). In our previous work, we used a two-step protocol with reduction of the sulfoxide groups and subsequent hydrolysis of the dithiane liberating an aldehyde function. From the plethora of methods available for the reduction of sulfoxides we chose for the formation of the corresponding dithioacetals a rhenium-catalyzed reduction with triphenylphosphine in dichloromethane (not anhydrous) at 45 °C, which was achieved in high yields exceeding 77% (Scheme 8).[30]



Scheme 8 Reduction of bissulfoxides (Table 5)

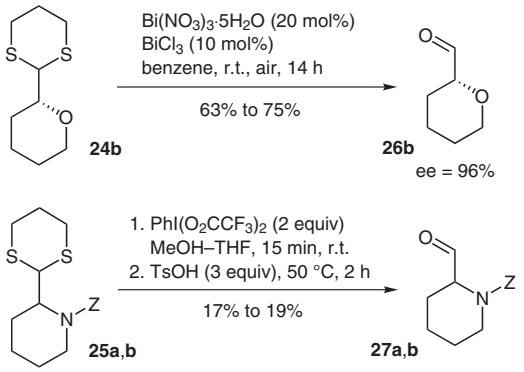
Similarly plenty of methods have been published for the hydrolysis of dithioacetals.[31] We found that this transformation is highly substrate-specific not allowing the utilization of a generally applicable method. It turned out that in very sensitive substrates partial racemization is difficult to avoid. We obtained satisfactory results in the cleavage of 2-(1,3-dithian-2-yl)tetrahydropyrans **24a** and **24b** for this transformation using bismuth nitrate in the presence of oxygen according to a published protocol (Scheme 9).[32]

Chiral aldehyde **26b** was obtained with 96% ee. This kind of hydrolysis failed for compound **25a**; best results were obtained with an slightly modified two-step protocol using $PhI(O_2CCF_3)_2$ in MeOH–THF followed by treatment with *p*-toluenesulfonic acid in dioxane–water as described by Danishefsky et al.[33] The high volatility of the aldehydes (e.g., **26**), their instability[25] and their tendency to racemize suggests an immediate transformation of these compounds, possibly even without extensive purification (**26** showed an ee of 86% after standing for several days at room temperature, **27** showed an ee of 70% after purification by column chromatography).

Table 5 Cleavage of the Auxiliary (Schemes 8 and 9)

Entry	Starting material	Dithiane[a]	Yield (%)	Hydrolysis	Aldehyde (config.)	Yield (%)
1	**21a**	**24a**	91	$Bi(NO_3)_3$	**26a** (*S*)	75
2	**21b**	**24b**	88	$Bi(NO_3)_3$	**26b** (*R*)	63
4	**23a**	**25a**	87	$PhI(O_2CCF_3)$	**27a** (*S*)	17
5	**23b**	**25b**	77	$PhI(O_2CCF_3)$	**27b** (*R*)	19

[a] Reduction was achieved with $ReOCl_3(PPh_3)_2/Ph_3P$ in CH_2Cl_2 at 45 °C.



Scheme 9 Hydrolysis of *S*,*S*-acetals (Table 5)

In conclusion, we have presented an auxiliary-based method for the preparation of α-functionalized cyclic aldehydes, which are hardly accessible in enantiomerically pure form by other routes. The stereochemical information of the auxiliary is introduced by means of diethyl tartrate, which is available and inexpensive in both enantiomeric forms. This gives access to each enantiomer of the target molecules, depending on the chosen configuration of the auxiliary. Application of this method to the preparation of 1,4-dicarbonyl compounds is currently under investigation in our group.

THF was distilled over sodium benzophenone ketyl and CH_2Cl_2 was distilled from CaH_2. Abbreviations: *tert*-butyloxycarbonyl (Boc), diethyl tartrate (DET), 3-(heptafluoropropylhydroxymethylene)-*d*-camphorate (hfc), thin-layer chromatography (TLC), trifluoroacetic acid (TFA), *tert*-butyldimethylsilyl (TBS), *p*-toluenesulfonyl (Ts), benzyloxycarbonyl (Z). All moisture-sensitive reactions were carried out under oxygen-free argon using oven-dried glassware and a vacuum line. Flash column chromatography[34] was carried out using Merck silica gel 60 (230–400 mesh) and TLC using commercially available Merck F_{254} pre-coated sheets. ^1H and ^{13}C NMR spectra were recorded on a Bruker Cryospek WM-250, AM-400, DRX 500, and Avance 600 spectrometers. The spectra were measured at r.t., unless otherwise stated. Chemical shifts are given in ppm downfield of TMS. ^{13}C NMR spectra were recorded with broad band proton decoupling and were assigned using DEPT experiments. Melting points were measured on a Büchi apparatus and are not corrected. IR spectra were recorded on a Bruker IFS-88 spectrometer. Elemental analyses were performed on a Heraeus, CHN-O-rapid or on an elementar vario MICRO apparatus. Electrical ionization and high-resolution mass spectra were recorded on a Finnigan MAT-90 spectrometer. Gas chromatography/mass spectrometry (GC-MS) measurements were performed on a GC (Agilent), model 6890 N on capillary column HP-5MS (length 30 m, inner diameter 0.25 mm, thickness of the film 0.25 μm); carrier gas: He. Mass spectrometer (Agilent) used was model 5975B VL MSD. Optical rotations were recorded on a Perkin–Elmer 241 polarimeter and specific optical rotations $[\alpha]_D^{20}$ are given in units of 10^{-1} deg cm^2 g^{-1}.

Ketene *S*,*S*-Acetals; General Procedure 1 (GP 1)

Propane-1,3-dithiol or ethane-1,2-dithiol (1.05 equiv) was added dropwise at 0 °C (in the case of ethane-1,2-dithiol: –78 °C) to a solution of CH_2Cl_2 (1 mL per mmol dithiol) and Me_3Al (2 M solution in toluene, 2.10 equiv). The formation of methane gas was observed. After removing the cooling bath, the solution was allowed to stir for 30 min at r.t. resulting in a milky solution. The corresponding ester, lactone, or lactam (1.00 equiv) in CH_2Cl_2 (1 mL per 2 mmol) was added within 15 min via a syringe pump. The resulting mixture was stirred at r.t. or refluxed for 12 h at 85 °C yielding a clear solution, which was concentrated in vacuo. Et_2O and Et_3N (3 drops) were added and moist Na_2SO_4 was carefully (**!**) added until evolution of gas ceased. After filtration over Celite and Na_2SO_4, the solvent was removed in vacuo. The crude product was obtained as a colorless liquid and either used without purification in the next step or purified by column chromatography.

Asymmetric Oxidation of Dithiolanes and Dithianes; General Procedure 2 (GP 2)

(+)-DET (2 equiv, traces of H_2O were removed by azeotropic distillation with toluene) and freshly distilled Ti(O-*i*-Pr)$_4$ (0.5 equiv) were dissolved in CH_2Cl_2 (2 mL per mmol DET) at r.t. under argon and stirred for 30 min. The solution became yellow. The (crude) ketene dithioacetal (1 equiv) was dissolved in CH_2Cl_2 (1 mL per mmol) and added to the mixture, which was then cooled to –45 °C and stirred for 2 h. Cumene hydroperoxide (80%; 4 equiv) in CH_2Cl_2 (1 mL per 10 mmol) was added over a period of 1 h. The mixture was stored for 12–24 h in a freezer (about –25 °C). Distilled H_2O (20 equiv) was added and the mixture was stirred vigorously for 1 h. The resulting gel was placed in an ultrasonic bath for 1 h to afford a filterable suspension, which was filtered by suction through a large sintered-glass funnel filled with Celite (1.5 cm height). The Celite pad was excessively washed with small portions of CH_2Cl_2 (at least 7 times) until TLC showed complete elution of the product. The filtrate was dried (Na_2SO_4) and evaporated to leave an oily material containing (+)-DET, cumene hydroxide, and the desired bissulfoxide. Pure bissulfoxide was obtained by column chromatography.

Rhenium-Catalyzed Reduction; General Procedure 3 (GP 3)

$ReOCl_3(PPh_3)_2$ (0.05 equiv), Ph_3P (1.90 equiv), and the corresponding bissulfoxide (1.00 equiv) were stirred for 14 h at 45 °C in CH_2Cl_2. After removal of the solvent in vacuo, the residue was purified by column chromatography to yield the desired pure dithioacetal.

***tert*-Butyl-(5-[1,3]dithian-2-ylidenepentyloxy)dimethylsilane (10)**

1,3-Dithiane (1.11 g, 9.24 mmol) was suspended in THF (30 mL) under argon. After cooling to –78 °C, a solution of *n*-BuLi in hexane (1.69 M, 5.74 mL, 9.70 mmol) was added dropwise. The solution was allowed to warm to 0 °C in 1 h followed by recooling to –78 °C. A solution of TMSCl (1.23 mL, 9.70 mmol) in THF (5 mL) was added and the mixture was allowed to warm to 0 °C within 1 h. After recooling to –78 °C, a solution of *n*-BuLi in hexane (1.69 M, 5.74 mL, 9.70 mmol) was added dropwise and the solution was warmed to 0 °C within 1 h. After recooling to –78 °C, 5-(*tert*-butyldimethylsilyloxy)pentanal (2.10 g, 9.70 mmol) in THF (10 mL) was added. After warming to r.t., aq sat. NH_4Cl solution (30 mL) was added. The aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The remaining crude ketene dithioacetal (3.1 g) was purified by column chromatography (hexanes–EtOAc, 10:1) to yield **10** (2.21 g, 75%) as a colorless oil; R_f = 0.64 (hexanes–EtOAc, 2:1).

IR (KBr): 2928, 2856, 1471, 1254, 1099, 836, 776 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 0.03 [s, 6 H, $Si(CH_3)_2$], 0.88 [s, 9 H, $SiC(CH_3)_3$], 1.47 (m, 4 H), 2.17 (m, 4 H), 2.84 (m, 4 H), 3.60 (t, *J* = 6.2 Hz, 2 H, OCH_2), 5.94 (t, *J* = 7.3 Hz, 1 H, H-5).

^{13}C NMR (101 MHz, $CDCl_3$): δ = –5.3 (q), 18.3 (q), 25.2 (t), 25.3 (t), 26.0 (t), 29.0 (t), 29.6 (t), 30.4 (t), 32.3 (t), 62.9 (t), 125.5 (s), 134.6 (d).

MS (EI, 70 eV): *m*/*z* (%) = 319 (10, $[M]^+$), 261 (87, $[M - t\text{-Bu}]^+$), 187 (100, $[M - OTBS]^+$), 75 (43).

HRMS-EI: *m/z* calcd for $C_{15}H_{30}OS_2Si$ $[M]^+$: 318.1507; found: 318.1504.

(2′*R*,6′*R*)-*tert*-Butyl-[5-(1,3-dioxo[1,3]dithian-2-ylidene)pentyloxy]dimethylsilane (15)

Oxidation of **10** according to GP 2 followed by column chromatography (CH_2Cl_2–acetone, 10:1 → 4:1) yielded **15** as an unstable colorless oil (1.22 g, 50%), which reacted upon standing at r.t. over some days yielding the solid addition product **21a**,**b**; $[\alpha]_D^{20}$ –12.2 (*c* 1.01, $CHCl_3$); R_f = 0.53 (CH_2Cl_2–acetone, 2:1).

IR (KBr): 3437, 2952, 2929, 2857, 1047 (S=O), 835, 775 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): 2 Rotamers, δ = 0.01 (0.04) [2 s, 6 H, $Si(CH_3)_2$], 0.87 (0.85) [2 s, 9 H, $SiC(CH_3)_3$], 1.56 (m, 4 H, H-3, H-2), 2.30–2.50 (m, 2 H, H-4), 2.62 (m, 2 H), 2.76 (m, 1 H), 3.03 (m, 1 H), 3.18 (m, 1 H), 3.59 (m, 3 H, H-1, dithiane-H), 6.65 (t, *J* = 8.0 Hz, 1 H, H-5).

^{13}C NMR (101 MHz, $CDCl_3$): 2 Rotamers (3:1), δ (major rotamer) = –3.7 (q), 14.8 (t), 17.9 [q, $C(CH_3)_3$], 25.1 (t), 25.8 (q), 28.6 (t), 31.7 (t), 48.7 (t), 55.2 (t), 61.9 (t), 140.7 (d, 1′-C), 144.2 (s, 1-C); δ (minor rotamer) = –5.4 (q), 14.8 (t), 18.2 [q, $C(CH_3)_3$], 25.3 (t), 25.6 (q), 28.8 (t), 32.0 (t), 48.8 (t), 55.3 (t), 62.3 (t), 140.8 (d), 144.1 (s).

MS (FAB): *m/z* = 351 $[M + H]^+$, 293 $[M - t\text{-Bu}]^+$.

5-([1,3]Dithian-2-ylidene)pentan-1-ol (9)

Following GP 1, ε-caprolactone (2.85 g, 24.8 mmol) reacted to yield crude **9** (5.0 g, quant) as a colorless liquid, which was used without further purification; R_f = 0.22 (hexane–EtOAc, 2:1).

IR (KBr): 3353, 2932, 2858, 1421, 1276, 1063, 912 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.36–1.64 (m, 5 H), 2.09–2.29 (m, 4 H), 2.80–2.87 (m, 4 H), 3.63 (t, *J* = 6.4 Hz, 2 H, CH_2OH), 5.93 (t, *J* = 7.3 Hz, 1 H, H-5).

MS (EI, 70 eV): *m/z* (%) = 204 (74, $[M]^+$), 145 (100), 71 (73).

HRMS-EI: *m/z* calcd for $C_9H_{16}OS_2$ $[M]^+$: 204.0642; found: 204.0639.

(2′*R*,6′*R*)-5-(1,3-Dioxo[1,3]dithian-2-ylidene)pentan-1-ol (14)

Crude **9** (5.00 g, 24.5 mmol) reacted following GP 2 (14 h at –25 °C). Purification by column chromatography (CH_2Cl_2–acetone, 2:1 → 1:1) afforded **14** together with the product of intramolecular addition **21a**,**b** (total yield: 5.06 g, 87%); R_f = 0.29 (CH_2Cl_2–MeOH, 10:1).

14

^1H NMR (250 MHz, $CDCl_3$): δ = 1.50–1.62 (m, 4 H), 2.28–2.84 (m, 5 H), 3.05 (tdd, *J* = 2.5, 13.0, 18.1 Hz, 1 H), 3.14–3.24 (m, 1 H), 3.57–3.64 (m, 3 H), 6.67 (t, *J* = 8.0 Hz, 1 H).

(2*S*,2′*R*,6′*R*) and (2*R*,2′*R*,6′*R*)-2-(1,3-Dioxo[1,3]dithian-2-yl)tetrahydropyran (21a,b)

*From Silyl Ether **15***: Compound **15** (1.46 g, 4.16 mmol) and $Bu_4NF{\cdot}3H_2O$ (1.19 g, 3.76 mmol) were dissolved in CH_2Cl_2 (20 mL) and the resulting solution was stirred for 45 min at r.t. [the reaction was monitored by TLC (CH_2Cl_2–MeOH, 10:1)]. After removal of the solvent in vacuo, the residue was purified by conventional chromatography (CH_2Cl_2–acetone, 2:1 → 1:1) yielding a mixture of **21a** and **21b** (45:55, 0.63 g, 64%). The diastereomers were separated by MPLC (CH_2Cl_2–MeOH, 100:1 → 20:1) affording **21a** and **21b** as pure isomers.

*From Alcohol **14***: Compound **14** (5.00 g, 21.1 mmol, containing small amounts of **21a**,**b**) as prepared above was dissolved in CH_2Cl_2 (100 mL). To this solution was added LiOH (5.0 g) and the mixture was stirred at 45 °C for 12 h [until TLC (CH_2Cl_2–MeOH, 10:1) showed complete addition]. H_2O (100 mL) and aq 1 M HCl (200 mL) were added and the mixture was extracted with portions of CH_2Cl_2 until monitoring by TLC (CH_2Cl_2–MeOH, 10:1) confirmed complete extraction. The organic layers were concentrated and the residue (4.0 g, 80%) containing a 45:55 mixture of **21a**:**21b** was purified by MPLC (CH_2Cl_2–MeOH, 100:1 → 20:1) to yield **21a** (1.80 g) and **21b** (2.20 g).

Using D-DET instead of L-DET in this sequence yielded a mixture of *ent*-**21a**/*ent*-**21b** = 55:45 in comparable yields.

21a

Mp 174–175 °C; $[\alpha]_D^{20}$ +165 (*c* 1.01, $CHCl_3$); R_f = 0.24 (CH_2Cl_2–acetone, 1:1), 0.40 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 2920, 2865, 1048 cm^{-1} (S=O).

^1H NMR (400 MHz, $CDCl_3$): δ = 1.58 (m, 3 H, H-4, H-5), 1.83 (ddd, *J* = 2.9, 5.5, 6.4 Hz, 1 H, H-3), 1.97 (m, 2 H, H-3, H-4), 2.59 (m, 2 H, dithiane-H), 3.00 (m, 2 H, dithiane-H), 3.37 (ddd, *J* = 3.0, 9.2, 12.9 Hz, 1 H, dithiane-H), 3.51 (m, 2 H, H-6), 3.95 (d, *J* = 2.8 Hz, 1 H, H-2), 4.03 (tdd, *J* = 1.8, 3.7, 11.2 Hz, 1 H, dithiane-H), 4.32 (td, *J* = 2.6, 11.6 Hz, 1 H, H-2).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.7 (dithiane-C), 23.2 (t, C-4), 25.2 (t, C-5), 29.7 (t, C-3), 46.1 (dithiane-C), 48.1 (dithiane-C), 68.9 (t, C-6), 69.9 (d, C-2′), 74.9 (d, C-2).

MS (FAB): *m/z* = 237 $[M + H]^+$.

ent-**21a**

$[\alpha]_D^{20}$ –156 (*c* 1.01, $CHCl_3$).

Further spectroscopic data were in full agreement with those of enantiomer **21a**.

21b

Mp 188–190 °C; $[\alpha]_D^{20}$ –37.5 (*c* 0.12, $CHCl_3$); R_f = 0.18 (CH_2Cl_2–acetone, 1:1), 0.30 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 2933, 2854, 1431, 1349, 1045 cm^{-1} (S=O).

^1H NMR (400 MHz, $CDCl_3$): δ = 1.57 (m, 3 H, H-4, H-5), 1.76 (m, 2 H, H-3), 1.90 (m, 1 H, H-4), 2.31 (m, 1 H, dithiane-H), 2.67 (m, 1 H, dithiane-H), 2.86 (m, 2 H, dithiane-H), 3.15 (m, 1 H, dithiane-H), 3.21 (d, *J* = 4.9 Hz, 1 H, H-2′), 3.50 (dt, *J* = 2.3, 11.7 Hz, 1 H, H-6), 3.61 (m, 1 H, dithiane-H), 4.10 (dtd, *J* = 1.6, 3.8, 5.8 Hz, 1 H, H-6), 4.23 (m, 1 H, H-2).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.6 (t, C-5′), 23.0 (t, C-4), 25.2 (t, C-5), 30.0 (t, C-3), 46.1 (dithiane-C), 52.1 (dithiane-C), 69.3 (t, C-6), 72.7 (d, C-2), 78.9 (d, C-2′).

MS (FAB): *m/z* = 237 $[M + H]^+$.

Anal. Calcd for $C_9H_{16}O_3S_2$: C, 45.74; H, 6.82; S, 27.13. Found: C, 45.65; H, 6.55; S, 27.26.

ent-**21b**

$[\alpha]_D^{20}$ +40.5 (*c* 0.97, $CHCl_3$).

Further spectroscopic data were in full agreement with those of enantiomer **21b**.

(2*SR*,2′*R*,5′*R*)-2-(1,3-Dioxo[1,3]dithiolan-2-yl)tetrahydropyran (19a,b)

Compound **6** [synthesized according to GP 1 starting from ε-caprolactone (4.54 g, 39.4 mmol)] was oxidized according to GP 2 and purified by column chromatography (CH_2Cl_2–acetone, 2:1) yielding **19** (6.47 g, 74%, over 2 steps) as a white solid mixture of isomers (85:15) not separable by column chromatography; R_f = 0.26 (CH_2Cl_2–acetone, 1:1).

IR (KBr): 2926, 2854, 1087, 1024 cm^{-1} (S=O).

^1H NMR (400 MHz, $CDCl_3$): δ = 1.45–1.76 (m, 4 H), 1.82–2.14 (m, 2 H), 3.40–3.75 (m, 7 H), 3.96–4.01 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): Mixture of isomers, δ (major isomer) = 22.6, 25.1, 31.1, 51.1, 51.9, 68.8, 71.7 (d), 94.7 (d); δ (minor isomer) = 22.7, 25.1, 30.6, 50.5, 51.3, 68.8, 70.4 (d), 96.5 (d).

MS (FAB): *m*/*z* = 223 $[M + H]^+$.

HRMS-FAB: *m*/*z* calcd for $C_8H_{14}O_3S_2$ $[M + H]^+$: 223.0462; found: 223.0465.

Anal. Calcd for $C_8H_{14}O_3S_2$: C, 43.22; H, 6.35; S, 28.85. Found: C, 43.15; H, 6.12; S, 28.36.

(2*S*,2′*R*,6′*R*) and (2*R*,2′*R*,6′*R*)-2-(1,3-Dioxo[1,3]dithian-2-yl)tetrahydrofuran (20a,b)

Compound **8** was synthesized according to GP 1 starting from freshly distilled δ-valerolactone (2.16 g, 21.6 mmol). After purification by column chromatography [cyclohexane–EtOAc, 2:1, R_f = 0.28 (hexane–EtOAc, 2:1)], **8** was obtained as a colorless oil (2.94 g, 64%), which was oxidized according to GP 2 and purified by column chromatography (CH_2Cl_2–acetone, 4:1 → 1:1) yielding **20a**,**b** (1.40 g, 45%) as a white solid mixture of diastereomers (**20a**/**20b**, 46:54), which could be separated by MPLC (CH_2Cl_2–MeOH, 50:1 → 20:1).

20a

Mp 92–94 °C; $[\alpha]_D^{20}$ +123.8 (*c* 1.01, $CHCl_3$); R_f = 0.28 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 3810, 3438, 2876, 2075, 1741, 1400, 1178, 1035 cm^{-1} (S=O).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.99 (m, 1 H, H-4), 2.07 (m, 1 H, H-4), 2.31 (td, *J* = 5.2, 13.8 Hz, 2 H, H-3), 2.61 (m, 2 H, dithiane-H), 3.02 (m, 2 H, dithiane-H), 3.33 (m, 1 H, dithiane-H), 3.47 (m, 1 H, dithiane-H), 3.86 (m, 1 H, H-5), 4.00 (m, 1 H, H-5), 4.11 (d, 1 H, *J* = 3.3 Hz, H-2′), 4.72 (dt, *J* = 3.6, 7.7 Hz, 1 H, H-2).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 14.6 (t), 25.3 (t, C-4), 29.9 (t, C-3), 45.8 (t), 48.1 (t), 69.1 (t, C-5), 72.0 (d, C-2), 74.0 (d, C-2′).

MS (EI, 70 eV): *m*/*z* (%) = 222 (58, $[M]^+$), 90 (51), 84 (100), 71 (92), 43 (80), 41 (81).

HRMS-EI: *m*/*z* calcd for $C_8H_{14}O_3S_2$ $[M]^+$: 222.0384; found: 222.0382.

Anal. Calcd for $C_8H_{14}O_3S_2$: C, 43.22; H, 6.35; S, 28.85. Found: C, 43.17; H, 6.05; S, 28.72.

20b

Mp 138–140 °C; $[\alpha]_D^{20}$ –2.0 (*c* 1.02, $CHCl_3$); R_f = 0.21 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 2950, 2950, 2900, 2880, 1728, 1424, 1041, 1021 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.96–2.10 (m, 3 H, H-3, H-4), 2.25–2.40 (m, 2 H, H-3, dithiane-H), 2.68–2.97 (m, 3 H, dithiane-H), 3.23 (dddd, *J* = 1.0, 2.7, 3.8, 14.2 Hz, 1 H, dithiane-H), 3.31 (d, *J* = 7.8 Hz, 1 H, H-2′), 3.61 (dddd, *J* = 1.0, 2.1, 5.6, 12.2 Hz, 1 H, dithiane-H), 3.85 (m, 1 H, H-5), 3.95 (td, *J* = 7.0, 13.8 Hz, 1 H, H-5), 4.66 (dd, *J* = 7.0, 14.5 Hz, 1 H, H-2).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.5 (t), 25.9 (t, C-4), 30.8 (t, C-3), 45.4 (t), 51.3 (t), 68.2 (t, C-5), 74.8 (d, C-2), 78.1 (d, C-2′).

MS (EI, 70 eV): *m*/*z* (%) = 222 (9, $[M]^+$), 90 (23), 84 (45), 71 (64), 63 (19), 55 (44), 43 (100), 41 (77).

HRMS-EI: *m*/*z* calcd for $C_8H_{14}O_3S_2$ $[M]^+$: 222.0384; found: 222.0388.

(2*SR*,2′*R*,5′*R*)-2-(1,3-Dioxo[1,3]dithiolan-2-yl)tetrahydrofuran (18a,b)

Compound **5** was synthesized starting from δ-valerolactone according to GP 1 and directly oxidized according to GP 2 and purified by column chromatography (CH_2Cl_2–acetone, 4:1 → 1:1) to give **18a** and **18b** as a white, solid, and inseparable mixture of isomers (51:49) (4.64 g, 56%, 2 steps). The diastereomers could not be assigned; R_f = 0.21 (CH_2Cl_2–acetone, 2:1).

IR (KBr): 2985, 2934, 2880, 1396, 1033 cm^{-1} (S=O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.90–2.06 (m, 3 H), 2.28–2.40 (m, 1 H), 3.52–3.95 (m, 7 H), 4.22–4.33 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): Mixture of isomers, δ = 25.6 (t), 25.9 (t), 30.5 (t), 31.7 (t), 51.4 (t), 51.5 (t), 51.6 (t), 52.2 (t), 68.5 (t), 69.0 (t), 72.0 (d), 72.8 (d), 94.3 (d), 95.9 (d).

MS (EI, 70 eV): *m*/*z* (%) = 208 (83, $[M]^+$), 132 (100, $[M - C_2H_4SO]^+$), 108 (22), 84 (47), 71 (73) $[C_4H_7O]^+$.

HRMS-EI: *m*/*z* calcd for $C_7H_{12}O_3S_2$ $[M]^+$: 208.0228; found: 208.0230.

Anal. Calcd for $C_7H_{12}O_3S_2$: C, 40.36; H, 5.81; S, 30.79. Found: C, 40.37; H, 5.60; S, 30.92.

***tert*-Butyl (2′*R*,5′*R*)-[5-(1,3-Dioxo[1,3]dithian-2-ylidene)pentyl]carbamate (17)**

Compound **12** was synthesized according to GP 1 starting from *tert*-butyl 2-oxoazepane-1-carboxylate (*N*-Boc-ε-caprolactam) and stirring overnight at reflux. The resulting crude colorless liquid was oxidized without further purification according to GP 2 and purified by column chromatography (CH_2Cl_2–acetone, 10:1 → 1:1) yielding **17** as a yellowish highly viscous oil (4.00 g, 63%, 2 steps).

Ketene *S*,*S*-Acetal 12

R_f = 0.52 (hexane–EtOAc, 2:1).

IR (KBr): 3348, 2931, 1698 (s, C=O), 1515, 1171 cm^{-1}.

MS (EI): *m*/*z* (%) = 303 (1, $[M]^+$), 205 (11), 164 (15), 113 (100), 85 (41), 84 (43), 57 (41), 55 (33), 41 (41).

HRMS: *m*/*z* calcd for $C_{14}H_{25}NO_2S_2$ $[M]^+$: 303.1327; found: 303.1326.

Bissulfoxide 17

$[\alpha]_D^{20}$ –18.9 (*c* 0.99, $CHCl_3$); R_f = 0.31 (CH_2Cl_2–acetone, 1:1).

IR (KBr): 3330, 2929, 1703 (s, C=O), 1526, 1170, 1050 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.41 (s, 9 H, *t*-C_4H_9), 1.52 (m, 4 H), 2.34 (m, 1 H), 2.46 (dt, *J* = 6.9, 14.1 Hz, 1 H, H-4), 2.63 (m, 2 H), 2.78 (ddd, *J* = 2.5, 11.9, 13.4 Hz, 1 H), 3.05 (m, 3 H), 3.18 (td, *J* = 3.3, 14.3 Hz, 1 H), 3.60 (dddd, *J* = 1.0, 2.1, 3.6, 7.7 Hz, 1 H), 4.60 (s br, 1 H, NH), 6.63 (t, *J* = 8.0 Hz, 1 H, H-5).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 14.8 (t), 25.8 (t), 28.4 [q, $C(CH_3)_3$], 28.5 (t), 29.5 (t), 39.9 (t), 48.9 (t), 55.4 (t), 79.2 (s), 140.2 (d, C-5), 144.8 (s), 155.9 (s).

MS (FAB): *m*/*z* = 336 $[M + H]^+$.

HRMS-FAB: *m*/*z* calcd for $C_{14}H_{25}NO_4S_2$ $[M + H]^+$: 336.1303; found: 336.1305.

Benzyl (2*S*,2′*R*,6′*R*)- and (2*R*,2′*R*,6′*R*)-2-(1,3-Dioxo[1,3]dithian-2-yl)piperidine-1-carboxylate (23a,b)

Boc-protected bissulfoxide **17** (4.10 g, 12.2 mmol) was dissolved in CH_2Cl_2 (100 mL). Deprotection was performed at r.t. by adding TFA (10 mL) followed by stirring at r.t. for 30–60 min (monitoring with TLC). The solution was concentrated and traces of TFA were removed by co-evaporation with $CHCl_3$ (3 × 15 mL). H_2O (100 mL) and Na_2CO_3 (10 g) were then added. The mixture was stirred for 1 h at 0 °C and warmed to r.t., Z-Cl (2.20 mL, 14.7 mmol) was added, and the stirring was continued overnight at r.t. The mixture was extracted with CH_2Cl_2 (5 × 25 mL), dried (Na_2SO_4), and concentrated. The resulting oil (^{1}H NMR: **23a**/**23b** 69:31) was purified by MPLC (CH_2Cl_2–MeOH, 50:1 → 20:1) yielding **23a** (2.83 g, 63%) and **23b** (1.27 g, 28%) as colorless, slowly solidifying oils.

23a

Mp 39–43 °C (softening range); $[\alpha]_D^{20}$ +92.8 (*c* 1.04, $CHCl_3$); R_f = 0.39 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 2938, 1692 (C=O), 1424, 1259, 1044 (S=O), 699 cm^{-1}.

^1H NMR (500 MHz, acetone-d_6): δ = 1.44–1.54 (m, 1 H), 1.62–1.70 (m, 2 H), 1.72–1.83 (m, 2 H), 2.27 (br d, *J* = 13.0 Hz, 1 H), 2.33–2.42 (m, 1 H), 2.51–2.61 (m, 1 H), 3.00 (ddd, *J* = 3.7, 9.4, 13.1 Hz, 1 H), 3.06–3.15 (m, 1 H), 3.17–3.26 (m, 2 H), 3.37 (ddd, *J* = 3.4, 7.9, 13.2 Hz, 1 H), 4.08 (br d, *J* = 13.4 Hz, 1 H), 4.29 (br d, *J* = 9.2 Hz, 1 H), 5.16 (m, 3 H), 7.28–7.44 (m, 5 H, Ph).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 11.5 (t), 18.7 (t), 24.4 (t), 26.8 (t), 40.7 (t), 42.2 (t), 42.6 (t), 48.2 (d), 67.4 (d), 70.4 (s), 127.9 (d), 128.0 (d), 128.3 (d), 136.1 (t), 155.0 (s).

MS (FAB): *m*/*z* (%) = 370 (40, $[M + H]^+$), 91 (100, $[C_7H_7]^+$).

HRMS-FAB: *m*/*z* calcd for $C_{17}H_{23}NO_4S_2$ $[M + H]^+$: 370.1147; found: 370.1152.

23b

$[\alpha]_D^{20}$ +29 (*c* 1.1, $CHCl_3$); R_f = 0.34 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 2928, 1694, 1662, 1423, 1262, 1042 cm^{-1} (S=O).

^1H NMR (400 MHz, $CDCl_3$): Rotamers, only selected signals are given, δ = 1.76–2.02 (m, 1 H), 3.58–3.65 (m, 1 H), 3.75–3.89 (m, 1 H), 3.90–4.24 (m, 1 H), 5.04–5.32 (m, 3 H), 7.24–7.44 (m, 5 H_{arom}).

MS (FAB): *m*/*z* (%) = 370 (100, $[M + H]^+$), 114 (91), 91 (64, $[C_7H_7]^+$).

HRMS-FAB: *m*/*z* calcd for $C_{17}H_{23}NO_4S_2$: $[M + H]^+$: 370.1147; found: 370.1143.

Benzyl (*S*)-2-([1,3]Dithian-2-yl)piperidine-1-carboxylate (25a)

Compound **23a** (1.13 g, 3.09 mmol) reacted according to GP 3 yielding **25a** (900 mg, 87%) as a colorless oil; $[\alpha]_D^{20}$ –26.5 (*c* 1.03, $CHCl_3$); R_f = 0.41 (hexane–EtOAc, 2:1).

IR (KBr): 2935, 1696 (C=O), 1423, 1255, 1169 cm^{-1}.

^1H NMR (500 MHz, 353 K, DMSO-d_6): δ = 1.30–1.40 (m, 1 H), 1.48–1.67 (m, 4 H), 1.71–1.80 (m, 1 H), 1.95–2.02 (m, 1 H), 2.05–2.11 (m, 1 H), 2.72 (ddd, *J* = 2.8, 9.9, 14.0 Hz, 1 H), 2.79–2.89 (m, 4 H), 3.94 (dd, *J* = 4.3, 14.0 Hz, 1 H), 4.39 (br s, 1 H), 4.55 (d, *J* = 10.9 Hz, 1 H), 5.10 (q, *J* = 12.7 Hz, 2 H, OCH_2), 7.27–7.32 (m, 1 H, C_6H_5), 7.34–7.40 (m, 4 H, C_6H_5).

^{13}C NMR (126 MHz, 353 K, DMSO-d_6): δ = 17.8, 24.1, 24.9, 25.0, 27.3, 27.4, 44.8, 52.5, 65.8, 126.9, 127.1, 127.8, 136.6, 154.2, 205.6.

MS (EI, 70 eV): *m*/*z* (%) = 337 (13, $[M]^+$), 262, 218 (100, $[M - C_4H_7S_2]^+$), 174, 119 $[C_4H_7S_2]^+$, 91 $[C_7H_7]^+$.

HRMS-EI: *m*/*z* calcd for $C_{17}H_{23}NO_2S_2$ $[M]^+$: 337.1170; found: 337.1173.

Benzyl (*R*)-2-([1,3]Dithian-2-yl)piperidine-1-carboxylate (25b)

Compound **23b** (800 mg) reacted according to GP 3 yielding **25b** (564 mg, 77%) as a colorless oil; $[\alpha]_D^{20}$ +25.6 (*c* 1.03, $CHCl_3$).

Further spectroscopic data were in full agreement with those of enantiomer **23a**.

***tert*-Butyl 5-([1,3]Dithiolan-2-ylidene)pentylcarbamate (11)**

Methyl *N*-*tert*-butyloxycarbonyl-6-aminohexanoate (4.56 g, 19.6 mmol) reacted according to GP 2 for 14 h at r.t. yielding after column chromatography (cyclohexane–EtOAc, 10:1) **11** as a colorless oil (3.46 g, 61%), which was immediately oxidized in the next step; R_f = 0.56 (cyclohexane–EtOAc, 2:1).

IR (KBr): 3356 (N–H), 2929, 1697 (C=O), 1598, 1516, 1365, 1276, 1170 cm^{-1}.

MS (FAB): *m*/*z* = 290 $[M + H]^+$, 234, 171, 131.

HRMS-FAB: *m*/*z* calcd for $C_{13}H_{23}NO_2S_2$ $[M + H]^+$: 290.1248; found: 290.1247.

***tert*-Butyl (2′*R*,6′*R*)-[5-(1,3-Dioxo[1,3]dithiolan-2-ylidene)pentyl]carbamate (16)**

Compound **11** (3.46 g, 12.0 mmol) reacted according to GP 2 followed by column chromatography (CH_2Cl_2–acetone, 2:1 → 1:1) yielding **16** (1.92 g, 50%) as a colorless oil, which solidified slowly. Product **16** was of limited stability; it partly decomposed during column chromatography; $[\alpha]_D^{20}$ –96.6 (*c* 1.00, $CHCl_3$); R_f = 0.18 (CH_2Cl_2–acetone, 1:1).

IR (KBr): 3356, 2972, 2052, 1683 (C=O), 1533, 1174, 1020 cm^{-1} (S=O).

^1H NMR (400 MHz, $CDCl_3$): δ = 1.44 (s, 9 H, *t*-C_4H_9), 1.54–1.68 (m, 4 H, 3-H, 2-H), 2.69–2.86 (m, 2 H, 4-H), 3.14 (m, 2 H, 1-H), 3.60–3.84 (m, 4 H, 3′-H, 4′-H), 4.78 (br, 1 H, NH), 7.33 (t, *J* = 7.8 Hz, 1 H, 5-H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 25.2 (t, C-2 or C-3), 28.3 [q, $C(CH_3)_3$], 29.4 (t, C-3 or C-2), 32.6 (t, C-4), 39.7 (t, C-1), 50.3 (t, C-3′ or C-4′), 50.6 (t, C-4′ or C-3′), 79.0 [s, $C(CH_3)_3$], 155.0 (d, C-5), 155.8 (s, C-2′ or C = O), 156.8 (C=O or C-2′).

MS (FAB): *m*/*z* = 322 $[M + H]^+$, 266.

HRMS-FAB: *m*/*z* calcd for $C_{13}H_{23}NO_4S_2$ $[M + H]^+$: 322.1147; found: 322.1144.

Benzyl (2*S*,2′*R*,6′*R*)- and (2*R*,2′*R*,6′*R*)-2-(1,3-Dioxo[1,3]dithiolan-2-yl)piperidine-1-carboxylate (22a,b)

Compound **16** (200 mg, 0.622 mmol) was dissolved in CH_2Cl_2 (10 mL). Deprotection (and concomitant addition) was performed at r.t. by adding TFA (1 mL) followed by stirring at r.t. for 30–60 min (monitoring with TLC). The solution was concentrated and traces of TFA were removed by co-evaporation with $CHCl_3$ (3 × 4 mL). H_2O (10 mL), Na_2CO_3 (1.3 g, 12.4 mmol), and Z-Cl (0.140 mL, 0.933 mmol) were added and the stirring was continued overnight at r.t. The mixture (^1H NMR: **22a/22b** ~1:1) was extracted with CH_2Cl_2 (5 × 5 mL), dried (Na_2SO_4), and concentrated. The resulting oil was purified by MPLC (CH_2Cl_2–MeOH, 50:1 → 20:1) to give **22** (137 mg, 62%). A pure fraction of one isomer was obtained, though its configuration could not be assigned unambiguously.

22; First Isomer

R_f = 0.29 (CH_2Cl_2–acetone, 1:1).

^1H NMR (400 MHz, acetone-d_6): δ = 1.44–1.56 (m, 1 H), 1.68–1.92 (m, 5 H), 3.06 (m, 1 H), 3.45 (m, 1 H), 3.52–3.92 (m, 3 H), 4.23 (br t, 1 H), 4.58 (dd, *J* = 4.3, 12.5 Hz, 1 H), 4.80 (m, 1 H), 5.04–5.26 (m, 2 H), 7.30–7.44 (m, 5 H).

^{13}C NMR (101 MHz, acetone-d_6): 2 Rotamers, δ = 20.2 (20.3) (t), 26.8 (27.1) (t), 29.5 (29.7) (t), 41.8 (42.4) (t), 48.7 (48.9) (d), 52.7 (52.9) (t), 54.5 (54.5) (t), 68.6 (68.7) (t), 93.2 (93.4) (d), 129.5 (d), 129.7 (129.8) (d), 130.3 (d), 138.8 (139.0) (s), 156.0 (156.7) (s)

22; Second Isomer

Spectroscopic data from the mixture of isomers.

R_f = 0.19 (CH_2Cl_2–acetone, 1:1).

IR (KBr): 3485, 2937, 2242, 1691 (C=O), 1340, 1259, 1032 cm^{-1} (S=O).

MS (FAB): *m*/*z* (%) = 356 (100, $[M + H]^+$), 91 (51, $[C_7H_7]^+$).

HRMS-FAB: *m*/*z* calcd for $C_{16}H_{21}NO_4S_2$ $[M + H]^+$: 356.0990; found: 356.0994.

(*S*)-2-([1,3]Dithian-2-yl)tetrahydropyran (24a)
Compound **21a** (998 mg) reacted according to GP 3 yielding **24a** (788 mg, 91%) as a colorless liquid; $[\alpha]_D^{20}$ –0.6 (*c* 1.01, $CHCl_3$); R_f = 0.50 (hexanes–EtOAc, 2:1).

IR (KBr): 2936, 2845, 1090 (C–O), 1049 (C–O) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.54 (m, 4 H, H-3, H-4, H-5), 1.77 (d, *J* = 12.9 Hz, 1 H, H-3), 1.90 (m, 2 H, H-5′, H-5), 2.11 (m, 1 H, H-5′), 2.88 (m, 4 H, H-4′, H-6′), 3.45 (dt, *J* = 2.1, 11.7 Hz, 1 H, H-6), 3.51 (ddd, *J* = 2.0, 5.5, 10.8 Hz, 1 H, H-2), 4.06 (tdd, *J* = 1.7, 3.9, 6.2 Hz, 1 H, H-6), 4.19 (d, *J* = 5.5 Hz, 1 H, H-2′).

^{13}C NMR (500 MHz, $CDCl_3$): δ = 23.1 (t), 25.6 (t), 26.1 (t, C-5′), 29.0 (t, C-3), 30.2 (t,), 30.3 (t), 52.7 (d, C-2′), 69.0 (t, C-6), 79.5 (d, C-2).

MS (EI, 70 eV): *m*/*z* (%) = 204 (49, $[M]^+$), 119 (74, $[C_4H_7S_2]^+$), 85 (100, $[C_5H_9O]^+$).

HRMS-EI: *m*/*z* calcd for $C_9H_{16}OS_2$ $[M]^+$: 204.0643; found: 204.0641.

(*R*)-2-([1,3]Dithian-2-yl)tetrahydropyran (24b)
Compound **21b** (540 mg) reacted according to GP 3 yielding **24b** (412 mg, 2.02 mmol, 88%) as a colorless liquid; $[\alpha]_D^{20}$ +0.6 (*c* 1.01, $CHCl_3$).

Further spectroscopic data were in full agreement with those of the enantiomer **24a**.

(*R*)-Tetrahydropyran-2-carbaldehyde (26b)
Finely ground $Bi(NO_3)_3 \cdot 5\ H_2O$ (196 mg, 0.403 mmol), $BiCl_3$ (64 mg, 0.20 mmol), and H_2O (73 μL) were added to a solution of **24b** (412 mg, 2.02 mmol) in anhyd benzene (20 mL) and the mixture was stirred for 14 h at r.t (monitoring with TLC). The reaction was quenched by the addition of H_2O (10 mL) and the mixture was extracted with Et_2O (5 × 20 mL). The combined organic layers were dried (Na_2SO_4) and carefully concentrated ($P \geq 100$ mbar). The resulting colorless liquid was purified by bulb-to-bulb distillation (60 °C/20 mbar, cooling the receiver with dry ice) to yield the highly volatile, characteristically smelling aldehyde **26b** (146 mg, 63%), which contained traces of benzene. Portionwise addition of $Eu(hfc)_3$ (19 mg) to **26b** (15 mg) led to a baseline separation in the ^1H NMR spectra of the signal at δ = 9.62 revealing an ee of 96%; $[\alpha]_D^{20}$ +12.8 (*c* 1.11, $CHCl_3$); R_f = 0.32 (hexane–EtOAc, 2:1).

IR (KBr): 3449, 2941, 2853, 1738 (C=O), 1208, 1095 (C–O), 1047 (C–O), 898, 733 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.40–1.66 (m, 4 H), 1.82–1.94 (m, 2 H), 3.54 (ddd, *J* = 2.3, 7.2, 12.4 Hz, 1 H), 3.83 (dd, *J* = 2.7, 11.0 Hz, 1 H), 4.07 (ddd, *J* = 2.6, 4.1, 11.6 Hz, 1 H), 9.62 (s, 1 H, CHO).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 22.5 (t), 25.5 (t), 26.2 (t), 68.2 (t), 81.5 (d, C-2), 201.9 (d, C-1′).

GC-MS (EI, 70 eV): *m*/*z* (%) = 114 (<1, $[M]^+$), 85 (100, $[M - HCO]^+$), 67 (28), 57 (27), 41 (44).

(*S*)-Tetrahydropyran-2-carbaldehyde (26a)
According to the procedure for the synthesis of **26b**, compound **24a** (788 mg, 3.86 mmol) yielded **26a** (330 mg, 75%) as a colorless liquid; $[\alpha]_D^{20}$ –13.0 (*c* 2.49, $CHCl_3$).

Further spectroscopic data were in full agreement with those of enantiomer **26b**.

Benzyl (*R*)-2-Formylpiperidine-1-carboxylate (27b)
A solution of **25b** (480 mg, 1.42 mmol) in MeOH–THF, (1:1, 20 mL) was treated with $PhI(O_2CCF_3)_2$ (1.26 g, 2.84 mmol) at r.t and stirred for 15 min. The reaction was quenched by the addition of aq sat. $NaHCO_3$ (20 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried (Na_2SO_4), concentrated, dissolved in dioxane–H_2O (10:1, 20 mL), treated with $TsOH \cdot H_2O$ (812 mg, 4.27 mmol), and stirred for 3 h at 50 °C. After cooling to r.t., the solution was diluted with Et_2O (30 mL) and washed successively with aq $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4), filtered over Celite and concentrated. Purification of the residue by chromatography over silica gel (cyclohexane–EtOAc, 4:1) afforded aldehyde **27b** (67 mg, 19%) as a colorless liquid.

A specific optical rotation of **27a** has been published: $[\alpha]_D^{20}$ –30.5 (*c* 1.4, $CHCl_3$).[25]

27b
$[\alpha]_D^{20}$ +24.4 (*c* 0.86, $CHCl_3$); R_f = 0.26 (hexane–EtOAc, 2:1).

IR (KBr): 3450, 2943, 2860, 1730 (C=O), 1703 (C=O), 1422, 1253, 1046, 699 cm^{-1}.

MS (EI, 70 eV): *m*/*z* (%) = 247 (<1, $[M]^+$), 218 (46, $[M - HCO]^+$), 174 (43), 91 (100, $[C_7H_7]^+$).

HRMS-EI: *m*/*z* calcd for $C_{14}H_{17}NO_3$ $[M]^+$: 247.1208; found: 247.1205.

Acknowledgment

We thank Pierre Keller and Oliver Geiseler for their help with the laboratory work. This work was supported by the Stiftung der Deutschen Wirtschaft (stipend for T.G.).

References

(1) (a) Sibi, M. P.; Manyem, S. *Tetrahedron* **2000**, *56*, 8033. (b) Berner, O. M.; Tedeschi, L.; Enders, D. *Eur. J. Org. Chem.* **2002**, 1877. (c) Guo, H.-C.; Ma, J.-A. *Angew. Chem. Int. Ed.* **2006**, *45*, 354; *Angew. Chem.* **2006**, *118*, 362. (d) Vicario, J. L.; Badía, D.; Carrillo, L. *Synthesis* **2007**, 2065. (e) Christoffers, J.; Koripelly, G.; Rosiak, A.; Rössle, M. *Synthesis* **2007**, 1279. (f) Tsogoeva, S. B. *Eur. J. Org. Chem.* **2007**, 1701. (g) Almaşi, D.; Alonso, D. A.; Nájera, C. *Tetrahedron: Asymmetry* **2007**, *18*, 299.

(2) For example: (a) Abbott, D. J.; Colonna, S.; Stirling, C. J. M. *J. Chem. Soc. D* **1971**, 471. (b) Tsuchihashi, G.-i.; Mitamura, S.; Inoue, S.; Ogura, K. *Tetrahedron Lett.* **1973**, 323. (c) Posner, G. H. In *Asymmetric Synthesis. Stereodifferentiating Addition Reactions*, Part A, Vol. 2; Morrison, J. D., Ed.; Academic Press: New York, **1983**, 225. (d) Solladie, G.; Moine, G. *J. Am. Chem. Soc.* **1984**, *106*, 6097. (e) Iwata, C.; Fujita, M.; Hattori, K.; Uchida, S.; Imanishi, T. *Tetrahedron Lett.* **1985**, *26*, 2221. (f) Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1986**, *108*, 7399. (g) Posner, G. H.; Weitzberg, M.; Hamill, T. G.; Asirvatham, E.; He, C.-H.; Clardy, J. *Tetrahedron* **1986**, *42*, 2919. (h) Yamazaki, T.; Ishikawa, N.; Iwatsubo, H.; Kitazume, T. *J. Chem. Soc., Chem. Commun.* **1987**, 1340. (i) Pyne, S. G.; Bloem, P.; Chapman, S. L.; Dixon, C. E.; Griffith, R. *J. Org. Chem.* **1990**, *55*, 1086. (j) Mandai, T.; Ueda, M.; Kashiwagi, K.; Kawada, M.; Tsuji, J. *Tetrahedron Lett.* **1993**, *34*, 111. (k) Wakasugi, D.; Satoh, T. *Tetrahedron* **2005**, *61*, 1245.

(3) Bäckvall, J.-E. In *Modern Oxidation Methods*; Bäckvall, J.-E., Ed.; Wiley-VCH: Weinheim, **2004**, 193.

(4) (a) Mikołajczyk, M.; Drabowicz, J.; Kiełbasiński, P. *Chiral Sulfur Reagents*; CRC Press: Boca Raton, **1997**. (b) Delouvrié, B.; Fensterbank, L.; Nájera, F.; Malacria, M. *Eur. J. Org. Chem.* **2002**, 3507. (c) See also: Fernández, I.; Khiar, N. *Chem. Rev.* **2003**, *103*, 3651.

(5) Aggarwal and co-workers investigated cycloadditions, epoxidations, and cyclopropanations of dithiane-derived alkylidenebissulfoxides: (a) Aggarwal, V. K.; Drabowicz, J.; Grainger, R. S.; Gültekin, Z.; Lightowler, M.; Spargo, P. L. *J. Org. Chem.* **1995**, *60*, 4962. (b) Aggarwal, V. K.; Gültekin, Z.; Grainger, R. S.; Adams, H.; Spargo, P. L. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2771. (c) Aggarwal, V. K.; Barrell, J. K.; Worrall, J. M.; Alexander, R. *J. Org. Chem.* **1998**, *63*, 7128. (d) Aggarwal, V. K.; Roseblade, S. J.; Barrell, J. K.; Alexander, R. *Org. Lett.* **2002**, *4*, 1227. (e) Aggarwal, V. K.; Roseblade, S.; Alexander, R. *Org. Biomol. Chem.* **2003**, *1*, 684.

(6) (a) Wedel, T.; Podlech, J. *Org. Lett.* **2005**, *7*, 4013. (b) Wedel, T.; Podlech, J. *Synlett* **2006**, 2043. (c) Wedel, T.; Müller, M.; Podlech, J.; Goesmann, H.; Feldmann, C. *Chem. Eur. J.* **2007**, *13*, 4273. (d) Wedel, T.; Gehring, T.; Podlech, J.; Kordel, E.; Bihlmeier, A.; Klopper, W. *Chem. Eur. J.* **2008**, 4631.

(7) (a) Brebion, F.; Delouvrié, B.; Nájera, F.; Fensterbank, L.; Malacria, M.; Vaissermann, J. *Angew. Chem. Int. Ed.* **2003**, *42*, 5342; *Angew. Chem.* **2003**, *115*, 5500. (b) Brebion, F.; Goddard, J.-P.; Fensterbank, L.; Malacria, M. *Synthesis* **2005**, 2449. (c) Brebion, F.; Goddard, J.-P.; Gomez, C.; Fensterbank, L.; Malacria, M. *Synlett* **2006**, 713. (d) For the addition of radicals, see also: Brebion, F.; Vitale, M.; Fensterbank, L.; Malacria, M. *Tetrahedron: Asymmetry* **2003**, *14*, 2889.

(8) Doelling, W. In *Science of Synthesis*, Vol. 24; de Meijere, A., Ed.; Georg Thieme Verlag: Stuttgart, **2006**, 461.

(9) (a) Seebach, D.; Kolb, M.; Gröbel, B.-T. *Chem. Ber.* **1973**, *106*, 2277. (b) Aggarwal, V. K.; Steele, R. M.; Ritmaleni; Barrell, J. K.; Grayson, I. *J. Org. Chem.* **2003**, *68*, 4087. (c) See also: Hwu, J. R.; Lee, T.; Gilbert, B. A. *J. Chem. Soc., Perkin Trans. 1* **1992**, 3219.

(10) See also: Juaristi, E.; Gordillo, B.; Valle, L. *Tetrahedron* **1986**, *42*, 1963.

(11) (a) Kruse, C. G.; Broekhof, N. L. J. M.; Wijsman, A.; van der Gen, A. *Tetrahedron Lett.* **1977**, 885. (b) Ceruti, M.; Balliano, G.; Rocco, F.; Milla, P.; Arpicco, S.; Cattel, L.; Viola, F. *Lipids* **2001**, *36*, 629.

(12) (a) Corey, E. J.; Beames, D. J. *J. Am. Chem. Soc.* **1973**, *95*, 5829. (b) Corey, E. J.; Kozikowski, A. P. *Tetrahedron Lett.* **1975**, 925.

(13) See also: (a) Sun, Y.; Liu, B.; Kao, J.; d'Avignon, D. A.; Moeller, K. D. *Org. Lett.* **2001**, *3*, 1729. (b) Liu, B.; Duan, S.; Sutterer, A. C.; Moeller, K. D. *J. Am. Chem. Soc.* **2002**, *124*, 10101.

(14) Okuyama, T.; Fujiwara, W.; Fueno, T. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 453.

(15) Padwa, A.; Coats, S. J.; Harring, S. R.; Hadjiarapoglou, L.; Semones, M. A. *Synthesis* **1995**, 973.

(16) (a) Chamberlin, A. R.; Chung, J. Y. L. *Tetrahedron Lett.* **1982**, *23*, 2619. (b) Chamberlin, A. R.; Nguyen, H. D.; Chung, J. Y. L. *J. Org. Chem.* **1984**, *49*, 1682.

(17) Gröbel, B.-T.; Seebach, D. *Synthesis* **1977**, 357.

(18) Taubinger, A. A.; Fenske, D.; Podlech, J. *Synlett* **2008**, 539.

(19) Pitchen, P.; Duñach, E.; Deshmukh, M. N.; Kagan, H. B. *J. Am. Chem. Soc.* **1984**, *106*, 8188.

(20) Di Furia, F.; Modena, G.; Seraglia, R. *Synthesis* **1984**, 325.

(21) For example: (a) Pandey, K. S.; Shriprakash Pandey, M.; Rao, K. M.; Vaidyanathaswamy, R. *Biosci. Biotechnol. Biochem.* **1994**, *58*, 1879. (b) Bhatt, U.; Christmann, M.; Quitschalle, M.; Claus, E.; Kalesse, M. *J. Org. Chem.* **2001**, *66*, 1885. (c) Bianchi, P.; Roda, G.; Riva, S.; Danieli, B.; Zabelinskaja-Mackova, A.; Griengl, H. *Tetrahedron* **2001**, *57*, 2213. (d) Hagmann, W. K.; Delaszlo, S. E.; Doherty, G.; Chang, L. L.; Yang, G. X. WO Patent 2001012183 A1, **2001**; *Chem. Abstr.* **2001**, *134*, 193737.

(22) Wedel, T. *Ph.D. Thesis*; University of Karlsruhe (TH): Karlsruhe, **2006**.

(23) CCDC 683981 (**19b**), CCDC 683980 (**20b**) and CCDC 683979 (**21b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(24) (a) Johnson, C. D. *Acc. Chem. Res.* **1993**, *26*, 476. (b) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734.

(25) Sánchez-Sancho, F.; Herradón, B. *Tetrahedron: Asymmetry* **1998**, *9*, 1951.

(26) For example: (a) Wallberg, A.; Nilsson, K.; Holm, B.; Nagard, M.; Granberg, K.; Slassi, A.; Edwards, L.; Isaac, M.; Xin, T.; Stefanac, T. U. S. US Patent 2007259862 A1, **2007**; *Chem. Abstr.* **2007**, *147*, 522250. (b) Gal, K.; Weber, C.; Wagner, G. A.; Bobok, A. A.; Nyeki, G.; Vastag, M.; Keserue, G.; Hada, V.; Koti, J. WO Patent 2007039782 A1, **2007**; *Chem. Abstr.* **2007**, *146*, 401989.

(27) For example: (a) Stehl, A.; Seitz, G.; Schulz, K. *Tetrahedron* **2002**, *58*, 1343. (b) Tong, S. T.; Barker, D. *Tetrahedron Lett.* **2006**, *47*, 5017. (c) Cremonesi, G.; Dalla Croce, P.; Fontana, F.; Forni, A.; La Rosa, C. *Tetrahedron: Asymmetry* **2007**, *18*, 1667.

(28) Seebach, D.; Dziadulewicz, E.; Behrendt, L.; Cantoreggi, S.; Fitzi, R. *Liebigs Ann. Chem.* **1989**, 1215.

(29) Wipf, P.; Graham, T. H. *Org. Biomol. Chem.* **2005**, *3*, 31.

(30) Arterburn, J. B.; Perry, M. C. *Tetrahedron Lett.* **1996**, *37*, 7941.

(31) Plietker, B. In *Science of Synthesis*, Vol. 25; Brückner, R., Ed.; Georg Thieme Verlag: Stuttgart, **2006**, 151.

(32) Komatsu, N.; Taniguchi, A.; Wada, S.; Suzuki, H. *Adv. Synth. Catal.* **2001**, *343*, 473.

(33) Meng, D.; Bertinato, P.; Balog, A.; Su, D.-S.; Kamenecka, T.; Sorensen, E. J.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1997**, *119*, 10073.

(34) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.