Enantio- and Diastereoselective Synthesis of (Protected) 2-Formyl- and 2-(Hydroxymethyl)-1-phenylalkane-1,3-diols from Chiral 2-Methoxy-3-tosyl-1,3-oxazolidines by Subsequent Asymmetric Formylation and Aldolization

Frank Steif, Birgit Wibbeling,[#] Oliver Meyer,[#] Dieter Hoppe*

Institut für Organische Chemie der Westfälischen Wilhelms-Universität Münster, Corrensstraße 40, D-48149 Münster, Germany
Fax +49(251)8339772

Received 5 January 2000

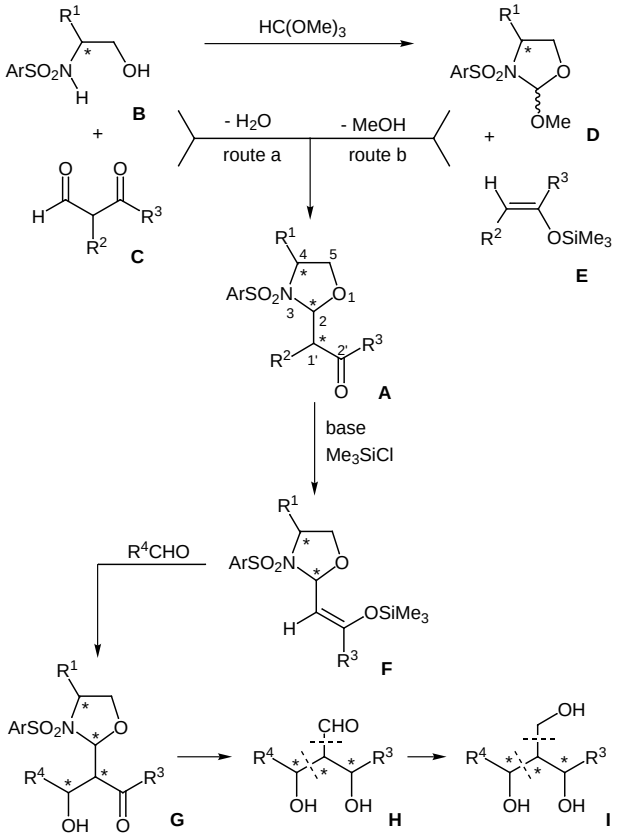
Abstract: Trimethylsilyl enol ethers are successively converted into chirally protected α-formyl ketones by asymmetric formylation with the 2-methoxy-1,3-oxazolidine **2**, transformed into the corresponding, thermodynamically determined (*Z*)-TMS enol ethers, and then are allowed to condense with aldehydes. All steps proceed with high stereoselectivity. Some synthetic options, arising from the three differentiated oxygen functionalities in the intermediates **8** are illustrated for the title target compounds.

Key words: chiral 3-arensulfonyl-1,3-oxazolidines, asymmetric formylation, diastereoselective aldolization, titanium enolates, chiral alkane-1,3-diols, ketones, chiral auxiliaries

Introduction

N-Arenesulfonyl-1,3-oxazolidines, derived from enantiomerically pure 1,2-amino alcohols, proved to be valuable templates for asymmetric synthesis. In particular, prochiral groups attached to the 2-position are attacked by nucleophiles or electrophiles with high diastereofacial selectivity.[1–6] Although diastereomerically enriched 2-(2-oxoalkyl)- or 2-(2-oxocycloalkyl)-1,3-oxazolidines **A** can be prepared from the corresponding β-keto aldehydes **C** and optically active *N*-arenesulfonyl-2-aminoalkan-1-ols **B**[1a,7], a more versatile route comprises the Lewis acid-catalyzed condensation of silyl enol ethers **E** with 2-methoxy-1,3-oxazolidines **D**, readily prepared from **B** (Scheme 1).[8,2g]

Route b is equivalent to an electrophilic formylation under the influence of the chiral auxiliary **B**, creating one (for R^2 = H) or two new stereogenic centers (for $R^2 \neq$ H) in **A** with high diastereoselectivity.[8] Under Lewis acid catalysis, equilibration of oxazolidines may take place giving rise to the 2,4-*cis*-disubstituted 1,3-oxazolidines in large excess (>98:2).[8e] In this study, we investigated the utilization of trimethylsilyl enol ethers **F**, derived from the oxazolidinyl-substituted ketones (**A**, R^1 = H), in aldol reactions of the Mukaiyama-type[9] to form hydroxy ketones **G**. Removal of the chiral auxiliary to form a protected or unprotected formyl group of **H** and the diastereoselective reduction to form triols **I** is possible by several means.[1,2]

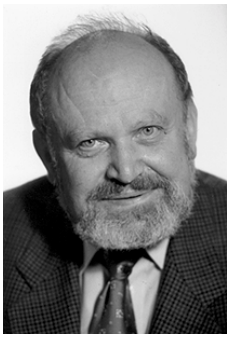


Scheme 1

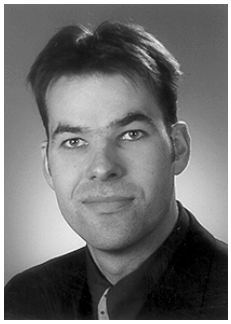
Results and Discussion

(*R*)-*N*-Tosyl-2-aminobutan-1-ol **(1)**[10] is smoothly condensed with trimethyl orthoformate to yield the cyclic amino acetal **2**[8e] in a *cis*/*trans* ratio of 86:14 (Scheme 2). It is usually utilized as a diastereoisomeric mixture in the following Lewis acid-catalyzed step, since a C-2 carbenium ion is the intermediate and the configuration of the precursor at C-2 has no influence on the product composition.[8e,f] The zinc dichloride-mediated condensation with the (*Z*)-trimethylsilyl enol ethers **3a**–**c** gave the *cis*-oxazolidines **4a**–**c** as single diastereoisomers (Table 1). Remarkably, also **4c**, which bears an additional stereogenic center in the side-chain is stereochemically homoge-

Biographical Sketches



Dieter Hoppe, born in 1941 in Berlin, worked as a chemically trained laboratory technician in Hannover before beginning his chemistry studies at the University of Göttingen in 1965. He received his doctorate in 1970 with U. Schöllkopf, submitting a dissertation on metalated isonitriles and completed his habilitation there in 1977 with a topic in the area of β-lactam chemistry. From 1977 to 1978 he was a postdoctoral fellow with R. B. Woodward at Harvard University in Cambridge (Massachusetts). After serving as a Privatdozent at the University of Göttingen he accepted a call to a C-4 professorship at the University of Kiel in 1985. Later, he followed a call to the University of Münster (1992), after he had declined a call to Hamburg (1991). His work was recognized in 1993 with an Otto-Bayer Award and in 1999 with a "Max-Planck Award for International Cooperation". He has been a coeditor of SYNTHESIS since 1988 and will retire from this duty during 2000. His areas of research relate to the development of stereoselective and especially enantioselective synthetic methods. The "(–)-sparteine method" for the generation of diverse chiral organolithium compounds is one of his major achievements.

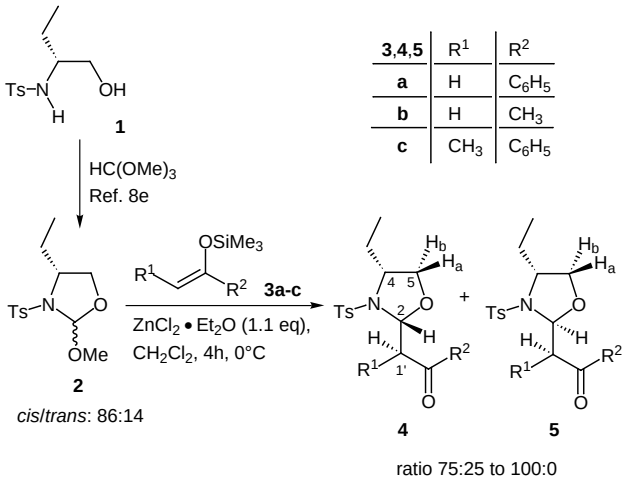


Frank Steif, born in 1970 in Oelde (Westfalia), began his studies in 1991 in Münster, and joined the research group of D. Hoppe in 1995. In 1996, he finished his diploma thesis. The topic of his dissertation, completed in 1999, is the application of enantiomerically pure *N*-tosyl-1,3-oxazolidines in stereoselective synthesis.

Birgit Wibbeling, born in 1958, got her education as a chemical-technical assistant in Bückeburg and started working at the Organisch-Chemisches Institut in Münster in 1979. First working more preparatively, she joined the X-ray laboratory in 1994 as a technician. Her main topics are crystal preparation, data collection, and routine structure analysis.

Oliver Meyer, born in 1971, studied chemistry in Münster and finished his diploma thesis on dihalocarbene addition to vinyl fluorides in 1997. He is currently completing his doctorate on the stereoselective cyclopropanation of vinyl fluorides under the supervision of Professor G. Haufe. Since 1997 he is working as an assistant for the X-ray crystallography department at the Institute of Organic Chemistry.

neous,[11] indicating that **3c** had been attacked exclusively onto the *Si*-face. The relative configuration *unlike*[12] (*u*,2*R*,1′*S*) in **4c** is concluded from the coupling constant $J_{2,1'}$ of 8.1 Hz in the ^{1}H NMR spectrum; as we have found in many examples, $J_{2,1'}$ in *u*-ketones is between 8 and 9 Hz, whereas the *l*-diastereomers exhibit 4−5 Hz.[13]



3,4,5	R^1	R^2
a	H	C_6H_5
b	H	CH_3
c	CH_3	C_6H_5

Scheme 2

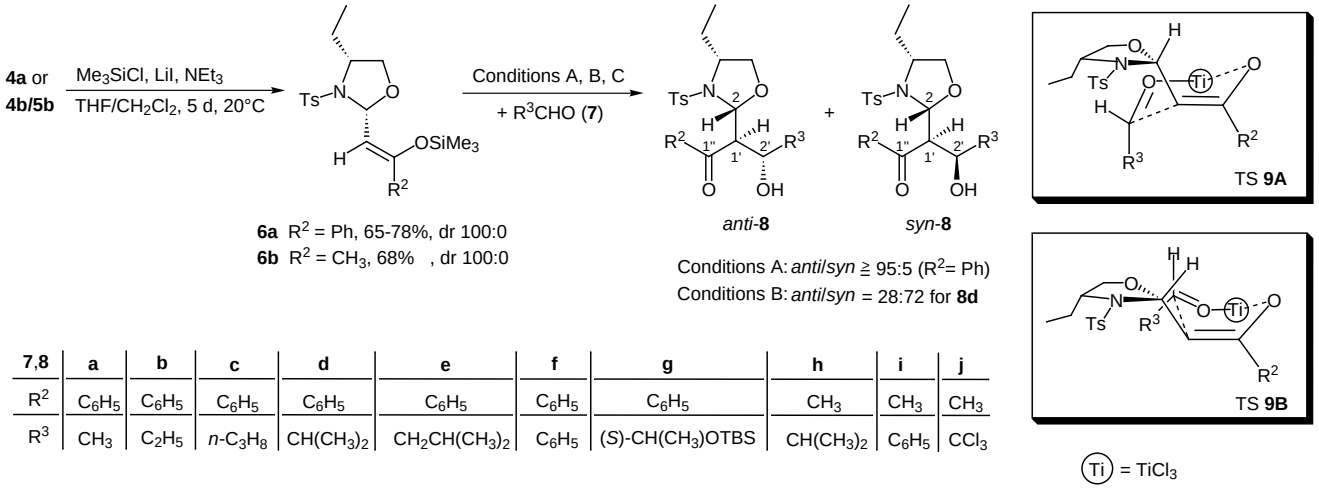
Ketones **4a** and **4b**/**5b** (75:25) were smoothly converted into the diastereomerically pure (*Z*)-silyl enol ethers **6a** or **6b**, respectively (Table 1), by applying Cazeau's conditions[14] for thermodynamically controlled enolization (Scheme 3). The expected (*Z*)-configuration was established by NOE in the ^{1}H NMR spectra. Fortunately, also from the *cis*-*trans* mixture **4b**/**5b**, only the *cis*-isomer **6b** was isolated (Table 1). Most probably, equilibration from 2,4-*trans* to the thermodynamically favoured 2,4-*cis* isomer is here a very facile process since the electron-donating power of the β-oxyvinyl group supports the formation of a ring-opened cationic intermediate.[15] We were unable to convert **4c** under these conditions into the corresponding trisubstituted TMS enol ether **6c**.

Several attempts to perform aldol additions of **4a,b** with aldehydes under Mukaiyama conditions failed.[9] Finally, the following procedure (Conditions A) turned out to be successful: To a solution of **4a,b** in dichloromethane, titanium(IV) tetrachloride was added at −78°C. The solution was allowed to warm to 0°C (light red colour) before the aldehyde **7** was added in five-fold excess to the reaction mixture. After aqueous workup, mixtures of *syn*/*anti*-aldols **8** with large excess of *anti*-**8** were isolated (Table 2). The pure diastereoisomers *anti*-**8a**−**j** were obtained by

Table 1 Compounds **4**−**6** Prepared

Substrates	R^1	R^2	Product[a]	Yield (%)	Ratio (dr)	mp (°C) (Et_2O)	$[\alpha]_D^{20}$ (*c*, CH_2Cl_2)	Configuration
2 + **3a**	H	C_6H_5	**4a**	85	>98:<2	182	+ 67.9 (1.13)	2*R*,4*R*
2 + **3b**	H	CH_3	**4b**	60[b]	75:25	oil	+ 13.0 (1.11)	2*R*,4*R*
	H	CH_3	**5b**	20[c]	–	oil	– 56.3 (1.08)	2*S*,4*R*
2 + **3c**	CH_3	C_6H_5	**4c**	85	>98:<2	113	+ 22.3 (1.09)	2*R*,2(1*S*),4*R*
2 + **4a**	H	C_6H_5	**6a**	65−78	>98:<2	138	+163.8 (0.98)	2(1*Z*),2*R*,4*R*
2 + **4b**/**5b**	H	CH_3	**6b**	68	>98:<2	oil	+ 89.6 (1.05)	2(1*Z*),2*R*,4*R*

[a] Satisfactory microanalyses obtained: C, H, N ± 0.4.
[b] Less polar diastereoisomer on silica gel.
[c] More polar diastereoisomer on silica gel.



7,8	a	b	c	d	e	f	g	h	i	j
R^2	C_6H_5	C_6H_5	C_6H_5	C_6H_5	C_6H_5	C_6H_5	C_6H_5	CH_3	CH_3	CH_3
R^3	CH_3	C_2H_5	*n*-C_3H_8	$CH(CH_3)_2$	$CH_2CH(CH_3)_2$	C_6H_5	(*S*)-$CH(CH_3)OTBS$	$CH(CH_3)_2$	C_6H_5	CCl_3

Reagents and conditions:
Conditions A: i) $TiCl_4$, −78°C, CH_2Cl_2; ii) **7a**−**g**, **7j**, 24 h, 0°C
Conditions B: i) $TiCl_4$, 20°C, CH_2Cl_2; ii) **7d**, 6 h, 20°C
Conditions C: i) $TiCl_4$, −78°C, CH_2Cl_2; ii) **7h,i**, $Ti(OPr\text{-}i)_4$, 24 h, 0°C
Scheme 3

flash chromatographic separation. The α-methyl silyl enol ether **4b**, under Conditions A, could be brought to condensation only with chloral (**7j**) (Table 2, Entry 11). The X-ray crystal structure[16] of the major diastereoisomer *anti*-**8d** (Figure 1) gives evidence for the correct stereochemical assignment.

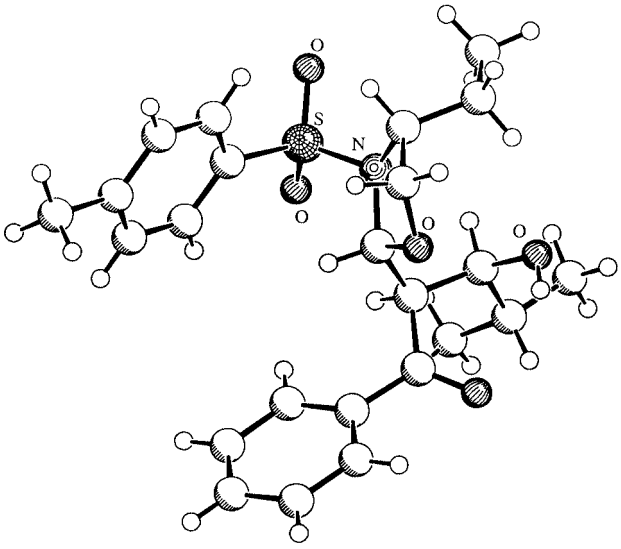


Figure 1 X-ray structure of *anti*-**8d**[16]

We assume that the aldol addition proceeds through intermediate titanium enolates.[17] Two cyclic transition states with the topicity *Si,Re*[18] lead to the observed configuration of the major diastereoisomers *anti*-**8**: TS **9A** has a chair-like topology, placing R^3 into a pseudoaxial position. Alternatively, a twist-boat TS **9B** with pseudoequatorial R^3 has to be discussed. Although few precedences for titanium-mediated *anti*-diastereoselective aldol reactions are known,[19] studies with stereodefined titanium ketone enolates are too scarce to give preference to one of these two pathways.[20]

Cyclic transition states (TS **9A** and TS **9B**) are considered to be typical for titanium enolates. Usually, Mukaiyama reactions, which are triggered by the activation of the carbonyl component, proceed through an open-chain transition state to give predominantly *syn*-aldols.[9]

A control experiment under Conditions B which supports the open-chain reaction path was performed with **4a** and 2-methylpropanal **(7d)** by mixing **4a**, $TiCl_4$ and **7d** in CH_2Cl_2 and keeping the solution at room temperature: *anti*-**8c** and *syn*-**8c** were isolated in a ratio of 28:72 (Table 2, Entry 5). The aldol reaction can be coupled also with efficient diastereofacial selectivity at the carbonyl group: **4a** furnished with (*S*)-*O*-TBS-lactaldehyde[21] **(7g)** the stereohomogeneous adduct *anti*-**8g** (Table 2, Entry 8).

For less reactive carbonyl compounds, addition of titanium tetra(isopropoxide) to the solution of the intermediate titanium enolate was required (Conditions C, Table 2, Entries 9–11). We assume that the effect of this additive is to slow down decomposition reactions. *syn*-**8** was produced in slight excess, giving evidence for an open-chain reaction mechanism to proceed. It is evident from the following arguments, that the second diastereoisomers *syn*-**8** differ from *anti*-**8** in the configuration at C-2' and not at C-1':

Table 2 Prepared Compounds **8a–j**

Entry	Substrates	R^2	R^3	Products[a]	Yield (%)	*anti*/*syn* (Conditions)	mp (°C) (Et_2O)	$[\alpha]_D^{20}$(*c*, CH_2Cl_2)	Configuration
1	**6a + 7a**	C_6H_5	CH_3	**8a**	74	>98:<2 (A)	oil	+25.6 (1.08)	2*R*,2(1*R*,2*S*),4*R*
2	**6a + 7b**	C_6H_5	C_2H_5	**8b**	77	>98:<2 (A)	46	+23.5 (1.15)	2*R*,2(1*R*,2*S*),4*R*
3	**6a + 7c**	C_6H_5	C_3H_8	**8c**	71	>98:<2 (A)	120	+22.7 (1.02)	2*R*,2(1*R*,2*S*),4*R*
4	**6a + 7d**	C_6H_5	$CH(CH_3)_2$	*anti*-**8d**	77[b]	94:6 (A)	117[b]	+23.0 (0.98)[b]	2*R*,2(1*R*,2*S*),4*R*
5	**6a + 7d**	C_6H_5	$CH(CH_3)_2$	*anti*-**8d** + *syn*-**8d**	58[c]	28:72 (B)	–[d]	–[d]	2*R*,2(1*R*,2*S*),4*R* 2*R*,2(1*R*,2*R*),4*R*
6	**6a + 7e**	C_6H_5	$CH_2CH(CH_3)_2$	**8e**	70	>98:<2 (A)	139–141	+20.1 (1.00)	2*R*,2(1*R*,2*S*),4*R*
7	**6a + 7f**	C_6H_5	C_6H_5	*anti*-**8f** + *syn*-**8f**	79[e]	90:10 (A)	138–140[e]	+23.3 (1.02)[e]	2*R*,2(1*R*,2*R*),4*R* 2*R*,2(1*R*,2*S*),4*R*
8	**6a + 7g**	C_6H_5	$CH(CH_3)OTBS$	**8g**	63	>98:<2 (A)	oil	+25.3 (0.99)	2*R*,2(1*R*,2*R*,3*S*),4*R*
9	**6b + 7d**	CH_3	$CH(CH_3)_2$	*anti*-**8h** + *syn*-**8h**	11[f] 29[g]	26:74 (C)	oil oil	–17.4 (0.51) –21.5 (0.42)	2*R*,2(1*R*,2*S*),4*R* 2*R*,2(1*R*,2*R*),4*R*
10	**6b + 7e**	CH_3	C_6H_5	*anti*-**8i** + *syn*-**8i**	70[h]	38:62 (C)	53–58[h]	+49.2 (1.02)[h]	2*R*,2(1*R*,2*R*),4*R* 2*R*,2(1*R*,2*S*),4*R*
11	**6a + 7j**	CH_3	CCl_3	**8j**	28	>98:<2 (A)	170	–13.5 (1.01)	2*R*,2(1*R*,2*R*),4*R*

[a] Satisfactory microanalyses obtained: C, H, N± 0.4.
[b] Diastereomeric mixture of *anti*-**8d** and *syn*-**8d** (94:6), which was not separable by flash chromatography.
[c] Diastereomeric mixture of *anti*-**8d** and *syn*-**8d** (28:72), which was not separable by flash chromatography.
[d] Not determined.
[e] Diastereomeric mixture of *anti*-**8f** and *syn*-**8f** (90:10), which was not separable by flash chromatography.
[f] Less polar diastereoisomer on silica gel.
[g] More polar diastereoisomer on silica gel.
[h] Diastereomeric mixture of *anti*-**8i** and *syn*-**8i** (38:62), which was not separable by flash chromatography.

• The ^{1}H NMR coupling constants between 2-H and 1'-H both in the adducts *anti*-**8** (6.3 Hz) and *syn*-**8** (5.4 Hz) are typical for a *like* relationship.[22] Thus, the second diastereoisomers have equal configuration at C-1' and must differ at the stereocenter C-2'.

• Only one diastereoisomer is detected from the reaction of the optically active aldehyde **7g** with silyl enol ether **6a**. According to the Felkin−Anh rule[23] *Re*-attack at the carbonyl group is expected to occur preferentially, enforcing the diastereoselectivity at C-2' for *Re*-attack but diminishing it for *Si*-attack.

The aldols **8** were reduced with diisobutylaluminium hydride[24] (DIBALH) in THF at −78°C (Conditions D, Scheme 4) or lithium aluminium hydride[25] (Et_2O, 0°C; Conditions E); Conditions D provided the *anti*-1,3-diols **10** in excess, whereas Conditions E gave rise preferentially to *syn*-diols **10**. Separation of the diastereomers **10** turned out to be very facile on the stage of the acetonides *cis*- and *trans*-**12**; therefore mixtures of *syn*- and *anti*-**10** were carried through the step of **11**. Thiolysis[1] of the oxazolidines with 1,3-propanedithiol in the presence of methanesulfonic acid yielded the 1,3-dithianes *syn*-/*anti*-**11**. The relative configuration of product *anti*-**11b** was established by an X-ray crystal structure analysis[26] (Figure 2).

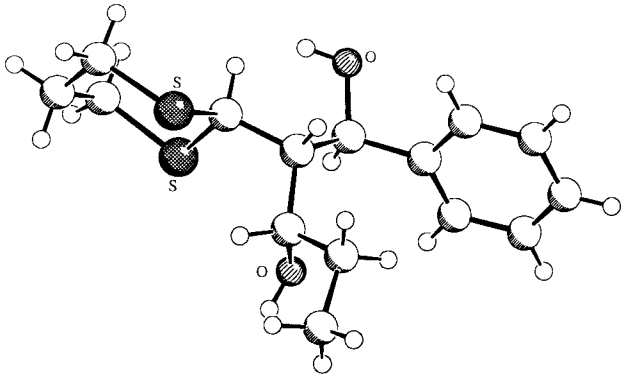
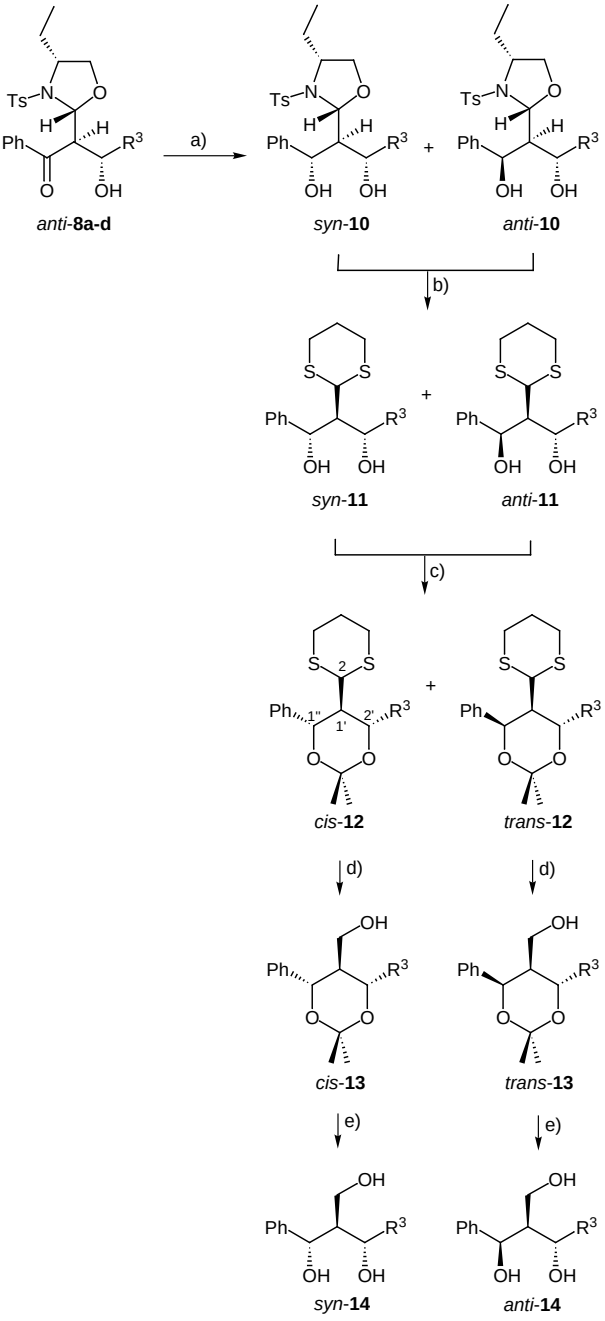


Figure 2 X-ray structure of *anti*-**11b**[26]

Diols **11** were protected by means of 2-methoxypropene/PPTS to form the acetonides *cis*- and *trans*-**12**, which could be separated by column chromatography, providing exclusively crystalline products. Deprotection of the masked formyl group was performed by the standard method[27,25b] (see step d in Scheme 4). The intermediate aldehydes were immediately reduced to give the alcohols *cis*- or *trans*-**13**. No epimerization could be detected in this step.

For any synthetic uses, many options are given, since the hydroxymethyl group in **13** can be brought selectively to the required oxidation level before further conversion.

With the conversion of some 1,3-dioxanes **13** into triols **14** (Table 3, Entries 30−36) we have demonstrated the feasability of complete deprotection.[28] Since triols **14** have a very good solubility in water, we chose a *trans*-dithioacetalization with propane-1,3-dithiol for removal of the isopropylidene bridge, since it does not require aqueous workup (Scheme 4, step e).



Reagents and conditions: a) DIBALH/THF, 24 h, −78°C (Conditions D) or $LiAlH_4/Et_2O$, 24 h, 0°C (Conditions E); b) $HS(CH_2)_3SH/CH_2Cl_2$, 7 h, 0 → 20°C; c) 2-methoxypropene, PPTS (cat.)/CH_2Cl_2, 2 h, 0°C; d) i. $CaCO_3$ (15 equiv)/CH_3I (20 equiv)/acetone/H_2O, 24 h, Δ; ii. $LiAlH_4$/THF, 2 h, 20°C; e) $HS(CH_2)_3SH/MeSO_3H$ (cat.)/CH_2Cl_2, 2 h, 0°C. For R^3, yields, and ratios, see Table 3.

Scheme 4

Table 3 Compounds **10**–**14** Prepared

Entry	Substrate	R^2	R^3	Product[a]	Yield (%)	Ratio (d.r., method)	mp (°C) (Et_2O)	$[\alpha]_D^{20}$ (*c*, CH_2Cl_2)	Configuration
1	**8a**	C_6H_5	CH_3	*anti*-**10a**	70	>98:<2 (D)	136	+92.2 (1.02)	2*R*,2(1*S*,2*S*),2{1(1*R*)},4*R*
2				*anti*-**10a** +					2*R*,2(1*S*,2*S*),2{1(1*R*)},4*R*
				syn-**10a**	72[b]	18:82 (E)	–[c]	–[c]	2*R*,2(1*S*,2*S*),2{1(1*S*)},4*R*
3	**8b**	C_6H_5	C_2H_5	*anti*-**10b**	65	>98:<2 (D)	128	+91.6 (0.72)	2*R*,2(1*S*,2*S*),2{1(1*R*)},4*R*
4				*anti*-**10b** +					2*R*,2(1*S*,2*S*),2{1(1*R*)},4*R*
				syn-**10b**	60[b]	18:82 (E)	–[c]	–[c]	2*R*,2(1*S*,2*S*),2{1(1*S*)},4*R*
5	**8d**	C_6H_5	$CH(CH_3)_2$	*anti*-**10c** + *syn*-**10c**	84[d]	91:9 (D)	155–157[d]	+93.8 (1.01)[d]	2*R*,2(1*S*,2*S*),2{1(1*R*)},4*R*
6				*anti*-**10c** +					
				syn-**10c**	62[b]	18:82 (G)	–[c]	–[c]	2*R*,2(1*S*,2*S*),2{1(1*S*)},4*R*
7	**8f**[e]	C_6H_5	C_6H_5	*anti*-**10d** +	89[f]	90:10 (D)	75	–74.1 (1.06)	2*R*,2(2*R*),2{1(1*R*)},4*R*
8				*syn*-**10d**	9[g]		191	+74.7 (0.50)	2*R*,2(1*S*,2*S*),2{1(1*R*)},4*R*
9	*anti*-**10a**	C_6H_5	CH_3	*anti*-**11a**	75	>98:<2	116	+55.6 (1.00)	1*R*,2*S*,3*S*
10	*syn*-**10a**			*anti*-**11a** +					1*R*,2*S*,3*S*
				syn-**11a**	60[b]	18:82	–[c]	–[c]	1*S*,2*S*,3*S*
11	*anti*-**10b**	C_6H_5	C_2H_5	*anti*-**11b**	79	>98:<2	92	+58.1 (1.04)	1*R*,2*S*,3*S*
12	*syn*-**10b**			*anti*-**11b** +					1*R*,2*S*,3*S*
				syn-**11b**	69[b]	18:82	–[c]	–[c]	1*S*,2*S*,3*S*
13	*anti*-**10c**	C_6H_5	$CH(CH_3)_2$	*anti*-**11c** + *syn*-**11c**	67[d]	91:9	101–103[d]	+68.2 (1.01)[d]	1*R*,2*S*,3*S*
14	*syn*-**10c**			*anti*-**11c** +		-			
				syn-**11c**	53[b]	18:82	_c	_c	1*S*,2*S*,3*S*
15	*anti*-**10d**	C_6H_5	C_6H_5	*anti*-**11d**	74	>98:<2	131	–33.7 (1.04)	1*R*,3*R*
16	*anti*-**11a**	C_6H_5	CH_3	*trans*-**12a**	92	-	114	+51.4 (1.07)	1*R*,2*S*,3*S*
17	*syn*-**11a**[b]			*cis*-**12a**	63[g]	-	136	+50.2 (1.01)	1*S*,2*S*,3*S*
18	*anti*-**11b**	C_6H_5	C_2H_5	*trans*-**12b**	87	-	124	+40.2 (0.99)	1*R*,2*S*,3*S*
19	*syn*-**11b**[b]			*cis*-**12b**	62[g]	-	150	+36.6 (1.01)	1*S*,2*S*,3*S*
20	*anti*-**11c**[d]	C_6H_5	$CH(CH_3)_2$	*trans*-**12c**	72[f]	-	155	+38.8 (1.06)	1*R*,2*S*,3*S*
21	*syn*-**11c**[b]			*cis*-**12c**	72[g]	-	126	+39.3 (1.00)	1*S*,2*S*,3*S*
22	*anti*-**11d**	C_6H_5	C_6H_5	*trans*-**12d**	88	-	189	+17.0 (1.02)	1*R*,3*R*
23	*trans*-**12a**	C_6H_5	CH_3	*trans*-**13a**	81	-	87	+100.9 (1.04)	1*R*,2*S*,3*S*
24	*cis*-**12a**			*cis*-**13a**	94	-	oil	–26.0 (0.99)	1*S*,2*S*,3*S*
25	*trans*-**12b**	C_6H_5	C_2H_5	*trans*-**13b**	81	-	63	+85.0 (1.00)	1*R*,2*S*,3*S*
26	*cis*-**12b**			*cis*-**13b**	89	-	76	–47.2 (1.03)	1*S*,2*S*,3*S*
27	*trans*-**12c**	C_6H_5	$CH(CH_3)_2$	*trans*-**13c**	73	-	48	+82.1 (1.10)	1*R*,2*S*,3*S*
28	*cis*-**12c**			*cis*-**13c**	78	-	78	–39.8 (1.08)	1*S*,2*S*,3*S*
29	*trans*-**12d**	C_6H_5	C_6H_5	*trans*-**13d**	85	-	91	–33.4 (1.01)	1*R*,3*R*
30	*trans*-**13a**	C_6H_5	CH_3	*anti*-**14a**	62	-	oil	+59.9 (0.45)	1*R*,2*S*,3*S*
31	*cis*-**13a**			*syn*-**14a**	76	-	oil	–32.5 (0.44)	1*S*,2*S*,3*S*
32	*trans*-**13b**	C_6H_5	C_2H_5	*anti*-**14b**	84	-	oil	+43.9 (1.03)	1*R*,2*S*,3*S*
33	*cis*-**13b**			*syn*-**14b**	77	-	oil	–44.5 (1.06)	1*S*,2*S*,3*S*
34	*trans*-**13c**	C_6H_5	$CH(CH_3)_2$	*anti*-**14c**	60	-	oil	+44.7 (1.12)	1*R*,2*S*,3*S*
35	*cis*-**13c**			*syn*-**14c**	60	-	oil	–40.2 (1.02)	1*S*,2*S*,3*S*
36	*trans*-**13d**	C_6H_5	C_6H_5	*anti*-**14d**	77	-	oil	–39.0 (0.97)	1*R*,3*R*

[a] Satisfactory microanalyses obtained: C, H, N ± 0.4.
[b] Diastereomeric mixture of *anti*/*syn* (18:82), which were not separable by flash chromatography.
[c] Not determined.
[d] Diastereomeric mixture of *anti*/*syn* (91:9), which were not separable by flash chromatography.
[e] Diastereomeric mixture of *anti*-**8f** and *syn*-**8f** (90:10).
[f] Less polar diastereoisomer on silica gel.
[g] More polar diastereoisomer on silica gel.

Conclusions

The strategy underlying this work, consists of the subsequent asymmetric formylation and aldolization, each with good stereocontrol, at a silyl enol ether at the same carbon atom to provide carbon chains with three consecutive stereocenters and α, β, γ-trifunctionalization. The chiral auxiliary, available in both enantiomeric forms[29] allows access to both enantiomeric series. Good flexibility is provided in the individual reaction steps, allowing the differentiation between the three functional groups. Moreover, the high crystallization tendency of *N*-sulfonyl-1,3-oxazolidines permits easy purification, diastereomer separation, and structural elucidation. It can be predicted, that many more substitution patterns than these which have

been demonstrated are easily accessible by the extension of substrates and applied reactions.

All experiments involving organometallic reagents were carried out under Ar in dried glassware. All solvents were purified by distillation and dried, if necessary, prior to use. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker WM 300 spectrometer. Optical rotations were recorded on a Perkin-Elmer polarimeter 241. Mps were obtained on Gallenkamp melting point apparatus MFB-595 and are uncorrected. Products were purified by flash column chromatography on silica gel (40-64 μm). Microanalyses were performed in the Organisch-Chemisches Institut der WWU Münster with a Perkin-Elmer Elemental Analyzer 240.

2-(2-Oxoalkyl)-1,3-oxazolidines 4a−5b; General Procedure

To a solution of (2*R*,4*R*)- and (2*S*,4*R*)-4-ethyl-2-methoxy-3-tosyl-1,3-oxazolidine **(2**; ratio 86:14; 2.85 g, 10.0 mmol) and the (*Z*)-trimethylsilyl enol ether[15] **3a−c** (11.0 mmol) in CH_2Cl_2 (30 mL) was added a 2.2 M solution of $ZnCl_2$•OEt_2 in CH_2Cl_2 (5.0 mL, 11.0 mmol) at 0°C and the mixture stirred at 0°C for 4 h. Then, sat. aq NaCl (20 mL) was added, the organic phase separated and the aqueous phase extracted with CH_2Cl_2 (3 × 15 mL). The combined CH_2Cl_2 solutions were dried (Na_2SO_4), evaporated to dryness, and the residue purified by crystallization from Et_2O (for **4a**) or by chromatography on silica gel with Et_2O/pentane (1:2 for **4c** and 1:1 for **4b**/**5b**). For yields, ratios, and data see Tables 1, 4, and 6.

β-(1,3-Oxazolidin-2-yl)alkenyl Trimethylsilyl Ethers 6a,b; General Procedure

To a stirred solution of the ketone **4a** (10.0 mmol) and anhyd LiI (400 mg, 3.00 mmol) in anhyd THF/CH_2Cl_2 (40 + 40 mL) was added Me_3SiCl (2.5 mL, 20 mmol) at ~20°C. After 30 min, Et_3N (1.7 mL, 12.0 mmol) was continuously added portionwise. The mixture was stirred for 5 d at 20°C and then carefully evaporated nearly to dryness. The crude product including Et_3N•HCl was diluted by adding CH_2Cl_2 (15 mL) and this mixture was filtered with Et_2O/pentane (1:3) through a column filled with silica gel, which had been suspended before with the same solvent. Elution of unreacted ketone **4a** was performed with EtOAc (500 mL). Best yields were achieved, when reusing the column after washing it with pentane (1 L). For yields and characterization see Tables 1, 4, and 6.

Aldols 8a−j; General Procedures

Conditions A

$TiCl_4$ (0.77 mL, 7.00 mmol) was added dropwise to a solution of silyl enol ether **6a** (3.12g, 7.00 mmol) in anhyd CH_2Cl_2 (70 mL) kept under Ar at −78°C. The solution turned to yellow in color and a red precipitate formed. After redissolution of the precipitate (15 min), the mixture was allowed to warm rapidly (within 5 min) to 0°C. Aldehyde **7** (35 mmol) was added before the reaction mixture had turned to dark red in color, and stirring was continued for 24 h at 0°C. For workup, H_2O (70 mL) was added, the mixture intensively stirred, and the phases separated (after adding sat. aq NaCl, 50 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL), the combined CH_2Cl_2 solutions dried (Na_2SO_4/$NaHCO_3$) and evaporated in vacuo. Purification of **8** was performed by recrystallization from Et_2O/pentane (1:1) for **8f** or by column chromatography (Et_2O/pentane, 1:1, 1% Et_3N, silica gel) for **8a−e**, **8g−j**. For yields, ratios, and data see Tables 2, 5, and 7.

Conditions B

$TiCl_4$ (0.05 mL, 0.46 mmol) was added dropwise to a solution of silyl enol ether **6a** (223 mg, 0.50 mmol) in anhyd CH_2Cl_2 (5 mL) kept under Ar at 20°C. The solution turned to dark red in color. Then 2-methylpropanal (**7d**; 0.23 mL, 2.52 mmol) was added and the mixture stirred at 20°C for 6 h. For workup and purification see Conditions A.

Conditions C

Silyl enol ether **6b** (2.69 g, 7.00 mmol) was treated as described in Conditions A. Ti(OPr-*i*)$_4$ (2.10 mL, 7.00 mmol) was added at 0°C before the aldehyde **7** (35 mmol). Stirring was continued for 24 h before workup was accomplished. Due to precipitation of titanium oxide hydrates, addition of H_2O (up to 800 mL) was required.

Diols 10; General Procedures

Reduction of Aldols 8 with Diisobutylaluminium Hydride (DIBALH); Conditions D

To a solution of aldol **8** (5.00 mmol) in anhyd THF (50 mL), kept under Ar at −78°C, was added dropwise a 1 M solution of DIBALH in hexane (20 mL, 20 mmol) and the mixture stirred at −78°C for 24 h. For workup, H_2O (20 mL, caution, H_2!) was carefully added and the mixture was allowed to warm to 20°C. The jelly percipitate formed was dissolved in Et_2O (50 mL) and 2 N NaOH (60 mL) with intensive stirring. The layers were separated, the aqueous phase extracted with Et_2O (3 × 100 mL, each), the combined organic solutions dried (Na_2SO_4), and evaporated in vacuo. The crude product was purified by flash chromatography (Et_2O/pentane, 1:1, silica gel). For yields, ratios and data see Tables 3, 5, and 7.

Reduction with $LiAlH_4$; Conditions E

A solution of aldol **8** (3.50 mmol) in anhyd Et_2O (30 mL) was added dropwise at 0°C to a suspension of $LiAlH_4$ (266 mg, 7.00 mmol) in Et_2O (30 mL) and the mixture stirred at 0°C for 24 h. For workup, 2 N HCl (20 mL, caution, H_2!) was carefully added, the layers were separated, the aqueous phase extracted with Et_2O (3 × 50 mL), the combined Et_2O solutions dried (Na_2SO_4/$NaHCO_3$), and evaporated in vacuo. Flash chromatography (Et_2O/pentane, 1:1, silica gel) yielded the pure diols **10**. For yields, ratios, and data see Tables 3, 5, and 7.

Table 4 Selected Spectroscopic Data of Compounds **4−6**

Product	IR (film) ν (cm^{-1})	^{1}H NMR (300 MHz, $CDCl_3$), δ, *J* (Hz)				
		2-H ($J_{2,1'}$)[a]	1'-H[a]	4-H ($J_{4,5a}$)[a]	5-H$_a$ ($J_{5a,5b}$)[a]	5-H$_b$ ($J_{4,5b}$)[a]
4b	1710, 1345, 1165	5.29 (d, 8.3)	2.85, 3.20 (dd)[b]	3.51−3.59 (m, 6.0)	3.24 (dd, 8.8)	3.64 (dd, 2.6)
4c	1665, 1335, 1150[c]	5.57 (d, 8.1)	3.78 (dq)	3.57−3.66 (m, 6.9)	3.33 (dd, 8.8)	3.51 (dd, 4.5)
5b	1710, 1345, 1165	5.50 (d, 7.9)	2.80, 3.32 (dd)[b]	3.87−3.94 (m, 6.5)	3.98 (dd, 8.3)	3.67 (dd, 3.1)
6a	1345, 1165, 845[c]	5.86 (d, 8.3)	5.22 (d)	3.75−3.81 (m, 6.2)	3.49 (dd, 8.7)	3.72 (dd, 3.1)
6b	1345, 1165, 845	5.72 (d, 8.3)	4.61 (dd)	3.58−3.67 (m, 6.2)	3.31 (dd, 8.8)	3.58−3.67 (m)

[a] d = doublet, q = quartet, m = multiplet.
[b] Diastereotopic protons.
[c] In KBr.

Table 5 Selected Spectroscopic Data of Compounds **8a–j** and **10–14**

Product	IR (KBr) ν (cm^{-1})	^{1}H NMR (300 MHz, $CDCl_3$), δ, *J* (Hz)					
		2-H[a,b] ($J_{2,1'}$)	1'-H[a,b]	2'-H[a,b] ($J_{1',2'}$)	2'-OH[a,b] ($J_{2',2'\text{-OH}}$)	1"-H[a,b] ($J_{1',1''}$)	1"-OH[a,b] ($J_{1'',1''\text{-OH}}$)
8a	3520, 1710, 1345, 1165[a]	5.48 (d, 6.2)	4.04 (dd)	4.36 (m, 2.6)	3.56–3.64 (m)	–	–
8b	3490, 1660, 1355, 1165	5.49 (d, 6.2)	4.07 (dd)	3.99–4.07 (m, 2.6)	3.55 (d, 8.6)	–	–
8c	3470, 1655, 1345, 1165	5.27 (d, 6.2)	4.04 (dd)	4.09–4.18 (m, 2.4)	3.55 (d, 8.8)	–	–
anti-**8d**	3550, 1670, 1345, 1165	5.48 (d, 6.3)	4.17 (dd)	3.70–3.78 (m, 2.1)	3.91 (d, 9.1)	–	–
syn-**8d**	3550, 1670, 1345, 1165	5.50 (d, 5.4)	4.31 (dd)	3.88 (d, 3.6)	3.46–3.59 (m)	–	–
8e	3490, 1670, 1345, 1165	5.64 (d, 6.4)	4.01 (dd)	4.24 (ddd, 2.4)	3.53 (d, 9.2)	–	–
8f	3440, 1660, 1345, 1165	5.44 (d, 6.9)	4.72 (dd)	5.22 (d, 2.9)	–[c]	–	–
8g	3430, 1690, 1335, 1165[d]	5.49 (d, 6.3)	4.26 (d)	4.80 (d)	3.93–3.98 (m)	–	–
anti-**8h**	3490, 1695, 1335, 1155[d]	5.24 (d, 5.3)	3.24 (dd)	3.88 (ddd, 4.1)	3.31 (d, 8.8)	–	–
syn-**8h**	3510, 1690, 1335, 1150[d]	5.62 (d, 8.9)	2.96 (dd)	3.75 (ddd, 3.3)	3.20 (d, 6.2)	–	–
8j	3380, 1690, 1355, 1165	5.42 (d, 8.6)	3.75 (d)	3.448 (dd, 1.2)	6.09 (d, 9.3)	–	–
anti-**10a**	3440–3320, 1335, 1155	4.60 (d, 1.2)	2.61 (m)	4.68 (dq, 1.4)	3.23 (s)	5.59 (d)	3.99 (d, 2.2)
syn-**10a**	3530–3340, 1340, 1160	5.03 (d, 6.2)	2.40 (m)	4.11 (m, 1.9)	2.85 (d, 7.4)	5.30 (t, 5.0)	3.38 (d, 4.5)
anti-**10b**	3510, 3400, 1330, 1150	4.61 (d, 0.9)	2.71 (t)	4.32 (dq, 1.2)	3.18 (d, 2.2)	5.52 (d)	4.01 (d, 2.1)
syn-**10b**	3590–3500, 1330, 1155	4.84 (d, 5.3)	2.46 (ddd)	3.87 (m, 1.7)	2.82 (d, 6.4)	5.25 (dd, 6.7)	3.35 (d, 4.5)
anti-**10c**	3510,1335, 1150	4.60 (d, 1.2)	2.94 (d)	3.94 (dd)	3.26 (d, 2.9)	5.50 (d)	4.11 (d, 2.2)
syn-**10c**	3460–3320, 1340, 1160	4.56 (d, 3.6)	2.75 (ddd)	3.67–3.71 (m, 1.7)	2.96 (d, 4.8)	5.17 (d, 8.1)	3.20 (d, 3.3)
anti-**10d**	3500–3400, 1330, 1150	5.94 (d, 9.4)	2.28 (dt)	5.74 (dd, 1.2)	3.96 (d, 5.7)	5.03 (d)	3.92 (d, 2.4)
anti-**11a**	3460–3370	4.39 (d, 2.9)	2.02 (m)	4.47 (ddq, 2.9)	2.53 (d, 4.5)	5.33 (t, 4.3)	3.63 (d, 3.8)
syn-**11a**	3600–3400	3.90 (d, 3.6)	2.07 (dq)	4.41 (dq, 1.9)	2.67–2.85 (m)	5.24 (d, 7.4)	3.36 (s)
anti-**11b**	3510–3400	4.39 (d, 3.1)	2.03 (m)	4.16–4.23 (m, 2.4)	2.58 (d, 5.0)	5.31 (t, 4.1)	3.66 (d, 3.6)
syn-**11b**	3420–3260	3.86 (d, 3.3)	2.10 (dt)	4.15–4.19 (m, 3.1)	2.65–2.89 (m)	5.25 (dd, 7.9)	3.32 (d, 1.3)
anti-**11c**	3540–3420	4.34 (d, 3.1)	2.26 (q)	3.97 (ddd, 2.2)	2.71 (d, 5.3)	5.35 (t, 3.4)	3.86 (d, 3.6)
syn-**11c**	3440–3390	3.83 (d, 3.1)	2.24 (m)	3.87–3.98 (m, 2.9)	2.55 (d, 6.2)	5.24 (dd, 8.1)	3.22 (d, 3.3)
anti-**11d**	3400–3200	4.33 (d, 3.6)	2.36 (q)	5.61 (dd, 2.6)	3.35 (d, 5.5)	5.14 (t, 3.8)	3.76 (d, 4.5)
trans-**12a**	3020, 2950, 2875	3.62 (d, 2.4)	2.20 (ddd)	4.35 (dq, 7.3)	–	5.17 (d, 5.3)	–
cis-**12a**	3050, 2970, 2880	3.91 (d, 1.4)	1.83 (dt)	4.26 (dq, 10.0)	–	4.98 (d, 10.5)	–
trans-**12b**	2960, 2910, 2870	3.63 (d, 2.4)	2.21 (m)	4.11 (dt, 7.4)	–	5.14 (d, 5.2)	–
cis-**12b**	2970, 2915, 2810	3.90 (d, 1.4)	1.90 (dt)	4.03 (ddd, 8.3)	–	4.96 (d, 10.5)	–
trans-**12c**	2965, 2915, 2870	3.66 (d, 2.4)	2.38 (ddd)	4.05 (dd, 7.2)	–	5.04 (d, 5.0)	–
cis-**12c**	3010, 2910, 2850	3.90 (d, 1.0)	1.94 (m)	3.97 (dd, 10.3)	–	4.95 (d, 10.3)	–
trans-**12d**	3015, 2965, 2870	3.68 (d, 2.4)	2.86 (ddd)	5.23 (d, 7.9)	–	5.41 (d, 5.3)	–
trans-**13a**	3220, 3010, 2970, 2870	3.30–3.48 (m)	1.98 (dq)	3.94 (dq, 7.4)	–	5.18 (d, 5.0)	–
cis-**13a**	3460–3380, 3010, 2970, 2885[d]	3.30 (dd, 5.5) 3.57 (dd, 7.2)	1.52 (m)	4.27 (dq, 10.3)	–	4.95 (d, 10.5)	–
trans-**13b**	3300–3240, 3010, 2965, 2890	3.34 (dd, 4.3) 3.45 (dd, 4.3)	2.01 (ddd)	3.73 (dt, 7.6)	–	5.17 (d, 4.8)	–
cis-**13b**	3500–3450, 3015, 2985, 2880	3.28 (d) 3.56 (dd, 2.6)	1.81 (ddt)	4.05 (dt, 10.7)	–	4.94 (d, 10.5)	–
trans-**13c**	3450–3440, 3010, 2980, 2860	3.34 (dt, 3.8) 3.45–3.52 (m)	2.08–2.14 (m)	3.61 (dd, 7.0)	–	5.12 (d, 4.5)	–
cis-**13c**	3470, 3010, 2980, 2900	3.27 (dt, 2.9) 3.55 (dt, 3.1)	1.65 (tt)	3.99 (dd, 10.5)	–	4.92 (d, 10.5)	–
trans-**13d**	3560, 3010, 2965, 2890	3.38–3.49 (m)	1.30 (dd)	4.90 (d, 7.9)	–	5.41 (d, 5.4)	–
anti-**14a**	3400–3240, 3010, 2950	3.62, 3.82 (d)	1.66 (m)	4.18 (qu, 5.9)	3.24 (s)	5.23 (t, 3.5)	4.02 (d,3.8)
syn-**14a**	3400–3240, 3010, 2950	3.41–3.46(m) 3.54 (dt, 3.6)	1.91–1.96 (m)	4.19 (m, 12.3)	3.41–3.46 (m)	4.91 (d, 8.29	3.61 (s)
anti-**14b**	3360–3240, 3005, 2870	3,62 (dd, 4.2) 3.84 (dd, 4.7)	1.58–1.77 (m)	3.95 (q, 4.5)	–[c]	5.27 (d, 3.3)	–[c]
syn-**14b**	3460–3380, 3010, 2970	3.45 (dd, 4.7) 3.56 (dd, 4.7)	1.99 (dt)	3.89 (ddd, 5.8)	–[c]	4.95 (d, 7.6)	–[c]
anti-**14c**	3400–3300, 3005, 2940	3.60–3.67 (m) 3.78–3.91 (m)	1.86 (ddd)	3.78–3.91 (m, 4.2)	2.90 (d, 5.3)	5.40 (t, 2.4)	3.78–3.91 (m)
syn-**14c**	3420–3340, 3005, 2940	3.42 (dd, 3.0) 3.61 (dd, 4.4)	2.04 (tt)	3.71 (t, 5.3)	1.84 (s)	5.11 (d, 7.1)	2.85 (s)
anti-**14d**	3510, 3010, 2980, 2880	3.37 (m, 3.1) 3.72 (dt, 4.3)	1.97 (m)	5.18 (m, 6.4)	3.64 (d, 3.6)	5.18 (m, 4.5)	3.93 (d, 4.3)

[a] For **13** and **14** the numbering does not follow the IUPAC nomenclature.
[b] s = singlet, d = doublet, t = triplet, q = quartet, qu = quintet, m = multiplet.
[c] Not detected.
[d] Film.

Table 6 Selected ^{13}C NMR Data of Compounds **4**–**6**

Product	^{13}C NMR (75 MHz, $CDCl_3$), δ		
	C-2	C-1'	C-2'
4b	88.33	50.61	204.88
4c	94.21	45.63	201.24
5b	87.23	47.45	204.58
6a	87.21	108.57	154.43
6b	86.94	106.99	153.00

Table 7 Selected ^{13}C NMR Data of Compounds **8a–j** and **10**–**14**

Product	^{13}C NMR (75 MHz, $CDCl_3$), δ			
	C-2[a]	C-1"[a]	C-2"[a]	C-1"'[a]
8a	91.57	55.77	66.52	201.81
8b	91.62	54.26	72.21	202.18
8c	91.62	54.52	70.32	202.24
anti-**8d**	92.49	51.49	76.49	202.86
syn-**8d**	93.23	51.58	77.64	201.64
8e	91.66	54.70	68.70	202.35
8f	91.78	56.93	73.48	199.84
8g	91.74	47.60	72.16	202.44
anti-**8h**	91.64	58.75	76.36	208.44
syn-**8h**	91.34	60.21	75.19	208.05
8j	90.62	52.83	83.97	211.81
anti-**10a**	92.10	51.67	66.52	70.81
syn-**10a**	92.88	53.31	66.25	72.41
anti-**10b**	92.19	49.94	71.20	72.22
syn-**10b**	93.10	52.00	72.17	72.89
anti-**10c**	92.33	47.75	71.48	76.44
syn-**10c**	93.38	49.14	73.54	76.05
anti-**10d**	91.08	54.66	73.61	69.42
anti-**11a**	55.97	47.85	67.87	72.52
syn-**11a**	55.92	50.45	69.54	74.03
anti-**11b**	54.15	47.98	72.61	73.79
syn-**11b**	54.28	50.69	73.54	73.74
anti-**11c**	51.00	48.16	72.80	77.88
syn-**11c**	51.82	51.25	73.64	77.43
anti-**11d**	56.85	47.61	72.14	73.90
trans-**12a**	54.21	49.17	65.52	71.00
cis-**12a**	52.39	48.20	67.41	74.19
trans-**12b**	52.00	49.44	70.54	71.24
cis-**12b**	49.92	48.98	72.18	74.28
trans-**12c**	49.85	49.41	71.61	72.89
cis-**12c**	49.12	47.26	74.30	74.46
trans-**12d**	53.19	49.82	71.62	72.16
trans-**13a**	61.24	51.08	66.27	69.70
cis-**13a**	59.48	49.85	66.40	73.52
trans-**13b**	61.40	49.24	70.05	71.18
cis-**13b**	59.34	47.34	70.90	73.63
trans-**13c**	61.95	46.73	70.65	73.59
cis-**13c**	59.24	45.05	73.22	73.92
trans-**13d**	60.65	51.13	70.31	71.94
anti-**14a**	61.09	52.07	67.73	73.43
syn-**14a**	61.87	52.76	69.21	75.64
anti-**14b**	61.29	50.03	73.33	73.81
syn-**14b**	62.44	51.11	74.59	75.29
anti-**14c**	61.31	47.17	73.24	77.80
syn-**14c**	62.28	47.99	76.00	78.79
anti-**14d**	60.32	52.80	72.88	73.93

[a] For **13** and **14** the numbering does not follow the IUPAC nomenclature.

β-(1,3-Dithian-2-yl)-α,γ-alkanediols 11; General Procedure

To a solution of oxazolidine **10** (3.00 mmol) in anhyd CH_2Cl_2 (30 mL) at 0°C were added propane-1,3-dithiol (1.36 mL, 13.5 mmol) and $MeSO_3H$ (0.19 mL, 3.00 mmol) and this mixture was stirred for 7 h. During this time, the temperature was allowed to rise to 20°C. For workup, solid powdered K_2CO_3 (620 mg, 4.5 mmol) was added, after 10 min stirring the solids were filtered off, the solvent evaporated, and the residue purified by column chromatography on silica gel with Et_2O/pentane (1:1). For yields, dr's, and data of **11** see Tables 3, 5, and 7.

5-(1,3-Dithian-2-yl)-1,3-dioxanes 12; General Procedure

A solution of diol **11** (2.00 mmol), pyridinium tosylate (PPTS, 151 mg, 0.60 mmol), and 2-methoxypropene (0.42 mL, 4.40 mmol) in anhyd CH_2Cl_2 (25 mL) was stirred for 2 h at 0°C. Sat. aq NaCl (20 mL) was added, the aqueous phase extracted with CH_2Cl_2 (3 × 20 mL, each). After drying (Na_2SO_4) and evaporation of the solvent, the acetonide **12** was purified by LC (Et_2O/pentane, 1:12, silica gel). Diastereomeric mixtures of *cis*- and *trans*-**12** could be separated by column chromatography. For yields and data see Tables 3, 5, and 7.

5-(Hydroxymethyl)-1,3-dioxanes *cis*- and *trans*-13; General Procedure

To a well-stirred mixture of acetonide **12** (1.00 mmol) and $CaCO_3$ (1.50 g, 15.0 mmol) in acetone/H_2O (8 + 1 mL) was added MeI (1.24 mL, 20.0 mmol). The mixture was refluxed for 24 h before $MgSO_4$ (approx. 0.5 g) was added for removal of H_2O. The solids were filtered off, the solvent evaporated, and the residue dissolved in THF (10 mL). This solution was added dropwise to a suspension of $LiAlH_4$ (190 mg, 5.00 mmol) in anhyd THF (15 mL) and stirring was continued for 3 h. After diluting the mixture with Et_2O (10 mL), successively H_2O (0.19 mL; caution, H_2!), 15% aq NaOH solution (0.19 mL), and H_2O (0.57 mL) were added. After addition of $MgSO_4$ (~0.5 g), the solids were filtered off, and the solution concentrated in vacuo. Purification was accomplished by column chromatography (Et_2O/pentane, 1:2, silica gel). For yields and data see Tables 3, 5, and 7.

Triols 14; General Procedure

A solution of acetonide **13** (1.00 mmol), propane-1,3-dithiol (0.30 mL, 3.00 mmol) and $MeSO_3H$ (2 drops) in CH_2Cl_2 (5 mL) was stirred for 4 h at 0°C. Solid K_2CO_3 (200 mg, 1.45 mmol) was added and stirring was continued for 10 min before the solids were filtered off and the solution was concentrated in vacuo. Column chromatography with Et_2O on silica gel yielded the triols **14** as colorless viscous oils. For obtainig analytically pure samples, drying at 0.1 mbar was essential. For yields and data see Tables 3, 5, and 7.

Acknowledgement

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

References

[#] X-Ray structure analyses.

(1) First reports:
(a) Hoppe, I.; Hoppe, D.; Wolff, C.; Egert, E.; Herbst, R. *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 67.
(b) Scolastico, C. *Pure Appl. Chem.* **1988**, *60*, 1689.

(2) (a) Hoppe, I.; Hoppe, D.; Herbst-Irmer, R.; Egert, E. *Tetrahedron Lett.* **1990**, *31*, 6859.
(b) Pasquarello, A.; Poli, G.; Scolastico, C. *Synlett* **1992**, 93.
(c) Hoffmann, H.; Bolte, M.; Berger, B.; Hoppe, D. *Tetrahedron Lett.* **1993**, *34*, 6537.

(d) Conde-Frieboes, K.; Harder, T.; Aulbert, D.; Strahringer, C.; Bolte, M.; Hoppe, D. *Synlett* **1993**, 921.
(e) Harder, T.; Löhl, T.; Bolte, M.; Wagner, K.; Hoppe, D. *Tetrahedron Lett.* **1994**, *35*, 7365.
(f) Prien, O.; Hoffmann, H.; Conde-Frieboes, K.; Krettek, T.; Berger, B.; Wagner, K.; Bolte, M.; Hoppe, D. *Synthesis* **1994**, 1313.
(g) Colombo, L.; Di Giacomo, M.; Brusotti, G.; Delogu, G. *Tetrahedron Lett.* **1994**, *35*, 2063.
(h) Poli, G.; Maccagni, E.; Manzoni, L.; Pilati, T.; Scolastico, C. *Synlett* **1995**, 71.
Winter, E.; Hoppe, D. *Tetrahedron* **1998**, *56*, 10329.

(3) For similiar uses of *N*-Boc-1,3-oxazolidines see:
(a) Agami, C.; Couty, F.; Lequesne, C. *Tetrahedron Lett.* **1994**, *35*, 3309.
(b) Colombo, L.; Di Giacomo, M. *Tetrahedron Lett.* **1999**, *40*, 1977; and references cited therein.

(4) Application of *N*-unsubstituted or alkyl-substituted 1,3-oxazolidines:
(a) Ukaji, Y.; Yamamoto, K.; Fukui, M.; Fujisawa, T. *Tetrahedron Lett.* **1991**, *32*, 2919.
(b) Mokhallalati, M. K.; Muralidharan, K. R.; Pridgen, L. N. *Tetrahedron Lett.* **1994**, *35*, 4267.
(c) Kanemasa, S.; Suenaga, H.; Onimura, K. *J. Org. Chem.* **1994**, *59*, 6949.

(5) For the use of chiral bicyclic 1,3-oxazolidines, see:
(a) Review: Romo, D.; Meyers, A. I. *Tetrahedron* **1991**, *47*, 9503.
(b) Leading reference to more recent work of A. I. Meyers et al.: Meyers, A. I.; Seefeld, M. A.; Lefker, B. A.; Blake, J. F.; Willard, P. G. *J. Am. Chem. Soc.* **1998**, *120*, 7429.
(c) Review: Ager, D. J.; Prakash, I.; Schaad, D. *Chem. Rev.* **1996**, *96*, 835.
(d) Leading reference to the work of H.-P. Husson et al.: François, D.; Lallemand, M.-C.; Selkti, M.; Tomas, A.; Kunesch, N.; Husson, H.-P. *J. Org. Chem.* **1997**, *62*, 8914.

(6) For related work with chiral 1,3-imidazolidines, see:
(a) Alexakis, A.; Sedrani, R.; Normant, J. F.; Mangeney, P. *Tetrahedron Asymmetry* **1990**, *1*, 283.
(b) Review: Alexakis, A.; Mangeney, P.; Jensen, N.; Tranchier, J.-P.; Gosmini, R.; Raussou, S. *Pure Appl. Chem.* **1996**, *68*, 531.

(7) Hoppe, I.; Hoffmann, H.; Gärtner, I.; Krettek, T.; Hoppe, D. *Synthesis* **1991**, 1157.

(8) (a) Conde-Frieboes, K.; Hoppe, D. *Synlett* **1990**, 99.
(b) Bernardi, A.; Cardani, S.; Carugo, O.; Colombo, L.; Scolastico, C.; Villa, R. *Tetrahedron Lett.* **1990**, *31*, 2779.
(c) Bernardi, A.; Piarulli, U.; Poli, G.; Scolastico, C.; Villa, R. *Bull. Soc. Chim. Fr.* **1990**, *127*, 751.
(d) Bernardi, A.; Cavicchioli, M.; Poli, G.; Scolastico, C.; Sidjimov, A. *Tetrahedron* **1991**, *47*, 7925.
(e) Conde-Frieboes, K.; Hoppe, D.; *Tetrahedron* **1992**, *48*, 6011.
(f) Bernardi, A.; Cardani, S.; Poli, G.; Potenza, D.; Scolastico, C. *Tetrahedron* **1992**, *48*, 1343.

(9) Reviews:
(a) Mukaiyama, T. *Org. React.* **1982**, *28*, 203.
(b) Mukaiyama, T. *Org. React.* **1994**, *46*, 1.
(c) Mukaiyama, T. *Aldrichim. Acta* **1996**, *29*, 59.

(10) Wilkinson, R. G.; Shepherd, R. G.; Thomas, J. P.; Baughn, C. *J. Am. Chem. Soc.* **1961**, *83*, 2212.

(11) For a similiar result with appropriate lithium and cesium enolates, see Ref. 2f.

(12) For *like* and *unlike* notation see:
Seebach, D.; Prelog, V. (see p. 4) *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 654.

(13) See Refs 7,8 for example.

(14) Cazeau, P.; Duboudin, F.; Moulines, F.; Babot, O.; Dunogues, J. *Tetrahedron* **1987**, *43*, 2075.

(15) Examples for Lewis acid-catalyzed epimerization, see Refs 7,8.

(16) X-ray crystal structure analysis of *anti*-**8d**: formula $C_{24}H_{31}NO_5S$, *M* = 445.56, colourless crystal 0.40 × 0.25 × 0.10 mm, *a* = 10.327(1), *b* = 10.918(1), *c* = 10.457(2) Å,β = 91.72(1)°, *V* = 1178.5(3) Å^3, ρ_{calc} = 1.256 g cm^{-3}, μ = 15.00 cm^{-1}, empirical absorption correction via ψ scan data (0.931 _*C* _ 0.999), *Z* = 2, monoclinic, space group $P2_1$ (No. 14), λ = 1.54178 Å, *T* = 223 K, ω/2θ scans, 2773 reflections collected (±*h*, ±*k*, −*l*), [(sinθ)/λ] = 0.62 Å^{-1}, 2619 independent and 2425 observed reflections [*I* _ 2 σ(*I*)], 286 refined parameters, *R* = 0.039, wR^2 = 0.103, max. residual electron density 0.33 (−0.27) e Å^{-3}, Flack parameter 0.00(2), hydrogens calculated and riding.

(17) (a) Review: Reetz, M. T. *Organotitanium Reagents in Organic Synthesis*; Springer: Berlin Heidelberg 1986; pp 149−162.
(b) Review: Weidmann, B.; Seebach, D. *Angew. Chem. Int. Ed. Engl.* **1983**, *22*,37.
c) Review: Mahrwald, R. *Chem. Rev.* **1999**, *99*, 1095.
(d) Reetz, M. T.; Peter, R. *Tetrahedron Lett.* **1981**, *22*, 4691.

(18) Note, that - compared to "ordinary" silyl enol ethers - the CIP-assignment is inverted due to the high priority of the oxazolidine residue.

(19) (a) Duthaler, R. O.; Herold, P.; Wyler-Helfer, S.; Riedicker, M. *Helv. Chim. Acta* **1990**, *73*, 659.
(b) Kanemasa, S.; Mori, T.; Tatsukawa, A. *Tetrahedron Lett.* **1993**, *34*, 8293.
(c) Solladié-Cavallo, A.; Koessler, J. L. *J. Org. Chem.* **1994**, *59*, 3240.
(d) Ghosh, A. K.; Onishi, M. *J. Am. Chem. Soc.* **1996**, *118*, 2527.

(20) (a) Evans, D. A.; Rieger, D. L.; Bilodeau, M. T.; Urpí, F. *J. Am. Chem. Soc.* **1991**, *113*, 1047.
(b) Yoshida, Y.; Matsumoto, N.; Hamasaki, R.; Tanabe, Y. *Tetrahedron Lett.* **1999**, *40*, 4227.
(c) Esteve, C.; Ferreró, M.; Romea, P.; Urpí, F.; Vilarrasa, J. *Tetrahedron Lett.* **1999**, *40*, 5083.

(21) Massad, S. K.; Hawkins, L. D.; Baker, D. C. *J. Org. Chem.* **1983**, *48*, 5180.

(22) The appropriate *unlike* diastereoisomers (2*R*,1'*S* or 2*S*,1'*R*) exhibit *J* = 8.0−9.0 Hz.

(23) (a) Felkin, H.; Cherest, M.; Prudent, N. *Tetrahedron Lett.* **1968**, *18*, 2199.
(b) Anh, N. T. *Top. Curr. Chem.* **1980**, *88*, 145.

(24) (a) Review: Winterfeldt, E. *Synthesis* **1975**, 617.
(b) Kiyooka, S.; Kuroda, H.; Shimasaki, Y. *Tetrahedron Lett.* **1986**, *26*, 3009.

(25) (a) Review: Gaylord, N. G. *J. Chem. Ed.* **1957**, *34*, 367.
(b) Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*, Vol. 1; Wiley: New York 1967; pp 581−595.

(26) X-ray crystal structure analysis of *anti*-**11b**: formula $C_{15}H_{22}O_2S_2$, *M* = 298.45, colourless crystal 0.40 × 0.35 × 0.20 mm, *a* = 8.847(2), *b* = 8.621(2), *c* = 10.871(2) Å, β = 109.63(1)°, *V* = 780.9(3) Å^3, ρ_{calc} = 1.269 g cm^{-3},μ = 30.50 cm^{-1}, empirical absorption correction via ψ scan data (0.975 _*C* _ 0.999), *Z* = 2, monoclinic, space group $P2_1$ (No. 4), λ = 1.54178 Å, *T* = 223 K, ω/2θ scans, 1782 reflections collected (±*h*, +*k*, +*l*), [(sinθ)/λ] = 0.62 Å^{-1}, 1696 independent and 1688 observed reflections [*I* _ 2 σ(*I*)], 176 refined parameters, *R* = 0.041, wR^2 = 0.109, max. residual electron density 0.62 (−0.48) e Å^{-3}, Flack parameter 0.04(2), hydrogens calculated and riding. Data sets were collected with an Enraf Nonius CAD4 diffractometer. Programs used: data reduction MolEN,

structure solution SHELXS-97, structure refinement SHELXL-97, graphics SCHAKAL-92. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CSD-138306 (*anti*-**8d**) and CSD-138307 (*anti*-**11b**). Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: int. Code +44(1223)336033, e-mail: deposit@ccdc.cam.ac.uk].

(27) (a) Fetizon, M.; Jurion, M. *J. Chem. Soc., Chem. Commun.* **1972**, 382.
(b) Wang Chang, H. L. *Tetrahedron Lett.* **1972**, *19*, 1989.

(28) For the synhesis of related triols see:
(a) Seebach, D.; Lapierre, J.-M.; Jaworek, W.; Seiler, P. *Helv. Chim. Acta* **1993**, *76*, 459
(b) Knochel, P.; Lütjens, H. *Tetrahedron Asymmetry* **1994**, *5*, 1161.

(29) The enantiomeric series is formed from *(S)-N*-tosylamino alkanols, derived from naturally occuring amino acids; see Refs 7,8.

Article Identifier:
1437-210X,E;2000,0,05,0743,0753,ftx,en;P00700SS.pdf