Asymmetric Syntheses of Chiral Allylic Alcohols

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Abstract: Chiral allylic alcohols **2** can easily be obtained by elimination from iodo ketals **10**. These are available from natural sources, or by application of the asymmetric Sharpless dihydroxylation to vinylogous esters **6**, subsequent reduction, halogenation and elimination. This protocol allows the synthesis of highly functionalized allylic alcohols, which can be used in asymmetric Claisen rearrangements.

Key words: asymmetric dihydroxylation, chiral allylic alcohol, diols, elimination, vinylogous esters

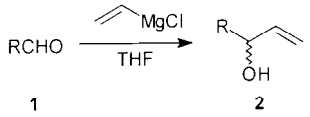
For several years, highly functionalized γ,δ-unsaturated amino acids have been of great interest because of their biological activity.[1] Many of them show antibiotic properties,[2] whereas they are also intermediates for the synthesis of complex amino acids and peptides.[3]

Besides electrophilic and nucleophilic allylations,[4] [3.3]-sigmatropic rearrangements are especially suited for the introduction of allylic side chains.[5] If the reaction is carried out with derivatives of chiral allylic alcohols or amines, the Claisen rearrangement yields optically active amino acids.[6] Therefore chiral allylic alcohols are highly interesting synthetic targets. Besides kinetic resolution procedures, e.g. via asymmetric Sharpless epoxidation,[7] or via enzymatic techniques,[8] the de novo syntheses of chiral allylic centers are of special interest. For this purpose also the Sharpless epoxidation of achiral alcohols can be used,[9] but other approaches, like the stereoselective reductions of vinylogous ketones,[10] or the addition of organometallics to aldehydes in the presence of chiral ligands,[11] are becoming more and more important.

Recently, we have developed a new variation of the ester enolate Claisen rearrangement proceeding via chelated allylic ester enolates.[12] This procedure is especially suitable for the generation of various types of γ,δ-unsaturated amino acids.[13] Because of our interest in the synthesis of polyhydroxylated amino acids and alkaloids,[14] we were looking for a general synthetic route especially to oxygenated allylic alcohols. Herein and in the following paper we describe the synthesis of functionalized chiral allylic alcohols and subsequent ester enolate Claisen rearrangement of the corresponding chiral allylic amino acid esters, which gives rise to the respective chiral amino acids in a highly enantio- as well as diastereoselective fashion.

The optically active allylic alcohols required for the preparation of the allylic esters were obtained in a few steps from chiral pool materials or via a dihydroxylation route, using the Sharpless protocol.[15]

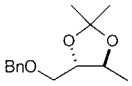
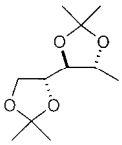
For analytical purposes, especially the determination of the optical purity of the allylic alcohols and the amino acids obtained by Claisen rearrangement, racemic and epimeric allylic alcohols were obtained by vinylmagnesium chloride addition to the corresponding aldehyde. Starting from achiral aldehydes **1** racemic alcohols **2** are obtained, while chiral aldehydes provide an epimeric mixture of *anti*- and *syn*-configurated alcohols (Scheme 1, Table 1).



1 2

Scheme 1

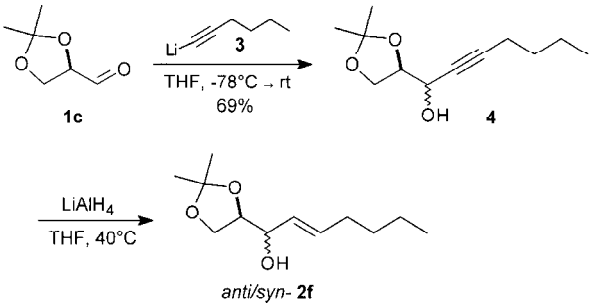
Table 1. Synthesis of Racemic and Epimeric Allylic Alcohols

Aldehyde	R	Yield (%)	Ratio *anti*/*syn*[a]	Product
1a	Ph	63	–	**2a**
1b	$BnOCH_2$	42	–	**2b**
1c		54	60:40	**2c**
1d		60	60:40	**2d**
1e		67	65:35	**2e**

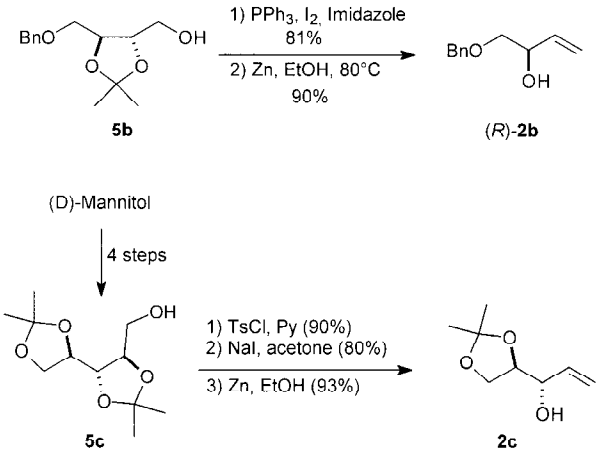
[a] Determined by HPLC and NMR.

The stereochemical outcome of the Grignard addition to 2,3-*O*-isopropylidene glyceraldehyde was investigated by Mulzer et al.[16] An *anti/syn* relationship of around 6:4 was observed in most cases. Similar results were also obtained in the vinylmagnesium chloride addition to various oxygenated chiral aldehydes (Table 1, entries 3–5). The *trans*-configurated substituted allylic alcohol **2f** was obtained from 2,3-*O*-isopropylidene-D-glyceraldehyde **(1c)** by addition of lithium acetylide **3** (*anti*/*syn* 6:4) and subsequent reduction of the propargylic alcohol **4** with $LiAlH_4$ (Scheme 2).

Highly oxygenated natural products like tartaric acid or sugars are especially suitable for the stereoselective synthesis of these functionalized allylic alcohols, and enantiomerically pure **2b** and **2c** were obtained by this approach (Scheme 3).



Scheme 2

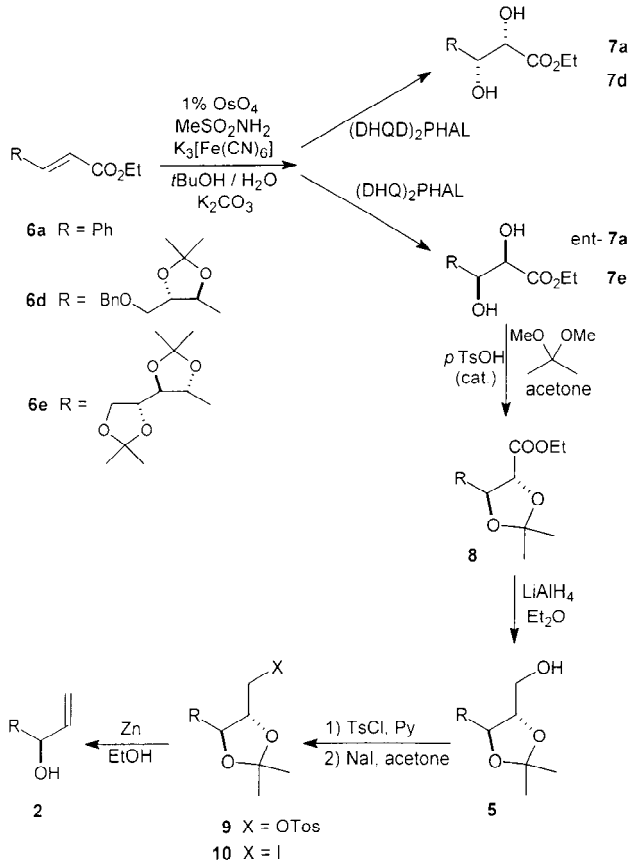


Scheme 3

Starting from dimethyl tartrate, alcohol **5b** was easily obtained.[17] Conversion into the iodide[18] and subsequent elimination using activated zinc[19] in ethanol provided **2b**[20] in overall good yield. According to Mulzer et al. alcohol **2c** was obtained from mannitol by a similar protocol. In this case the iodide was obtained by Finkelstein reaction from the corresponding tosylate.[21]

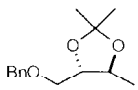
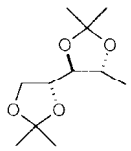
The Sharpless dihydroxylation[15] of olefins is especially suitable for the de novo generation of chirality centers. Starting from easy accessible α,β-unsaturated esters **6**, asymmetric dihydroxylation (AD) leads to chiral diols **7** (Scheme 4).

Both enantiomeric diols **7a** and ent-**7a** can be obtained in a highly stereoselective fashion (98% ee) from achiral cinnamoyl esters **6a**, depending on the ligand used (Table 2, entries 1, 2). Using chiral α,β-unsaturated esters like **6d**[22] and **6e**,[23] AD proceeded via double diastereoselection with particularly high *anti*-selectivities (98% ds) in



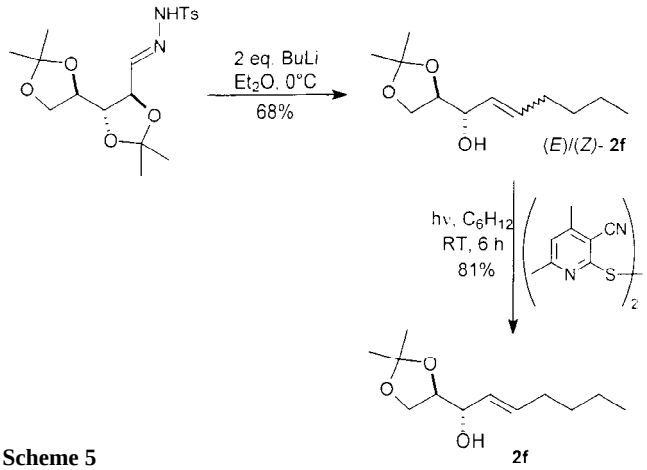
Scheme 4

Table 2. Synthesis of Chiral Allylic Alcohols via Sharpless Dihydroxylation

Ester	Sharpless Dihydroxylation				Ketalization		Reduction		Iodination		Elimination		
	R	Ligand	Yield (%)	Diol	Yield (%)	Ketal	Yield (%)	Alcohol	Yield (%)	Iodide	Yield (%)	Alcohol	Config
6a	Ph	$(DHQD)_2PHAL$	88	**7a**	97	**8a**	92	**5a**	81	**10a**	89	**2a**	(*S*)
6a	Ph	$(DHQ)_2PHAL$	85	ent-**7a**	96	ent-**8a**	89	ent-**5a**	80	ent-**10a**	86	ent-**2a**	(*R*)
6d		$(DHQD)_2PHAL$	74	**7d**	90	**8d**	88	**5d**	86	**10d**	86	**2d**	(2*S*,3*S*,4*S*)
6e		$(DHQ)_2PHAL$	94	**7e**	88	**8e**	98	**5e**	81	**10e**	93	**2e**	(2*S*,3*R*, 4*S*,5*R*)

the matched case (entries 3, 4).[24] Protection of the diols **7** to the corresponding ketals **8** and reduction of the ester functionality yielded the alcohols **5**. These were treated as described before. Tosylation of the primary hydroxy group gave **9** and subsequent iodination resulted in the formation of the iodide **10**. After elimination with zinc in ethanol, the *anti*-configurated chiral allylic alcohols **2** were obtained in good yields and in nearly optically pure form (98% ds).[25]

The *anti*-configurated substituted alcohol **2f** was synthesized (Scheme 5) from the tosyl hydrazone of protected D-aldehydo arabinose.[26] Reaction with 2 equivalents of BuLi gave the expected allylic alcohol as an *E/Z* mixture (*E/Z* 2:1).



Scheme 5

This mixture was converted into the pure *E*-alcohol by photochemical isomerization. Therefore the mixture was irradiated in cyclohexane with a 150-W UV lamp for 12 hours in the presence of bis(3-cyano-4,6-dimethyl-2-pyridyl) disulfide[27] until no *Z*-isomer could be detected by GC.

In conclusion, we have described a general applicable procedure for the synthesis of highly functionalized chiral allylic alcohols. These alcohols can be converted into the corresponding allylic esters, which are suitable substrates for asymmetric Claisen rearrangements (see following paper).

Most reactions were carried out in oven-dried glassware (100 °C) under argon. All solvents were dried before use. THF was distilled from sodium benzophenone, CH_2Cl_2 and i-Pr_2NH from CaH_2. The starting materials and the products were purified by flash chromatography on silica gel (32–63 μm). Mixtures of EtOAc and petroleum ether (40–60 °C) were generally used as eluents. TLC: commercially precoated Polygram© SIL-G/UV 254 plates (Macherey–Nagel). Visualization was accomplished with UV light, I_2, and $KMnO_4$ soln. ^1H and ^{13}C NMR: Bruker AC-300 spectrometer. Enantiomeric and diastereomeric ratios were determined by analytical HPLC using a Knauer Eurosphere column (250 × 4 mm, Si80, 5 μm, flow: 2 mL/min), as well as a Chiracel-OD-H column (Daicel) (0.5 mL/min) and a Knauer UV detector. Optical rotations were measured on a Perkin–Elmer polarimeter PE 241.

Asymmetric Dihydroxylation of *α,β*-Unsaturated Esters 6; General Procedure:
Following the Sharpless protocol,[15] $K_3[Fe(CN)_6]$ (3 mmol), K_2CO_3 (3 mmol) and methanesulfonamide (1 mmol) were suspended in water (5 mL) and *t*-BuOH (5 mL). Under vigorous stirring OsO_4 (0.01 mmol) and the corresponding ligand [$(DHQ)_2PHAL$ or $(DHQD)_2PHAL$] (0.01 mmol) were added at 0 °C. Stirring was continued for further 5 min, before the vinylogous ester **6** (1 mmol) was added. The vigorously stirred mixture was allowed to warm to r.t. overnight. The mixture was cooled to 0 °C again, before solid Na_2SO_3 (12 mmol) was added. After stirring for 1 h, H_2O was added slowly, until all salts were dissolved. The aqueous layer was extracted three times with EtOAc, the combined organic layers were dried (Na_2SO_4), and the solvent was removed in vacuo. The crude product was purified by flash chromatography (EtOAc/petroleum ether).

Ketalization of the Diols 7; General Procedure:
To a solution of diol **7** (1 mmol) in acetone (0.5 mL) and 2,2-dimethoxypropane (1 mL) *p*-TsOH (0.05 mmol) was added. After stirring for 24 h, anhyd Na_2CO_3 (1 mmol) was added. After filtration, the solvent was removed in vacuo. The residue obtained was purified by flash chromatography (EtOAc/petroleum ether).

Reduction of the Esters 8; General Procedure:
A solution of **8** (1 mmol) in Et_2O (2 mL) was added slowly to a stirred suspension of $LiAlH_4$ (1.1 mmol) in abs Et_2O at 0 °C under argon. The mixture was allowed to warm to r.t. during 12 h. After repeated cooling to 0 °C water (0.05 mL), 15% NaOH (0.05 mL) and water (0.15 mL) were successively added. The precipitate formed (after stirring for 1 h) was removed by filtration and the solvent was evaporated in vacuo. The residue obtained was purified by flash chromatography (EtOAc/petroleum ether).

Tosylation of the Alcohols 5; General Procedure:
p-TsCl (1.5 mmol) in abs pyridine (0.5 mL) was added to a solution of alcohol **5** (1 mmol) in abs pyridine (1 mL) at 0 °C. After removal of the ice bath, the mixture was stirred for 24 h, before water and Et_2O (10 mL each) were added, and the layers were separated. The aqueous layer was extracted with Et_2O (2 × 10 mL). The combined organic layers were subsequently washed with 1 N $KHSO_4$ and brine, and dried (Na_2SO_4). After evaporation of the solvent in vacuo, the residue obtained was crystallized from CH_2Cl_2/petroleum ether.

Finkelstein Reaction with Tosylates 9; General Procedure:
A suspension of tosylate **9** (1 mmol) and NaI (50 mmol) in a mixture of acetone (20 mL) and MeCN (8 mL) was refluxed for 24 h. If the reaction was complete (TLC control), water and Et_2O were added, until two layers were formed. After separation of the organic layer, the aqueous layer was extracted twice with Et_2O. The combined organic layers were dried (Na_2SO_4), and the solvent was removed in vacuo. The crude product was purified by flash chromatography (EtOAc/petroleum ether).

Synthesis of Allylic Alcohols 2; General Procedure:
Zinc dust (8.5 mmol) was added to a solution of iodide **10** (1 mmol) in abs EtOH (25 mL), and the suspension was refluxed for 4 h. After filtration through Celite, the solvent was removed in vacuo. The crude product was purified by flash chromatography (EtOAc/petroleum ether).

(2*R*,3*S*,4*E*)-1,2-(Isopropylidenedioxy)non-4-en-3-ol (2f):
2f was obtained by photochemical isomerization of the corresponding (*E/Z*)-mixture, which was obtained according to the literature.[26]

Table 3. Analytical and Spectroscopic Data of Compounds **2, 5** and **7–10**

Compound	$[\alpha]_D^{20}$ (*c*, Solvent)	^{1}H NMR (300 MHz, $CDCl_3$) δ, *J* (Hz)	^{13}C NMR (75 MHz, $CDCl_3$) δ
2a[28]	+ 5.2 (0.3, $CHCl_3$)	2.03 (s_{br}, 1H, O*H*), 5.17–5.24 (m, 1H, C*H*OH), 5.20 (d, *J* = 9.9, 1H, CHCH=CH*H*^{t}), 5.36 (ddd, *J* = 17.3, 1.1, 1.1, 1H, CHCH=CH*H*^{c}), 6.06 (ddd, *J* = 16.5, 9.9, 6.1, 1H, CHC*H*=CH_2), 7.28–7.39 (m, 5H, Ar*H*)	75.38 (d, *C*–OH), 115.13 (t, C=*C*H_2), 126.34, 127.77, 128.58 (3d, Ar*C*), 140.27 (d, *C*H=CH_2), 142.62 (s, quart. Ar*C*)
ent-**2a**[29]	–5.2 (0.3, $CHCl_3$)	2.03 (s_{br}, 1H, O*H*), 5.17–5.25 (m, 1H, C*H*OH), 5.20 (d, *J* = 9.9, 1H, CH=CH*H*^{t}), 5.35 (ddd, *J* = 17.3, 1.1, 1.1, 1H, CH=CH*H*^{c}), 6.06 (ddd, *J* = 16.5, 9.9, 6.1, 1H, C*H*=CH_2), 7.26–7.40 (m, 5H, Ar*H*)	75.39 (d, *C*HOH), 115.13 (t, C=*C*H_2), 126.36, 127.78, 128.59 (3d, Ar*C*), 140.28 (d, *C*H=CH_2), 142.64 (s, quart. Ar*C*)
2b[20]	+ 5.4 (0.36, $CHCl_3$)	2.58 (s_{br}, 1H, O*H*), 3.39 (dd, *J* = 9.6, 8.1, 1H, BnOC*H*$_2$), 3.55 (dd, *J* = 9.6, 3.4, 1H, BnOC*H*$_2$), 4.33–4.38 (m, 1H, C*H*OH), 4.58 (s, 2H, PhC*H*$_2$), 5.20 (dd, *J* = 10.6, 1.4, 1H, CH=CH*H*^{t}), 5.37 (dd, *J* = 17.3, 1.5, 1H, CH=CH*H*^{c}), 5.85 (ddd, *J* = 17.2, 10.6, 5.5, 1H, C*H*=CH_2), 7.26–7.42 (m, 5H, Ar*H*)	71.53 (t, PhC*H*$_2$), 73.41 (t, BnOC*H*$_2$), 74.09 (d, *C*HOH), 116.41 (t, C=*C*H_2), 127.80, 127.84, 128.49 (3d, Ar*C*), 136.70 (d, *C*H=CH_2), 137.89 (s, quart. Ar*C*)
2c[21]	+ 1.7 (1.2, $CHCl_3$)	1.36 (s, 3H, C*H*$_3$), 1.44 (s, 3H, C*H*$_3$), 2.19 (s_{br}, 1H, O*H*), 3.90 (dd, *J* = 8.3, 6.8, 1H, C*H*$_2$O), 3.96 (dd, *J* = 8.3, 6.5, 1H, C*H*$_2$O), 4.12 (m_c, 1H, C*H*OC), 4.29 (m_c, 1H, C*H*OH), 5.24 (ddd, *J* = 10.6, 1.5, 1H, CH=CH*H*^{t}), 5.38 (ddd, *J* = 17.3, 1.5, 1.5, 1H, CH=CH*H*^{c}), 5.83 (ddd, *J* = 17.2, 10.6, 5.5, 1H, C*H*=CH_2)	25.12 (q, *C*H$_3$), 26.43 (q, *C*H$_3$), 64.72 (t, *C*H$_2$O), 71.89 (d, *C*HOC), 78.11 (d, *C*HOH), 109.44 [s, *C*(CH$_3$)$_2$], 116.92 (t, C=*C*H_2), 135.77 (d, *C*H=CH_2)
2d	–21.6 (1.1, $CHCl_3$)	1.43 (s, 3H, C*H*$_3$), 1.44 (s, 3H, C*H*$_3$), 2.71 (d, *J* = 2.6, 1H, OH), 3.61 (dd, *J* = 12.9, 4.8, 1H, C*H*$_2$OBn), 3.64 (dd, *J* = 12.9, 5.2, 1H, C*H*$_2$OBn), 3.84 (dd, *J* = 8.1, 5.5, 1H, C*H*OC), 4.14 (ddd, *J* = 7.7, 5.2, 4.8, 1H, C*H*OC), 4.25 (m_c, 1H, C*H*OH), 4.58 (d, *J* = 12.1, 1H, PhC*H*$_2$), 4.63 (d, *J* = 12.1, 1H, PhC*H*$_2$), 5.29 (ddd, *J* = 10.3, 1.5, 1.5, 1H, CH=CH*H*^{t}), 5.23 (ddd, *J* = 17.3, 1.5, 1.5, 1H, CH=CH*H*^{c}),5.86 (ddd, *J* = 17.3, 10.3, 5.5, 1H, C*H*=CH_2), 7.28–7.39 (m, 5H, Ar*H*)	26.94 (q, *C*H$_3$), 70.70 (t, PhC*H*$_2$), 72.29 (d, *C*HOH), 73.61 (t, *C*H$_2$O), 76.96 (d, *C*HOC), 80.91 (d, *C*HOC), 109.37 [s, *C*(CH$_3$)$_2$], 116.68 (t, C=*C*H_2), 127.79, 127.85, 128.44, (3d, Ar*C*), 136.02 (s, quart. Ar*C*), 136.06 (d, *C*H=CH_2)
2e[30]	+ 22.9 (3.4, $CHCl_3$)	1.37–1.45 (m, 12H, C*H*$_3$), 3.34 (d, *J* = 2.6, 1H, OH), 3.72–3.84 (m, 2H, C*H*O), 3.98–4.21 (m, 4H, C*H*O), 5.26 (ddd, *J* = 10.5, 1.4, 1.4, 1H, CH=CH*H*^{t}), 5.43 (ddd, *J* = 17.2, 1.5, 1.5, 1H, CH=CH*H*^{c}), 6.00 (ddd, *J* = 17.2, 10.7, 6.1, 1H, C*H*=CH_2)	25.12 (q, *C*H$_3$), 26.42 (q, *C*H$_3$), 26.88 (q, *C*H$_3$), 67.87 (t, *C*H$_2$O), 73.30 (d, *C*HO), 76.59 (d, *C*HO), 80.47 (d, *C*HO), 83.16 (d, *C*HO), 109.62 [s, *C*(CH$_3$)$_2$], 110.17 [s, *C*(CH$_3$)$_2$], 116.69 (t, C=*C*H_2), 136.79 (d, *C*H=CH_2)
2f[26]	+ 29.4 (1.1, $CHCl_3$)	0.89 (t, *J* = 7.1, 3H, CH$_2$C*H*$_3$), 1.29–1.35 (m, 4H, C*H*$_2$), 1.36 [s, 3H, C(C*H*$_3$)$_2$], 1.44 [s, 3H, C(C*H*$_3$)$_2$], 2.01–2.16 (m, 3H, C=CHC*H*$_2$, OH), 3.85–3.98 (m, 2H, C*H*$_2$O), 4.10 (dt, *J* = 6.6, 4.0, 1H, C*H*OC), 4.25 (m_c, 1H, C*H*OH), 5.39 (ddt, *J* = 15.4, 6.4, 1.4, 1H, CHOHC*H*=C), 5.77 (ddt, *J* = 14.9, 6.9, 1.1, 1H, C=C*H*CH$_2$)	13.85 (q, CH$_2$*C*H$_3$), 22.15 (t, *C*H$_2$CH$_3$), 25.18 [q, C(*C*H$_3$)$_2$], 26.42 [q, C(*C*H$_3$)$_2$], 31.16 (t, *C*H$_2$), 32.01 (t, *C*H$_2$), 64.67 (t, *C*H$_2$O), 71.65 (d, *C*HO), 78.48 (d, *C*HO), 109.29 [s, *C*(CH$_3$)$_2$], 127.18 (d, CHOH*C*H=C), 134.47 (d, C=*C*HCH$_2$)
5a[31]	+ 19.4 (3.0, CH_2Cl_2)	1.53 (s, 3H, C*H*$_3$), 1.59 (s, 3H, C*H*$_3$), 2.15 (dd, *J* = 8.2, 4.4, 1H, OH), 3.64 (ddd, *J* = 12.6, 8.2, 4.4, 1H, C*H*OC), 3.84–3.90 (m, 2H, C*H*$_2$OH), 4.91 (d, *J* = 8.5, 1H, PhC*H*O), 7.29–7.42 (m, 5H, Ar*H*)	27.11 (q, *C*H$_3$), 27.15 (q, *C*H$_3$), 53.40 (t, *C*H$_2$OH), 78.69 (d, *C*HO), 83.61 (d, *C*HO), 109.32 [s, *C*(CH$_3$)$_2$], 126.54, 128.34, 128.65 (3d, Ar*C*), 127.75 (s, quart. Ar*C*)
ent-**5a**[32]	–19.5 (3.1, CH_2Cl_2)	1.53 (s, 3H, C*H*$_3$), 1.59 (s, 3H, C*H*$_3$), 2.14 (dd, *J* = 8.2, 4.3, 1H, OH), 3.64 (ddd, *J* = 12.6, 8.2, 4.3, 1H, C*H*OC), 3.82–3.91 (m, 2H, C*H*$_2$OH), 4.91 (d, *J* = 8.2, 1H, PhC*H*O), 7.29–7.42 (m, 5H, Ar*H*)	27.11 (q, *C*H$_3$), 27.16 (q, *C*H$_3$), 53.41 (t, *C*H$_2$OH), 78.69 (d, *C*HO), 83.62 (d, *C*HO), 109.32 [s, *C*(CH$_3$)$_2$], 126.55, 128.35, 128.65 (3d, Ar*C*), 137.75 (s, quart. Ar*C*)
5d	–14.5 (1.2, $CHCl_3$)	1.31 (s, 3H, C*H*$_3$), 1.38 (s, 3H, C*H*$_3$), 1.39 (s, 3H, C*H*$_3$), 1.43 (s, 3H, C*H*$_3$), 2.16 (s_{br}, 1H, OH), 3.59 (dd, *J* = 10.6, 6.0, C*H*OC), 3.70–3.84 (m, C*H*OC, C*H*$_2$OH), 4.03 (ddd, *J* = 8.1, 8.1, 4.0, 1H, C*H*OC), 4.20 (ddd, *J* = 6.3, 6.3, 4.2, 1H, C*H*OC), 4.59 (d, *J* = 12.4, 1H, PhC*H*$_2$), 4.63 (d, *J* = 12.4, 1H, PhC*H*$_2$), 7.27–7.35 (m, 5H, Ar*H*)	26.80 (q, *C*H$_3$), 26.93 (q, *C*H$_3$), 27.04 (q, *C*H$_3$), 62.62 (t, *C*H$_2$OH), 70.21 (t, *C*H$_2$OBn), 73.43 (t, PhC*H*$_2$O), 77.87 (d, *C*HO), 79.18 (d, *C*HO), 80.35 (d, *C*HO), 80.97 (d, *C*HO), 109.04 [s, *C*(CH$_3$)$_2$], 110.22 [s, *C*(CH$_3$)$_2$], 127.54, 127.64, 128.28 (3d, Ar*C*), 138.10 (s, quart. Ar*C*)
5e	+ 7.2 (3.6, $CHCl_3$)	1.33–1.43 (m, 18H, C*H*$_3$), 2.23 (dd, *J* = 8.2, 4.7, 1H, OH), 3.71 (ddd, *J* = 12.2, 8.2, 4.3, 1H, C*H*$_2$OH), 3.79–4.13 (m, 7H, 1-H^b, C*H*OC, C*H*$_2$OH, C*H*$_2$OC), 4.23 (dd, *J* = 11.9, 5.0, 1H, C*H*$_2$OC)	25.34, 26.40, 26.57, 26.88, 27.07, 27.51 (6q, *C*H$_3$), 62.69 (t, *C*H$_2$OH), 65.98 (t, *C*H$_2$OC), 76.06, 78.98, 79.45, 79.97, 90.07 (5d, *C*HO), 109.55, 109.65, 110.52 [3s, *C*(CH$_3$)$_2$]

Table 3. continued

Compound	$[\alpha]_D^{20}$ (*c*, Solvent)	^{1}H NMR (300 MHz, $CDCl_3$) δ, *J* (Hz)	^{13}C NMR (75 MHz, $CDCl_3$) δ
7d	+ 8.8 (1.0, $CHCl_3$)	1.30 (t, *J* = 7.1, 3H, CH_2CH_3), 1.39 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 3.11 (d, *J* = 6.9, 1H, 2-OH), 3.37 (d, *J* = 4.3, 1H, 3-OH), 3.54 (dd, *J* = 9.3, 7.0, 1H, CHOH), 3.73 (dd, *J* = 9.3, 4.8, 1H, CHOH), 3.90 (dd, *J* = 15.1, 9.8, 2H, CH_2OBn), 4.11 (m_c, 1H, CHOC), 4.28 (dq, *J* = 7.1, 1.5, 2H, CH_2CH_3), 4.39 (d, *J* = 6.6, 1H, CHOC), 4.56 (d, *J* = 12.1, 1H, PhCH_2O), 4.62 (d, *J* = 12.1, 1H, PhCH_2O), 7.28–7.37 (m, 5H, ArH)	14.17 (q, CH_2CH_3), 26.23 (q, CH_3), 26.92 (q, CH_3), 61.97 (t, CH_2CH_3), 70.53 (t, CH_2OBn), 70.83 (d, CHOC), 73.76 (d, CHOC), 73.82 (t, PhCH_2O), 78.50 (d, CHOH), 78.64 (d, CHOH), 109.68 [s, $C(CH_3)_2$], 127.98, 128.07, 128.54 (3d, ArC), 136.99 (s, quart. ArC), 173.24 (s, C=O)
7e[23]	–9.9 (1.3, $CHCl_3$)	1.31 (t, *J* = 7.1, 3H, CH_2CH_3), 1.34 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 3.02 (d, *J* = 8.0, 1H, OH), 3.05 (d, *J* = 7.9, 1H, OH), 3.75–3.80 (m, 2H, CHOH), 3.88 (d, *J* = 9.0, 1H, CHOC), 3.97–4.09 (m, 3H, CHOC), 4.20 (dd, *J* = 8.2, 5.7, 1H, CHOC), 4.25–4.30 (m, CH_2CH_3)	14.18 (q, CH_2CH_3), 25.04 (q, CH_3), 26.31 (q, CH_3), 26.91 (q, CH_3), 61.82 (t, CH_2CH_3), 67.96 (t, CH_2OC), 70.89 (d, CHOC), 73.66 (d, CHOC), 76.40 (d, CHOC), 78.96 (d, CHOH), 81.19 (d, CHOH), 109.93 [s, $C(CH_3)_2$], 110.37 [s, $C(CH_3)_2$], 173.21 (s, C=O)
8d	+ 7.6 (1.1, $CHCl_3$)	1.28 (t, *J* = 7.1, CH_2CH_3), 1.41 (2s, 6H, CH_3), 1.43 (2s, 6H, CH_3), 3.61 (dd, *J* = 10.4, 5.5, 1H, CH_2OBn), 3.69 (dd, *J* = 10.4, 3.8, 1H, CH_2OBn), 3.99 (dd, *J* = 7.4, 6.4, 1H, CHOC), 4.20–4.27 (m, 3H, CHOC, CH_2CH_3), 4.35 (dd, *J* = 6.1, 6.1, 1H, CHOC), 4.53 (d, *J* = 5.8, 1H, CHOC), 4.60 (s_{br}, 2H, PhCH_2O), 7.27–7.34 (m, 5H, ArH)	14.08 (q, CH_2CH_3), 26.02, 26.97, 27.12, 27.23 (4q, CH_3), 61.44 (t, CH_2CH_3), 70.56 (t, CH_2OBn), 73.51 (t, PhCH_2O), 77.04, 78.11, 78.42, 79.92 (4d, CHOC), 110.14 [s, $C(CH_3)_2$], 112.01 [s, $C(CH_3)_2$], 127.61, 127.65, 128.33 (3d, ArC), 138.06 (s, quart. ArC), 170.95 (s, C=O)
8e	+ 3.7 (0.6, $CHCl_3$)	1.29 (t, *J* = 7.2, 3H, CH_2CH_3), 1.33–1.42 (m, 18H, CH_3), 3.92–4.02 (m, 2H, CH_2CH_3), 4.04–4.14 (m, 2H, CH_2OC), 4.18–4.31 (m, 3H, CHOC), 4.46 (dd, *J* = 6.0, 4.4, 1H, CHOC), 4.63 (d, *J* = 6.1, CHOC)	14.12 (q, CH_2CH_3), 15.23, 25.92, 26.47, 26.98, 27.25, 27.57 (6q, CH_3), 61.45 (t, CH_2CH_3), 67.18 (t, CH_2OC), 75.74, 76.76, 78.43, 79.35, 79.56 (5d, CHOC), 109.77, 110.40, 111.88 [3s, $C(CH_3)_2$], 171.34 (s, C=O)
9a	–0.3 (3.9, $CHCl_3$)	1.45 (2s, 3H, CH_3), 1.52 (2s, 3H, CH_3), 2.45 (s, 3H, ArCH_3), 3.90 (ddd, *J* = 8.4, 4.1, 3.3, 1H, CHOC), 4.11 (dd, *J* = 11.0, 4.2, 1H, CH_2OC), 4.24 (dd, *J* = 11.0, 3.2, 1H, CH_2OC), 4.83 (d, *J* = 8.5, 1H, PhCHOC), 7.26–7.38 (m, 7H, ArH), 7.77 (d, *J* = 8.3, 2H, ArH)	21.63 (q, ArCH_3), 26.73 (q, CH_3), 27.04 (q, CH_3), 67.37 (t, CH_2OTos), 79.05 (d, CHOC), 80.63 (d, CHOC), 110.01 [s, $C(CH_3)_2$], 126.51, 128.03, 128.59, 128.73, 129.85 (5d, ArC), 132.88 (s, ArCCH$_3$), 136.97 (s, quart. ArC), 144.94 (s, quart. ArC)
ent-**9a**	+ 0.3 (3.2, $CHCl_3$)	1.45 (s, 3H, CH_3), 1.52 (s, 3H, CH_3), 2.45 (s, 3H, ArCH_3), 3.91 (ddd, *J* = 8.2, 4.1, 3.4, 1H, CHOC), 4.11 (dd, *J* = 11.0, 4.2, 1H, CH_2OTos), 4.24 (dd, *J* = 11.0, 3.2, 1H, CH_2OTos), 4.83 (d, *J* = 8.5, 1H, PhCHOC), 7.24–7.37 (m, 7H, ArH), 7.77 (d, *J* = 8.3, 2H, ArH)	21.63 (q, ArCH_3), 26.74 (q, CH_3), 27.04 (q, CH_3), 67.38 (t, CH_2OTos), 79.06 (d, CHOC), 80.63 (d, CHOC), 110.01 [s, $C(CH_3)_2$], 126.52, 128.03, 128.60, 128.73, 129.85 (5d, ArC), 132.89 (s, ArCCH$_3$), 136.98 (s, quart. ArC), 144.94 (s, quart. ArC)
9d	+ 3.8 (3.3, $CHCl_3$)	1.27 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 2.44 (s, 3H, ArCH_3), 3.40 (d, *J* = 10.9, 1H, CH_2OBn), 3.56 (dd, *J* = 10.6, 5.9, 1H, CH_2OBn), 3.69–3.78 (m, 2H, CHOC), 4.06–4.13 (m, 3H, CHOC, CH_2OTos), 4.29 (dd, *J* = 12.4, 4.2, 1H, CH_2OTos), 4.57 (d, *J* = 12.2, 1H, PhCH_2O), 4.62 (d, *J* = 12.2, 1H, PhCH_2O), 7.26–7.34 (m, 7H, ArH), 7.80 (d, *J* = 7.8, 2H, ArH)	21.61 (q, ArCH_3), 26.76, 26.94, 27.03 (3q, CH_3), 69.23 (t, CH_2OTos), 70.22 (t, CH_2OBn), 73.48 (t, PhCH_2O), 77.71, 78.07, 78.19, 80.20 (4d, CHOC), 110.21 [s, $C(CH_3)_2$], 110.64 [s, $C(CH_3)_2$], 127.62, 127.66, 128.08, 128.32, 129.76 (5d, ArC), 133.04 (s, ArCCH$_3$), 138.12 (s, quart. ArC) 144.79 (s, quart. ArC)
9e	–7.3 (0.5, MeOH)	1.31–1.40 (m, 18H, CH_3), 2.44 (s, 3H, ArCH_3), 3.86–4.20 (m, 8H, CHOC, CH_2OTos), 4.27 (dd, *J* = 10.5, 2.5, 1H, CH_2OTos), 7.33 (d, *J* = 8.1, 2H, ArH), 7.80 (d, *J* = 8.3, 2H, ArH)	21.61 (q, ArCH_3), 25.31, 26.41, 26.86, 26.97, 27.41, 27.45 (6q, CH_3), 66.19 (t, CH_2OC), 69.29 (t, CH_2OTos), 76.07, 77.12, 77.27, 79.54, 79.84 (5d, CHOC), 109.68, 110.48, 110.52 [3s, $C(CH_3)_2$], 128.06, 129.78 (2d, ArC), 133.00 (s, ArCCH$_3$), 144.84 (s, quart. ArC)
10a	+ 35.7 (3.9, $CHCl_3$)	1.51 (s, 6H, CH_3), 3.17 (dd, *J* = 11.0, 5.0, 1H, CH_2I), 3.33 (dd, *J* = 11.0, 3.7, 1H, CH_2I), 3.53 (ddd, *J* = 8.1, 4.8, 3.5, 1H, CHOC), 4.66 (d, *J* = 8.0, 1H, PhCHOC), 7.26–7.34 (m, 5H, ArH)	4.56 (t, CH_2I), 27.27 (q, CH_3), 27.36 (q, CH_3), 81.36 (d, CHO), 83.27 (d, CHO), 109.52 [s, $C(CH_3)_2$], 126.63, 128.61, 128.73 (3d, ArC), 137.00 (s, quart. ArC)

Table 3. continued

Compound	$[\alpha]_D^{20}$ (*c*, Solvent)	^{1}H NMR (300 MHz, $CDCl_3$) δ, *J* (Hz)	^{13}C NMR (75 MHz, $CDCl_3$) δ
ent-**10a**	–35.9 (3.9, $CHCl_3$)	1.51 (s, 6H, CH_3), 3.17 (dd, *J* = 11.2, 5.0, 1H, CH_2I), 3.33 (dd, *J* = 11.1, 3.7, 1H, CH_2I), 3.53 (ddd, *J* = 8.1, 4.8, 3.7, 1H, C*H*OC), 4.66 (d, *J* = 8.1, 1H, PhC*H*OC), 7.26–7.34 (m, 5H, Ar*H*)	4.56 (t, CH_2I), 27.26 (q, *C*H$_3$), 27.36 (q, *C*H$_3$), 81.34 (d, *C*HO), 83.26 (d, *C*HO), 109.52 [s, *C*(CH$_3$)$_2$], 126.62, 128.61, 128.72 (3d, Ar*C*), 137.00 (s, quart. Ar*C*)
10d	+ 5.7 (0.5, $CHCl_3$)	1.30 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 3.36 (dd, *J* = 10.8, 5.5, 1H, CH_2I), 3.49 (dd, *J* = 10.7, 3.3, 1H, CH_2I), 3.56 (dd, *J* = 10.8, 5.8, 1H, C*H*OC), 3.67–3.80 (m, 4H, C*H*OC), 4.16–4.19 (m, 1H, C*H*OC), 4.57 (d, *J* = 13.6, 1H, PhCH_2), 4.62 (d, *J* = 13.6, 1H, PhCH_2), 7.24–7.33 (m, 5H, Ar*H*)	7.06 (t, CH_2I), 26.84, 26.88, 27.02, 27.17 (4q, *C*H$_3$), 70.08 (t, *C*H$_2$OBn), 73.24 (t, PhCH_2), 77.65, 78.95, 79.96, 81.62 (4d, *C*HO), 109.86 [s, *C*(CH$_3$)$_2$], 110.01 [s, *C*(CH$_3$)$_2$], 127.34, 127.44, 128.08 (3d, Ar*C*), 137.91 (s, quart. Ar*C*)
10e	–12.4 (1.0, $CHCl_3$)	1.36–1.47 (m, 18H, CH_3), 3.32 (dd, *J* = 10.8, 5.2, 1H, CH_2I), 3.50 (dd, *J* = 10.8, 3.5, 1H, CH_2I), 3.83 (dd, *J* = 14.0, 7.0, 1H, C*H*OC), 3.88–3.93 (m, 1H, C*H*OC), 3.95–4.00 (m, 2H, C*H*OC), 4.05–4.12 (m, 2H, C*H*OC, CH_2OC), 4.20 (dd, *J* = 12.1, 6.0, 1H, CH_2OC)	7.51 (t, CH_2I), 25.33, 26.49, 27.26, 27.51, 27.72 (5q, *C*H$_3$), 66.20 (t, *C*H$_2$O), 76.16, 78.15, 79.50, 79.86, 81.24 (5d, *C*HO), 109.70, 109.98, 110.58 [3s, *C*(CH$_3$)$_2$]

Therefore a solution of (*E*/*Z*)-**2f** (1 g, 4.67 mmol, *E*/*Z* 7:3) and bis(3-cyano-4,6-dimethyl-2-pyridyl) disulfide[27] (14 mg, 0.05 mmol) in cyclohexane (500 mL) was irradiated for 5 h in a photoreactor with a 150-W high pressure lamp At this point an *E*/*Z* ratio of 86:14 was obtained. After addition of further bis(3-cyano-4,6-dimethyl-2-pyridyl) disulfide (14 mg, 0.05 mmol) and irradiation for 8 h, no *Z*-isomer could be detected by GC. Flash chromatography (EtOAc/petroleum ether 15:85) gave **2f** (810 mg, 81%) as a colorless oil.

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