One-Pot Generation and Conversion of Trichloroacetimidates for the Racemization-Free Allylation and Benzylation of α-Hydroxyesters and the Enantiopure Synthesis of a Chiral Diglycole

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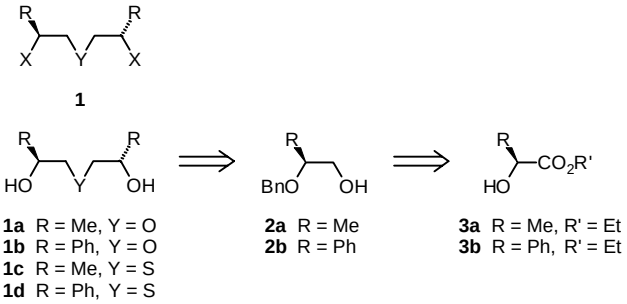
Abstract. *O*-Allylations and *O*-benzylations of α-hydroxy esters (**3a**–**3c**) are performed without racemization. The reagents applied, *O*-allyl- and *O*-benzyltrichloroacetimidate (**5a**, **5b**) are prepared and converted in a one-pot-procedure. After protection by benzylation (*S*)-(–)-ethyl lactate (**3a**) is converted by a sequence of carbonyl reduction, alcohol activation, ether formation, and deprotection to the optically active diglycole derivative **1a**.

In the course of our combinatorial catalysis project on asymmetric Michael reactions [1] we are interested in the synthesis of optically active C_2-symmetric tripodal ligands of the general type **1** (Scheme 1) [2]. The chiral diglycoles **1a** and **1b** and thiodiglycoles **1c** and **1d** are useful intermediates for the preparation of such ligands **1** (X = P, S; Y = O, S) since the transformations OH → SR, OH → PR_2 are readily performed [3].



Scheme 1 C_2-Symmetric diglycoles and thiodiglycoles (**1a**–**1d**) derived from ethyl lactate and mandelate (**3a**, **3b**)

Reasonable starting materials for the preparation of **1a**–**1d** are (*S*)-ethyl lactate (**3a**) and mandelate (**3b**), because the stereoinformation is received from the chiral pool and the secondary hydroxy functions are preexisting. The synthesis of intermediates **2a** and **2b** can be achieved by different routes [4], *e.g.* by ring opening of optically active epoxides with BnOH (**4a**), but however, the regioselectivity and stereospecificity of this reaction are not satisfying [5]. The protection of α-hydroxy esters **3** turned out to be a crucial step in our approach: Although the alkylation of (*S*)-ethyl lactate (**3a**) with NaH–BnBr was reported in the literature to proceed without (at least partial) racemization [6], this result could not be reproduced in our hands. And alternatively, the alkylation with Ag_2O–BnBr [7] seemed not to be very attractive for upscaling. However, *O*-benzylation can be performed under non-basic conditions with *O*-benzyl trichloroacetimidate (**5a**) [8], which is commercially available, but rather expensive. This reagent was reported to alkylate hydroxy functions under acidic conditions in good [9] to moderate [10] yields. Herein, we wish to report on a new one-pot protocol for the generation and conversion of this reagent **5a** as well as for the allyl congener **5b**. Moreover, we report on the application of this method in the synthesis of the optically active diglycole **1a**.

Results and Discussion

Trichloroacetimidates

Benzyl and allyl trichloroacetimidates (**5a** and **5b**) are prepared from the corresponding alcoholes, CCl_3CN, and a catalytic amount of NaH in Et_2O. After quenching with MeOH, the reaction mixture was acidified with a small excess of triflic acid and the α-hydroxy esters **3a**–**3b** as well as dimethyl maleate (**3c**) (0.5 eq.) were added (Scheme 2). After stirring over night at ambient temperature and aqueous workup chromatography yielded products **6a**–**6f** in 71–30% yield. Importantly, compared to procedures applying the reagents **5a** and **5b** in

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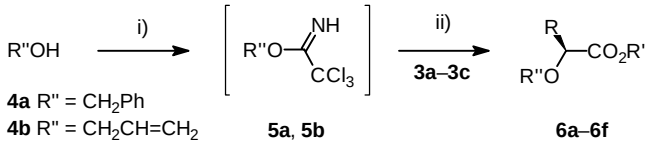
substance the yields of this one-pot protocol are in the same range (69–70% for **6a** [11], 60–68% for **6c** [9a, 12]). Moreover, since the reaction conditions are strictly Brönstedt acidic, no racemization was detectable by comparison of optical rotations.

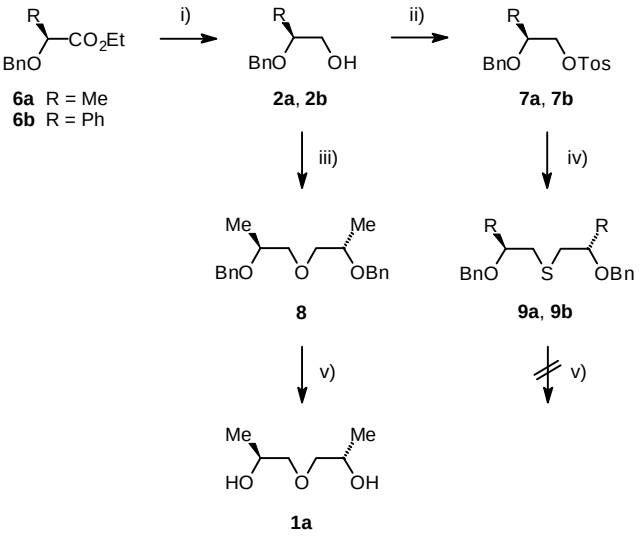


Starting Materials	Product	R	R'	R''	Yield (%)
3a, **4a**	**6a**	Me	Et	CH_2Ph	59
3b, **4a**	**6b**	Ph	Et	CH_2Ph	71
3c, **4a**	**6c**	CH_2CO_2Me	Me	CH_2Ph	65
3a, **4b**	**6d**	Me	Et	$CH_2CH=CH_2$	43
3b, **4b**	**6e**	Ph	Et	$CH_2CH=CH_2$	45
3c, **4b**	**6f**	CH_2CO_2Me	Me	$CH_2CH=CH_2$	30

Scheme 2 One pot-generation and conversion of trichloroacetimidates for the racemization-free benzylation and allylation of optically active α-hydroxy esters. Reagents and conditions: i) 1. 0.1 eq. NaH, Et_2O or THF; 2. 0.95 eq. CCl_3CN, 90 min; 3. 0.1 eq. MeOH, 15 min. ii) 1. 0.15 eq. CF_3SO_3H; 2. 0.5 eq. **3a**–**3c**, 18 h

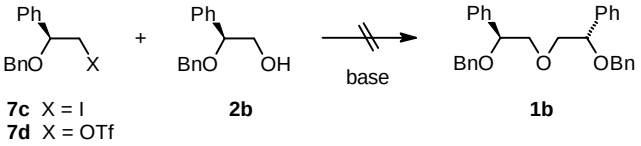
Diglycoles and Thiodiglycoles

Further conversion towards target compounds **1a**–**1d** followed standard procedures (Scheme 3): Benzyloxy esters **6a** and **6b** were reduced with $LiAlH_4$ in THF followed by tosylation of the primary hydroxy function in **2a** and **2b** to give sulfonates **7a** and **7b**. Ether synthesis starting from lactic acid derivatives **2a** and **7a** with 1 eq. NaH in DMF at 50 °C proceeded successfully to give protected ether **8** in 71% yield. In the case of the mandelic derivatives **2b** and **7b** no formation of the corresponding ether was observed under a number of different reaction conditions. Bis-benzyloxy compound **8** was deprotected by Pd-catalyzed hydrogenolysis to give compound **1a** in 36% overall yield in five steps from ethyl lactate (**3a**), which is not a significant improvement of the route reported by us previously (33% from **3a** by the use of an acetal protective group) [13]. Aiming at the synthesis of dihydroxy thioether intermediates **1c** and **1d** we prepared the bis-benzyloxy thioethers **9a** and **9b** by conversion of tosylates **7a** and **7b** with an excess of Na_2S in DMF or acetone. However, we were not able to deprotect compounds **9a** and **9b** by application of a number of different protocols. Presumably, the thioether function prevents every catalyzed hydrogenolysis by coordination to the metal centers. Since we have meanwhile been able to access compounds **1c** and **1d** by the choice of a different protective group [13], we did not further follow the route reported here.



Scheme 3 Preparation of C_2-symmetric diglycole **1a**. Reagents, conditions, and yields: i) $LiAlH_4$, THF, 23 °C, 90 min, **2a**: 98%, **2b**: 86%; ii) TosCl, pyridine, 23 °C, 16 h, **7a**: 94%, **7b**: 93%; iii) + **7a**, NaH, DMF, 50 °C, 3 h, **8**: 73%; iv) Na_2S, 16 h, **9a**: DMF, 50 °C, 92%, **9b**: acetone, 70 °C, 85%; v) Pd–C, H_2 (1 bar), EtOH, 23 °C, 16 h, **1a**: 90%

To date we have not been able to prepare compound **1b** from mandelic acid. Beside tosylate **7b** other electrophiles have been utilized in nucleophilic substitutions with deprotonated **2b**, *e.g.* iodo-compound **7c** (prepared from **7b** with NaI–DMF in 79% yield) or triflate **7d** (from **2b** and Tf_2O-pyridine in 24% yield) (Scheme 4). We presume that nucleophilic substitutions leading to **1b** are prevented by either steric congestion or intramolecular electrophilic attack of the phenyl ring in the activated compounds **7b**–**7d**.



Scheme 4 Ether **1b** can not be synthesized from electrophiles **7c** and **7d** with alcoholate derived from **2b**.

Summary

Benzyl and allyl trichloroacetimidates (**5a** and **5b**) were generated and converted in a one-pot procedure with α-hydroxy esters **3a**–**3c**. The yields of this protocol are similar to those achieved by application of **5a** and **5b** in

substance. Importantly, no racemization took place under the reaction conditions. From one benzylation product (**6a**) the optically active C_2-symmetric diglycole derivative **1a** was prepared in 36% overall yield from ethyl lactate (**3a**).

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Experimental

Absolute Et_2O was freshly distilled from sodium and THF from potassium, abs. DMF was purchased from Aldrich. Column chromatography was accomplished with Merck silica gel (type 60, 0.063–0.200 mm) using *tert*-butyl methyl ether (MTB) and petroleum ether (*b.p.* 40–60 °C) (PE). All starting materials were commercially available. All reagents were used as purchased. – ^{1}H NMR: Bruker AM 400 (400 MHz) and AC 200 (200 MHz). – ^{13}C NMR: Bruker AC 200 (50 MHz), resonances were assigned by DEPT experiments. – HRMS (EI, 70 eV): Varian MAT 955Q. – IR: Nicolet Magna IR 750. – Elemental analyses: Analytik Jena Vario EL. – Optical rotations: Perkin Elmer polarimeter 341. – Spectroscopic data of compounds **6a** [7d], **6c** [9a], **6d** [7b], **6e** [7b], **2a** [7a] (except ^{13}C NMR), **2b** [5c], **7a** [11b] (except ^{13}C-NMR), **7b** [5c], and **1a** [13] were in accordance with the literature.

Benzylation and Allylation (General Procedure)

Under an inert atmosphere (Ar or N_2) a solution of alcohol **4** (21.0 mmol) in abs. Et_2O or THF (5 ml) was added to a suspension of NaH (84 mg of a 60% dispersion in mineral oil, 2.10 mmol) in abs. Et_2O or THF (5 ml) at ambient temperature (water cooling bath). After the mixture became homogeneous CCl_3CN (2.89 g, 20.0 mmol) was added dropwise at 0 °C and the mixture stirred at ambient temperature for 90 min. After addition of MeOH (68.0 mg, 2.10 mmol) followed by 15 min stirring, CF_3SO_3H (450 mg, 3.00 mmol) and the hydroxy ester **3** (10.0 mmol, dissolved in 5 ml Et_2O or THF for **3b** or **3c**) were added. Stirring of the reaction mixture over night at ambient temperature was followed by dilution with MTB (100 ml). Subsequently, the mixture was extracted two times with saturated aqueous $NaHCO_3$ solution (each 50 ml) and brine (50 ml). Drying of the organic layer ($MgSO_4$) and evaporation yielded a residue, which was redissolved in cyclohexane (100 ml). After filtration and evaporation of the filtrate the crude product was submitted to column chromatography (SiO_2, MTB–PE) to yield the *O*-protected hydroxy ester **6**.

Ethyl (S)-(–)-2-Benzyloxypropionate (**6a**)

Following the general procedure alcohol **4a** (4.54 g, 42.0 mmol) in THF, NaH (126 mg, 80% dispersion in mineral oil, 4.20 mmol), CCl_3CN (5.78 g, 40.0 mmol), MeOH (135 mg, 4.20 mmol), CF_3SO_3H (900 mg, 6.00 mmol), and hydroxy ester **3a** (2.36 g, 20.0 mmol) were converted to yield the title compound **6a** (2.46 g, 11.8 mmol, 59%) after chromatography on SiO_2 (MTB–PE 1 : 5, R_f = 0.33) as a colorless oil. – $[\alpha]_D^{23}$ = –81.2 (c 10.6, $CHCl_3$); ref. [7d]: –83 (c 2.52, $CHCl_3$), ref. [11a]: –74.5 (c 2.94, $CHCl_3$).

$C_{12}H_{16}O_3$	Calcd.:	C 69.21	H 7.74
(208.26)	Found:	C 68.93	H 7.70.

Ethyl (S)-(+)-2-Benzyloxy-2-phenylacetate (**6b**)

Following the general procedure alcohol **4a** (2.27 g, 21.0 mmol) in Et_2O, NaH (84.0 mg, 2.10 mmol), CCl_3CN (2.89 g, 20.0 mmol), MeOH (68.0 mg, 2.10 mmol), CF_3SO_3H (450 mg, 3.00 mmol), and hydroxy ester **3b** (1.80 g, 10.0 mmol) were converted to yield the title compound **6b** (1.93 g, 7.14 mmol, 71%) after chromatography on SiO_2 (MTB–PE 1 : 5, R_f = 0.25) as a colorless oil. – $[\alpha]_D^{23}$ = +78.8 (c 20.0, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.21 (t, J = 7.2 Hz, 3H), 4.10–4.26 (m, 2H), 4.60 (s, 2H), 4.92 (s, 1H), 7.22–7.52 (m, 10H). – ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$): δ/ppm = 13.84 (CH_3), 60.91 (CH_2), 70.93 (CH_2), 79.53 (CH), 127.12 (2CH), 127.65 (CH), 127.79 (2CH), 128.20 (2CH), 128.35 (2CH), 128.40 (CH), 136.26 (C), 137.04 (C), 170.50 (C). – IR(ATR): $\tilde{\nu}$/cm^{-1} = 1746.
Mol. mass calcd. 197.0966 (for $C_{14}H_{13}O$), found 197.0962 ($M^+ - CO_2Et$).

$C_{17}H_{18}O_3$	Calcd.:	C 75.53	H 6.71
(270.33)	Found:	C 75.03	H 6.68.

Dimethyl (S)-(–)-2-Benzyloxybutanedioate (**6c**)

Following the general procedure alcohol **4a** (2.27 g, 21.0 mmol) in Et_2O, NaH (84.0 mg, 2.10 mmol), CCl_3CN (2.89 g, 20.0 mmol), MeOH (68.0 mg, 2.10 mmol), CF_3SO_3H (450 mg, 3.00 mmol), and hydroxy ester **3c** (1.62 g, 10.0 mmol) were converted to yield the title compound **6c** (1.63 g, 6.47 mmol, 65%) after chromatography on SiO_2 (MTB–PE 1 : 2, R_f = 0.30) as a yellowish oil. – $[\alpha]_D^{23}$ = –71.8 (c 11.1, $CHCl_3$); ref. [12]: –68.5 (c 11.4, $CHCl_3$).

Ethyl (S)-(–)-2-Allyloxypropionate (**6d**)

Following the general procedure alcohol **4b** (1.22 g, 21.0 mmol) in Et_2O, NaH (84.0 mg, 2.10 mmol), CCl_3CN (2.89 g, 20.0 mmol), MeOH (68.0 mg, 2.10 mmol), CF_3SO_3H (450 mg, 3.00 mmol), and hydroxy ester **3a** (1.18 g, 10.0 mmol) were converted to yield the title compound **6d** (675 mg, 4.27 mmol, 43%) after chromatography on SiO_2 (MTB–PE 1 : 3, R_f = 0.39) as a yellowish oil. – $[\alpha]_D^{23}$ = –64.2 (c 11.9, $CHCl_3$), –69.7 (c 10.6, EtOH); ref. [7b]: –73.6 (EtOH).

Ethyl (S)-(+)-2-Allyloxy-2-phenylacetate (**6e**)

Following the general procedure alcohol **4b** (1.22 g, 21.0 mmol) in Et_2O, NaH (84.0 mg, 2.10 mmol), CCl_3CN (2.89 g, 20.0 mmol), MeOH (68.0 mg, 2.10 mmol), CF_3SO_3H (450 mg, 3.00 mmol), and hydroxy ester **3b** (1.80 g, 10.0 mmol) were converted to yield the title compound **6e** (982 mg, 4.46 mmol, 45%) after chromatography on SiO_2 (MTB–PE 1 : 3, R_f = 0.45) as a colorless oil. As a second fraction starting material **3b** was recovered (995 mg, 5.52 mmol, 55%, R_f = 0.12). – $[\alpha]_D^{23}$ = +87.0 (c 11.1, $CHCl_3$), +86.8 (c 10.7, EtOH); ref. [7b]: +80.5 (EtOH).

Dimethyl (S)-(–)-2-Allyloxybutanedioate (**6f**)

Following the general procedure alcohol **4b** (1.22 g, 21.0 mmol) in Et_2O, NaH (84.0 mg, 2.10 mmol), CCl_3CN (2.89 g, 20.0 mmol), MeOH (68.0 mg, 2.10 mmol), CF_3SO_3H (450 mg, 3.00 mmol), and hydroxy ester **3c** (1.62 g,

10.0 mmol) were converted to yield the title compound **6f** (613 g, 3.03 mmol, 30%) after chromatography on SiO_2 (MTB–PE 1 : 2, R_f = 0.33) as a colorless oil. As a second fraction starting material **3c** was recovered (120 mg, 0.740 mmol, 7%, R_f = 0.06). – $[\alpha]_D^{23}$ = –49.8 (c 11.2, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 2.76 (dd, J = 16.0 Hz, J = 7.6 Hz, 1H), 2.81 (dd, J = 16.0 Hz, J = 5.1 Hz, 1H), 3.71 (s, 3H), 3.77 (s, 3H), 4.02 (ddt, J = 12.5 Hz, J = 6.1 Hz, J = 1.1 Hz, 1H), 4.22 (ddt, J = 12.5 Hz, J = 5.6 Hz, J = 1.3 Hz, 1H), 4.35 (dd, J = 7.6 Hz, J = 5.1 Hz, 1H), 5.18–5.23 (m, 1H), 5.24–5.32 (m, 1H), 5.89 (ddt, J = 17.2 Hz, J = 10.5 Hz, J = 5.9 Hz, 1H). – ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$): δ/ppm = 37.54 (CH_2), 51.75 (CH_3), 52.01 (CH_3), 71.85 (CH_2), 73.96 (CH), 117.81 (CH_2), 133.62 (CH), 170.28 (C), 171.68 (C). – IR (ATR): $\tilde{\nu}$/cm^{-1} = 1740 (vs). – $C_9H_{14}O_5$ (202.21): mol. mass calcd. 203.0919 (for $C_9H_{15}O_5$), found 203.0916 (M^+ + H).

(S)-(+)-2-Benzyloxy-1-propanol (**2a**)

Under an inert atmosphere a solution of ester **6a** (2.27 g, 10.9 mmol) in abs. THF (5 ml) was added dropwise at 0 °C to a suspension of $LiAlH_4$ (827 mg, 21.8 mmol) in THF (15 ml). After stirring for 90 min at ambient temperature water (60 ml) was added carefully and the mixture was extracted three times with MTB (each 50 ml). The combined organic extracts were washed with water (two times 50 ml), brine (50 ml), dried ($MgSO_4$), and evaporated. Column chromatography (SiO_2, MTB–PE 5 : 1, R_f = 0.38) yielded the title compound **2a** (1.77 g, 10.6 mmol, 98%) as a colorless oil. – $[\alpha]_D^{23}$ = +45.3 (c 10.5, $CHCl_3$); ref. [7a]: +45.8 (c 6.5, $CHCl_3$). – ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$): δ/ppm = 15.67 (CH_3), 65.66 (CH_2), 70.35 (CH_2), 75.27 (CH), 127.19 (CH), 127.32 (2CH), 127.97 (2CH), 138.22 (C).

(S)-(+)-2-Benzyloxy-2-phenylethanol (**2b**)

According to the previous procedure for **2a** the ester **6b** (1.72 g, 6.38 mmol) was reduced with $LiAlH_4$ (484 mg, 12.8 mmol) to give the title compound **2b** (1.25 g, 5.48 mmol, 86%) as a colorless oil after chromatography (SiO_2, MTB–PE 1 : 1, R_f = 0.34). – $[\alpha]_D^{23}$ = +117 (c 2.3, $CHCl_3$); ref. [4c]: +104 (c 2.16, $CHCl_3$).

$C_{15}H_{16}O_2$	Calcd.:	C 78.92	H 7.06
(228.29)	Found:	C 78.41	H 7.05.

(S)-(–)-2-Benzyloxypropyl 4-toluenesulfonate (**7a**)

TosCl (1.09 g, 5.72 mmol) was added to a solution of alcohol **2a** (475 mg, 2.86 mmol) in pyridine (4 ml), and the resulting mixture was stirred over night at ambient temperature. After addition of water (30 ml) and extraction with CH_2Cl_2 (three times 30 ml) the combined organic layers were washed with hydrochloric acid (18%, two times 50 ml) and brine (50 ml), dried ($MgSO_4$), and evaporated. Column chromatography of the residue (SiO_2, MTB–PE 1 : 1, R_f = 0.44) yielded the title compound **7a** (864 mg, 2.70 mmol, 94%) as a yellowish oil. – $[\alpha]_D^{23}$ = –4.0 (c 4.3, MeOH); ref. [11b]: –2.80 (c 4.43, MeOH). – ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$): δ/ppm = 16.66 (CH_3), 21.56 (CH_3), 71.21 (CH_2), 72.28 (CH), 72.62 (CH_2), 127.52 (2CH), 127.58 (CH), 127.86 (2CH), 128.27 (2CH), 129.75 (2CH), 132.88 (C), 138.01 (C), 144.71 (C).

$C_{17}H_{20}O_4S$	Calcd.:	C 63.73	H 6.29
(320.41)	Found:	C 63.75	H 6.32.

(S)-(+)-2-Benzyloxy-2-phenylethyl 4-toluenesulfonate (**7b**)

According to the previous procedure for **7a** the alcohol **6b** (274 mg, 1.20 mmol) was converted with TosCl (458 mg, 2.40 mmol) to yield the title compound **7b** (428 mg, 1.12 mmol, 93%) as a colorless oil after chromatography (SiO_2, MTB–PE 1 : 2, R_f = 0.34). – $[\alpha]_D^{23}$ = +75 (c 2.1, $CHCl_3$); ref. [5c]: +66.6 (c 2.20, $CHCl_3$).

$C_{22}H_{22}O_4S$	Calcd.:	C 69.09	H 5.80
(382.48)	Found:	C 68.98	H 5.85.

(S,S)-(–)-Bis(2-benzyloxy-1-propyl)-ether (**8**)

Under an inert atmosphere solutions of tosylate **7a** (320 mg, 1.00 mmol) in DMF (1 ml) and alcohol **2a** (166 mg, 1.00 mmol) in DMF (1 ml) were added to NaH (60.0 mg of a 80% dispersion in mineral oil, 2.00 mmol) at ambient temperature. The mixture was stirred for 3 h at 50 °C, water (10 ml) was added, and after extraction with MTB (three times 25 ml) the combined organic layers were washed with water (two times 50 ml) and brine (50 ml), dried ($MgSO_4$), and evaporated. Column chromatography of the residue (SiO_2, MTB–PE 1 : 3, R_f = 0.40) yielded the title compound **8** (230 mg, 0.732 mmol, 73%) as a colorless oil. – $[\alpha]_D^{23}$ = –0.476 (c 10.5, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.20 (d, J = 6.3 Hz, 6H), 3.46 (dd, J = 10.1 Hz, J = 4.6 Hz, 2H), 3.56 (dd, J = 10.1 Hz, J = 6.1 Hz, 2H), 3.69–3.79 (m, 2H), 4.62 (s, 4H), 7.20–7.40 (m, 10H). – ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$): δ/ppm = 17.05 ($2CH_3$), 70.88 ($2CH_2$), 73.71 (2CH), 75.39 ($2CH_2$), 127.15 (2CH), 127.32 (4CH), 128.05 (4CH), 138.76 (2C). – IR (ATR): $\tilde{\nu}$/cm^{-1} = 2971 (s), 2867 (s), 1496 (s), 1453 (s), 1374 (s), 1343 (s), 1112 (vs), 1062 (vs), 1028 (s), 696 (vs). – $C_{20}H_{26}O_3$ (314.42): mol. mass calcd. 223.1334 (for $C_{13}H_{19}O_3$), found 223.1339 ($M^+ - C_7H_7$).

(S,S)-(+)-Bis(2-hydroxypropyl)-ether (**1a**)

A mixture of ether **8** (63.0 mg, 0.200 mmol) and Pd–C (25.0 mg, 10% Pd) in EtOH (2 ml) was stirred over night at ambient temperature under an atmosphere of H_2 (1 bar). After filtration through SiO_2 and washing of the residue with MTB evaporation of the solvent yielded diol **1a** (24.0 mg, 0.179 mmol, 90%) as a colorless oil. – $[\alpha]_D^{23}$ = +42 (c 2.3, $CHCl_3$).

(S,S)-(–)-Bis(2-benzyloxypropyl)-thioether (**9a**)

In a tightly closed reaction flask a mixture of tosylate **7a** (843 mg, 2.63 mmol), Na_2S-hydrate (65%, 258 mg, 2.15 mmol), and DMF (2 ml) was heated over night at 50 °C. MTB (30 ml) was added and the solution was washed with water (three times 30 ml), dried ($MgSO_4$), and evaporated. Column chromatography of the residue (SiO_2, MTB–PE 1 : 10, R_f = 0.36) yielded thioether **9a** (401 mg, 1.21 mmol, 92%) as a colorless oil. – $[\alpha]_D^{23}$ = –2.30 (c 16.5, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.28 (d, J = 6.2 Hz, 6H), 2.60 (dd, J = 13.2 Hz, J = 6.3 Hz, 2H), 2.81 (dd, J = 13.2 Hz, J = 5.7 Hz, 2H), 3.62–3.74 (m, 2H), 4.51 (d, J = 11.8 Hz, 2H), 4.57 (d, J = 11.8 Hz, 2H), 7.22–7.38 (m, 10H). – ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$): δ/ppm = 19.13 ($2CH_3$), 38.95 ($2CH_2$), 70.50 ($2CH_2$), 74.77 (2CH), 127.29 (2CH), 127.42 (4CH), 128.11 (4CH), 138.44 (2C). – IR (ATR): $\tilde{\nu}$/cm^{-1} =

1132 (s), 1089 (vs), 1072 (vs), 1028 (s), 696 (vs). – $C_{20}H_{26}O_2S$ (333.49): mol. mass calcd. 330.1654 (for $C_{20}H_{26}O_2S$), found 330.1651 (M^+).

(S,S)-(+)-Bis(2-benzyloxy-2-phenylethyl)-thioether (**9b**)

Following the previous procedure for **9a** tosylate **7b** (764 mg, 2.00 mmol) and Na_2S-hydrate (65%, 312 mg, 2.60 mmol) were converted in acetone (3 ml) at 70 °C to yield the thioether **9b** (386 mg, 0.849 mmol, 85%) as a colorless oil after chromatography (SiO_2, MTB–PE 1 : 10, R_f = 0.29). – $[\alpha]_D^{23}$ = +110 (c 3.0, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 2.72 (dd, J = 5.0 Hz, J = 13.6 Hz, 2H), 2.97 (dd, J = 13.6 Hz, J = 8.1 Hz, 2H), 4.28 (d, J = 11.9 Hz, 2H), 4.46 (dd, J = 8.1 Hz, J = 5.0 Hz, 2H), 4.47 (d, J = 11.9 Hz, 2H), 7.20–7.46 (m, 20H). – ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$): δ/ppm = 40.57 ($2CH_2$), 70.60 ($2CH_2$), 81.67 (2CH), 126.83 (4CH), 127.49 (2CH), 127.74 (4CH), 127.95 (2CH), 128.29 (4CH), 128.46 (4CH), 138.22 (2C), 140.97 (2C). – IR (ATR): ν/cm^{-1} = 1092 (s), 697 (vs). – $C_{30}H_{30}O_2S$ (454.63): mol. mass calcd. 545.2514 (for $C_{37}H_{37}O_2S$), found 545.2521 ($M^+ + C_7H_7$).

(S)-(+)-2-Benzyloxy-1-iodo-2-phenyl-ethane (**7c**)

NaI (150 mg, 1.00 mmol) was added to a solution of tosylate **7b** (182 mg, 0.467 mmol) in DMF (1 ml). The mixture was heated over night in a tightly closed reaction flask to 70 °C, and subsequently chromatographed on SiO_2 (MTB–PE 1 : 5, R_f = 0.55) to yield the iodo-derivative **7c** (127 mg, 0.376 mmol, 79%) as a colorless oil. – $[\alpha]_D^{23}$ = +93 (c 4.6, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 3.36 (dd, J = 4.5 Hz, J = 10.4 Hz, 1H), 3.43 (dd, J = 10.4 Hz, J = 8.5 Hz, 1H), 4.36 (d, J = 11.6 Hz, 1H), 4.50 (dd, J = 8.5 Hz, J = 4.5 Hz, 1H), 4.53 (d, J = 11.6 Hz, 1H), 7.26–7.44 (m, 10H). – ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$): δ/ppm = 10.45 (CH_2), 71.10 (CH_2), 81.05 (CH), 126.70 (2CH), 127.72 (CH), 127.93 (2CH), 128.33 (2CH), 128.47 (CH), 128.73 (2CH), 137.69 (C), 139.89 (C). – IR (ATR): ν/cm^{-1} = 1090 (s), 734 (s), 696 (vs). – Mol. mass calcd. 338.0168 (for $C_{15}H_{15}IO$), found 338.0166 (M^+).

(S)-2-Benzyloxy-2-phenylethyl trifluoromethanesulfonate (**7d**)

Under an atmosphere of argon pyridine (79.1 mg, 1.00 mmol) was added to a solution of alcohol **2b** (228 mg, 1.00 mmol) in CH_2Cl_2 (2 ml) at 0 °C and the mixture was stirred for 30 min. Subsequently, $(CF_3SO_2)_2O$ (125 mg, 0.543 mmol) was added dropwise at 0 °C, and the mixture was stirred over night at ambient temperature. After addition of water (10 ml) and extraction with MTB (three times 20 ml) the combined organic layers were washed with saturated aqueous NH_4Cl-solution (30 ml) and brine (30 ml), dried ($MgSO_4$), and evaporated. The residue was chromatographed on SiO_2 (MTB–PE 1 : 5, R_f = 0.40) to yield the triflate **7d** (46.0 mg, 0.128 mmol, 24%) as a yellowish oil, which decomposed at ambient temperature within hours, and even at –20 °C within days. – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 4.39 (d, J = 12.0 Hz, 1H), 4.47 (dd, J = 10.6 Hz, J = 3.0 Hz, 1H), 4.52–4.68 (m, 2H), 4.73 (dd, J = 8.4 Hz, J = 3.0 Hz, 1H), 7.15–7.47 (m, 10H). – ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$): δ/ppm = 70.81 (CH_2), 78.05 (CH_2), 78.14 (CH), 127.15 (2CH), 127.76 (2CH), 127.90 (CH), 128.45 (2CH), 129.05 (2CH), 129.23 (CH), 135.47 (C), 137.17 (C).

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