Thiazole Masked Chiral Butanals from D-Glyceraldehyde Acetonide and 2-Trimethylsilylthiazole

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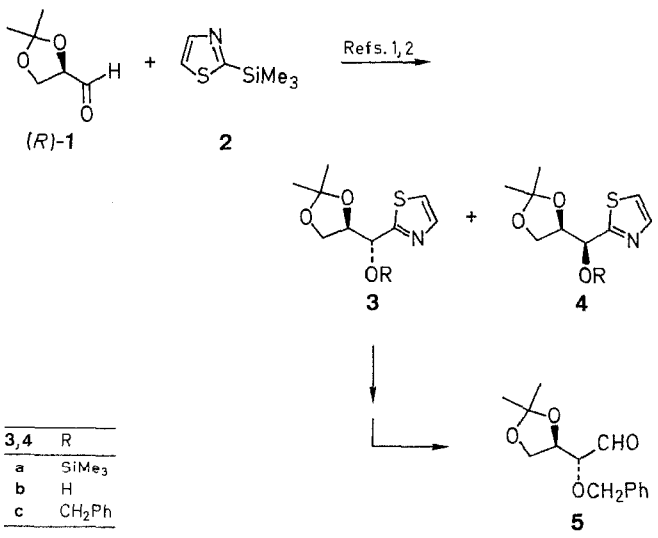
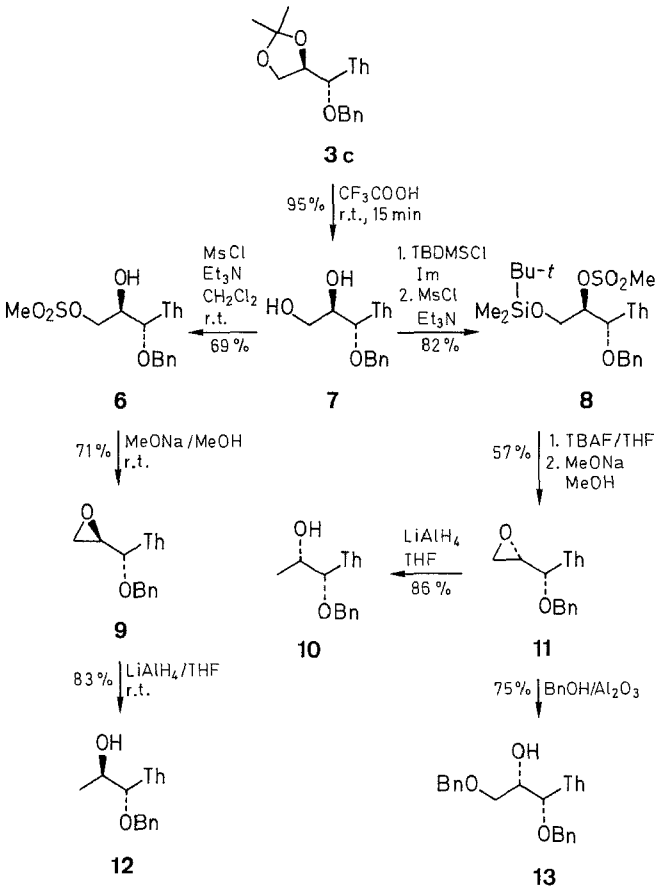
1,2-*O*-Isopropylidene-3-(2-thiazolyl) glycerol **3** (thiazole D-erythrose) obtained from (*R*)-2,3-*O*-isopropylideneglyceraldehyde **(1)** and 2-trimethylsilylthiazole **(2)** is elaborated into thiazole-masked chiral hydroxy-, epoxy-, and azidobutanals.

We reported earlier[1,2] that the reaction of (*R*)-2,3-*O*-isopropylideneglyceraldehyde[3] **(1)** with 2-trimethylsilylthiazole **(2)** proceeds with high degree of diastereoselectivity (ds ≥ 95%) affording the *anti*-adduct **3a**; this is desilylated *in situ* to the thiazolyl glycerol acetonide **3b**, which is isolated in excellent yield.[4] Releasing the aldehyde from the thiazole nucleus in the protected *O*-benzyl derivative **3c**, produced (*R*)-3,4-*O*-isopropylidene-2-*O*-benzylerythrose **(5)** in good overall yield. The iterative repetition of this thiazole-mediated one-carbon extension (Thiazole Route) over five more cycles converted **3c** into a series of *anti* 1,2-glycitols up to a C-9 term sequence.[2] We would like to report here some selective hydroxy group elaborations of thiazolyl glycerols **3b, c** to give functionalized chiral butanals which may serve as building blocks of biologically



3,4	R
a	$SiMe_3$
b	H
c	CH_2Ph

active molecules.[5] Unfortunately, the application of these concepts to the *syn*-diastereomer **4** is somewhat conditioned by its low availability due to the profound *anti*-selectivity of the addition of **2** to **1** under various conditions.[6]

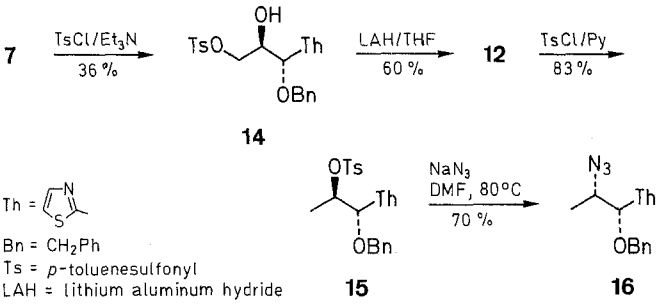


Th = , Bn = CH_2Ph, TBDMS = *tert*-butyldimethylsilyl, Im = imidazole, Ms = methanesulfonyl, TBAF = tetrabutylammonium fluoride

Scheme A

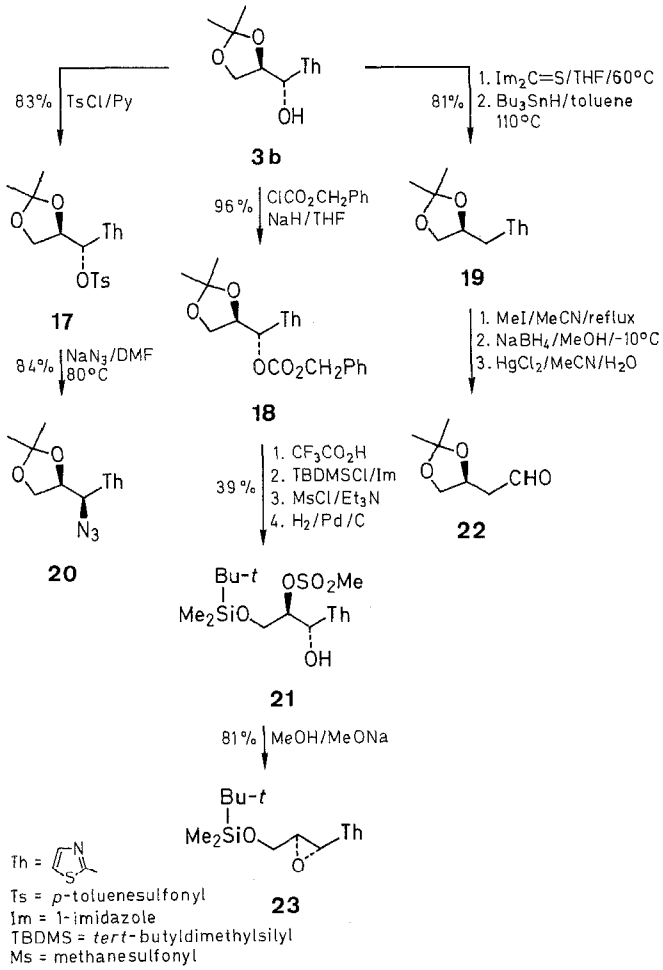
The 1,3-dioxolane ring cleavage by trifluoroacetic acid of the *O*-benzyl derivative **3c** gave the thiazolyl glycerol **7** which was used as a common precursor to the diastereomeric epoxy alcohols **9** and **11** (Scheme A). To this end, the primary hydroxy group of **7** was protected as *O*-mesylate (mesyl chloride[7] in dichloromethane/triethylamine) to give **6**, which upon treatment with sodium methoxide in methanol afforded the thiazolyl *anti*-2,3-epoxypropanol **9** in ca. 70% yield. On the other hand, the sequential silylation (*tert*-butyldimethylsilyl chloride in dichloromethane/imidazole[8]) and mesylation of **7** gave the *O*-mesylate **8** which on treatment with tetrabutylammonium fluoride in tetrahydrofuran and then with sodium methoxide in methanol produced the thiazolyl *syn*-2,3-epoxypropanol **11** in ca. 57% yield.[9] The absolute configuration at the chiral centre of the oxirane ring in the diastereomeric epoxy alcohols **9** and **11** was assigned on the basis of the reasonable assumption that they arised from the respective precursors by intramolecular S_N2 reaction. Consistent ^{1}H-NMR data were in fact obtained as the H-1 signal of the *anti*-product **9** was at $\delta = 4.91$ ($J = 3.2$ Hz) whereas that of the *syn*-product was at $\delta = 4.51$ ppm ($J = 5.2$ Hz). Interestingly enough, compound **11** appears to be a potential precursor towards L-sugars through our iterative thiazole-mediated extension procedure[2]. Homologation should be feasible starting either from **11** or from thiazole L-threose **13** which was obtained from the latter by oxirane ring opening using benzyl alcohol absorbed over aluminum oxide.[10] It is worth noting that **13** is the formal *syn*-adduct of 2-trimethylsilylthiazole (**2**) to L-glyceraldehyde,[11] namely, the product of the so far elusive stereochemical outcome in reactions of **2** with polyoxygenated aldehydes.

The reductive oxirane ring cleavage of epoxides **9** and **11** with lithium aluminum hydride in tetrahydrofuran afforded thiazole deoxy-D-erythrose **12** and L-threose **10** respectively in 80–90% yield.[12] The stereochemistry of **12** and by inference of its precursor **9**, was confirmed by its preparation by a more direct route (Scheme B) starting from the *O*-benzyl thiazolyl glycerol **7** *via* the *O*-tosylate **14**. Compound **12** was readily transformed through the *O*-tosylate **15** into the azide **16**, namely a potential precursor to 3,4-dideoxy-3-amino-L-threose.



Th = , Bn = CH_2Ph
Ts = *p*-toluenesulfonyl
LAH = lithium aluminum hydride

Scheme B



Th =
Ts = *p*-toluenesulfonyl
Im = 1-imidazole
TBDMS = *tert*-butyldimethylsilyl
Ms = methanesulfonyl

Scheme C

In Scheme **C** are presented some hydroxy group elaborations starting from the thiazolyl glycerol **3b**. Since various attempts at debenzylation of **8** (Scheme **A**) failed under standard conditions, **3b** was protected as benzyloxycarbonyl derivative **18**.[13]

The 1,3-dioxolane ring cleavage in **18** followed by sequential silylation and mesylation as described for the conversion of **7** into **8** and reductive cleavage of the *O*-benzyloxycarbonyl group, gave the key intermediate **21**, which upon treatment with sodium methoxide in methanol afforded the chiral *O*-silylated 2,3-epoxy alcohol **23** (81 % yield). Also in this case the stereochemistry at the oxirane ring was assigned by similar reasonings as for **9** and **11**. Tosylation of **3b** under standard conditions followed by reaction of the resulting *O*-tosylate **17** with sodium azide in dimethylformamide afforded the azide **20**, a potential precursor of 2-deoxy-2-amino-D-threose. Finally, deoxygenation of **3b** by thiocarbonyldiimidazole and tributyltin hydride according to the Barton procedure[14] gave the thiazole masked (*R*)-3,4-dihydroxybutanal acetonide **19**, which was converted into the aldehyde **22**.[1,2,4]

In conclusion, the synthetic Schemes **A, B,** and **C** show relatively straightforward elaborations of the *O*-protected thiazolyl glycerols **3b** and **3c** into various chiral substrates which, by virtue of the thiazole-formyl equivalence, can be considered as functionalized masked butanals. In particular, masked epoxy aldehydes[15] **9, 11,** and **23** should by useful starting materials in a variety of asymmetric syntheses,[12,15,16] where the formyl group has to be protected and deblocked under neutral conditions.

All melting points are uncorrected. ^{1}H-NMR spectra were obtained on a 80 MHz Bruker WP80 spectrometer. Chemical shifts are given in parts per million from TMS. Mass spectra were recorded at 70 eV on a Varian Mat CH7 high-resolution mass spectrometer. IR spectra were obtained on a Perkin Elmer 297 grating spectrophotometer.

(2*R*,3*R*)-1,2-*O*-Isopropylidene-3-(2-thiazolyl)-1,2,3-propanetriol **(3b)** was obtained via the 3-*O*-trimethylsilyl derivative **3a** from (*R*)-2,3-isopropylideneglyceraldehyde **(1)** and 2-trimethylsilylthiazole **(2)** as described.[2] Benzylation of **3b** to **3c** and unmasking of the formyl from thiazole to give (2*R*,3*R*)-1,2-*O*-isopropylidene-3-*O*-benzyl-D-erythrose **(5)** was carried out as reported.[2]

All experiments were carried out under nitrogen atmosphere and with freshly distilled and dried solvents.

(2*R*,3*R*)-3-Benzyloxy-3-(2-thiazolyl)-1,2,3-propanetriol (7); Typical Procedure:

A solution of 99 % CF_3CO_2H (2 mL) and water (0.2 mL) is added to the 1,3-dioxolane derivative **3c** (0.5 g, 1.6 mmol) at 0 °C. After stirring for 15 min, the mixture is neutralized with $NaHCO_3$ and extracted with EtOAc (2 × 30 mL). The organic layer is dried (Na_2SO_4), and the solvent is removed *in vacuo* to give the crude diol **7**, which is crystallized from EtOAc/*n*-hexane; yield: 0.4 g (95 %); mp 65–67 °C.

$C_{13}H_{15}NO_3S$	calc.	C 58.86	H 5.70	N 5.28
(265.3)	found	58.89	5.72	5.30

^{1}H-NMR ($CDCl_3/D_2O$): δ = 3.71 (d, 2 H, J = 4 Hz, CH_2OD); 3.97 (m, 1 H, CHOD); 4.65 (d, 2 H, J = 2 Hz, $OC\underline{H}_2Ph$); 4.85 (d, 1 H, J = 6.4 Hz, C$\underline{H}$OBn); 7.32 (m, 6 H, C_6H_5, + 5 H_{th}); 7.72 (d, 1 H, J = 3.3 Hz, 4-H_{th}).

(2*R*,3*R*)-3-Benzyloxy-1-methylsulfonyloxy-3-(2-thiazolyl)-1,2,3-propanetriol (6); Typical Procedure:

A solution of Et_3N (0.67 mL, 4.8 mmol) in CH_2Cl_2 (10 mL) is added dropwise to a solution of the diol **7** (1 g, 3.7 mmol) and CH_3SO_2Cl (0.37 mL, 4.8 mmol) in the same solvent (30 mL). After stirring for 12 h, the mixture is washed with brine (2 × 10 mL). The organic layer is dried (Na_2SO_4), the solvent removed *in vacuo* and the residue chromatographed on silica gel (eluent: CH_2Cl_2/EtOAc, 8:2) to give the *O*-mesylate **6**; yield: 0.89 g (69 %); oil.

$C_{14}H_{17}NO_5S_2$	calc.	C 48.98	H 4.99	N 4.08
(343.4)	found	50.01	5.00	4.10

^{1}H-NMR ($CDCl_3$): δ = 3.01 (s, 3 H, CH_3); 3.92 (br, 1 H, OH); 4.15 (m, 1 H, C$\underline{H}$OH); 4.38 (d, 2 H, J = 4 Hz, CH_2OMs); 4.65 (AB quartet, 2 H, $OC\underline{H}_2Ph$); 4.8 (d, 1 H, J = 6.8 Hz, C$\underline{H}$OBn); 7.3 (m, 6 H, C_6H_5 + 5-H_{Th}); 7.72 (d, 1 H, J = 3 Hz, 4-H_{Th}).

(2*R*,3*R*)-3-Benzyloxy-1-*tert*-butyldimethylsilyloxy-2-methylsulfonyloxy-3-(2-thiazolyl)-1,2,3-propanetriol (8):

Step 1:

To a solution of the diol **7** (2.24 g, 8.45 mmol) and dimethyl-*tert*-butylsilyl chloride (1.39 g, 9.3 mmol) in CH_2Cl_2 (50 mL) is added imidazole (0.63 g, 9.3 mmol) in one portion. After stirring for 4 h, the mixture is washed with brine (2 × 20 mL). The organic layer is dried (Na_2SO_4), the solvent removed *in vacuo* and the residue chromatographed on silica gel (eluent: cyclohexane/ether, 9:1) to give the 1-*tert*-butyldimethylsilyloxy derivative of **7**; yield: 2.7 g (84 %); oil.

^{1}H-NMR ($CDCl_3/D_2O$): δ = 0.05 (s, 6 H, Me_2Si); 0.87 (s, 9 H, *t*-BuSi); 3.71 (m, 2 H, CH_2O); 3.9 (m, 1 H, CHOD); 4.52 (AB quartet, 2 H, $OC\underline{H}_2Ph$); 4.8 (d, 1 H, J = 6 Hz, C$\underline{H}$OBn); 7.23 (m, 6 H, C_6H_5 + 5-H_{Th}); 7.71 (d, 1 H, J = 3.2 Hz, 4-H_{Th}.

Step 2:

A solution of the 1-*tert*-butyldimethylsiloxy derivative of **7** (2.7 g, 7.1 mmol) and CH_3SO_2Cl (0.66 mL, 8.5 mmol) in CH_2Cl_2 (50 mL) is treated dropwise with a solution of Et_3N (1.2 mL, 8.6 mmol). After 2 h, the mixture is worked up as above for compound **6**, and the residue is chromatographed on silica gel (eluent: CH_2Cl_2/ether, 9:1) to give the protected triol **8**; yield: 3.18 g (98 %); oil.

$C_{20}H_{31}NO_5SiS_2$	calc.	C 52.48	H 6.83	N 3.06
(457.7)	found	52.45	6.85	3.03.

^{1}H-NMR ($CDCl_3$): δ = 0.045 (s, 6 H, Me_2Si); 0.86 (s, 9 H, *t*-BuSi); 2.92 (s, 3 H, CH_3SO_2); 3.8 (m, 2 H, CH_2O); 4.62 (s, 2 H, $OC\underline{H}_2Ph$); 5.05 (m, 2 H, C$\underline{H}$OMs + C$\underline{H}$OBn); 7.25 (m, 5 H, C_6H_5); 7.3 (d, 1 H, J = 3.2 Hz, 5-H_{Th}); 7.72 (d, 1 H, J = 3.2 Hz, 4-H_{Th}).

(1*R*,2*R*)-1-Benzyloxy-2,3-epoxy-1-(2-thiazolyl)propanol (9); Typical Procedure:

To a solution of the *O*-mesylate **6** (0.46 g, 1.34 mmol) in MeOH (20 mL) is added NaOMe (0.08 g, 1.48 mmol). After stirring for 2 h at room temperature the solvent is removed under vacuum and the residue chromatographed on silica gel (eluent: CH_2Cl_2/EtOAc, 8:2) to give the epoxide **9**; yield: 0.23 g (71 %); oil; $[\alpha]_D^{25}$ + 96.0° (c = 2.8, $CHCl_3$).

$C_{13}H_{13}NO_2S$	calc.	C 63.15	H 5.30	N 5.67
(247.3)	found	63.11	5.32	5.69

^{1}H-NMR ($CDCl_3$): δ = 2.73 (d, 2 H, J = 3.4 Hz, CH_2O); 3.41 (q, 1 H, J = 3.2 Hz, CHO); 4.62 (s, 2 H, $OC\underline{H}_2Ph$); 4.91 (d, 1 H, J = 3.2 Hz, C$\underline{H}$OBn); 7.29 (m, 6 H, C_6H_5 + 5 H_{Th}); 7.72 (d, 1 H, J = 3.2 Hz, 4-H_{Th}).

MS: m/z (%) = 247 (M^+, 10); 141 (35); 112 (52); 91 (100).

(1*R*,2*S*)-1-Benzyloxy-2,3-epoxy-1-(2-thiazolyl)propanol (11):

Step 1:

The *O*-trialkylsilyl derivative **8** (1.2 g, 2.6 mmol) is treated with 1 M THF solution of Bu_4NF (2.6 mL, 2.6 mmol) diluted with THF (20 mL). After 2 h stirring, the solvent is removed under vacuum and water is added (20 mL). The mixture is extracted with CH_2Cl_2 (2 × 20 mL), the organic layer is dried (Na_2SO_4), and the solvent removed *in vacuo*. Chromatography of the residue on silica gel (eluent: CH_2Cl_2/EtOAc, 8:2) gives the desilylated product of **8**; yield: 0.75 g (84 %); oil.

^{1}H-NMR ($CDCl_3/D_2O$): δ = 2.92 (s, 3 H, CH_3); 3.78 (m, 2 H, CH_2OD); 4.64 (s, 2 H, $OC\underline{H}_2Ph$); 5.1 (m, 2 H, C$\underline{H}$OMs + C$\underline{H}$OBn); 7.27 (s, 5 H, C_6H_5); 7.34 (d, 1 H, J = 3.2 Hz, 5-H_{Th}); 7.74 (d, 1 H, J = 3.2 Hz, 4-H_{Th}).

Step 2:

A solution of the desilylated compound (0.34 g, 1 mmol) and NaOMe (0.067 g, 1.2 mmol) in MeOH (10 mL) is stirred for 2 h at room temperature and the solvent evaporated. Chromatography of the residue on silica gel (eluent: CH_2Cl_2/EtOAc; 8:2) affords the epoxide **11**; yield: 0.17 g (68 %); oil; $[\alpha]_D^{25}$ + 14.1° (c = 1.74, $CHCl_3$).

$C_{13}H_{13}NO_2S$	calc.	C 63.15	H 5.30	N 5.67
(247.3)	found	63.17	5.31	5.66

^{1}H-NMR ($CDCl_3$): δ = 2.87 (d, 2 H, J = 2.2 Hz, CH_2O); 3.37 (m, 1 H, CHO); 4.51 (d, 1 H, J = 5.2 Hz, C$\underline{H}$OBn); 4.77 (s, 2 H, $OC\underline{H}_2Ph$); 7.36 (m, 6 H, C_6H_5 + 5 H_{Th}); 7.79 (d, 1 H, J = 3.2 Hz, 4-H_{Th}).

Reductive Opening of the Epoxides 9 and 11; Typical Procedure:
To a suspension of $LiAlH_4$ (16 mg, 0.4 mmol) in THF (2 mL) is added a solution of the epoxide **9** or **11** (90 mg, 0.35 mmol) in the same solvent (3 mL). After 30 min stirring, the mixture is diluted with ether (10 mL) and water is added (0.1–0.2 mL). After filtration, the solvent is removed *in vacuo* and the residue chromatographed on silica gel (eluent: CH_2Cl_2/EtOAc, 8:2) to give the corresponding alcohol **12** and **10**.

(1R,2R)-1-Benzyloxy-1-(2-thiazolyl)-1,2-propanediol **(12)**; yield: 71 mg (83%); oil; $[\alpha]_D^{25}$ +86.2° (c = 0.98, $CHCl_3$).

$C_{13}H_{15}NO_2S$	calc.	C 62.64	H 6.07	N 5.62
(249.3)	found	62.68	6.09	5.64

^{1}H-NMR ($CDCl_3$): δ = 1.16 (d, 3H, J = 8.4 Hz, CH_3); 3.5 (br, 1H, OH); 4.12 (m, 1H, CHOH); 4.61 (AB quartet, 2H, OCH_2Ph); 4.66 (d, 1H, J = 5.0 Hz, CHOBn); 7.34 (m, 6H, C_6H_5 + 5-H_{Th}); 7.79 (d, 1H, J = 3.5 Hz, 4-H_{Th}).

MS: m/z (%) = 249 (M^+, 5); 205 (8); 143 (15); 125 (25); 114 (100); 91 (87).

(1R,2S)-1-Benzyloxy-1-(2-thiazolyl)-1,2-propanediol **(10)**; yield: 75 mg (86%); oil; $[\alpha]_D^{25}$ +85.1° (c = 1.416, $CHCl_3$).

$C_{13}H_{15}NO_2S$	calc.	C 62.64	H 6.07	N 5.62
(249.3)	found	62.69	6.06	5.63

^{1}H-NMR ($CDCl_3$): δ = 1.11 (d, 3H, J = 6.4 Hz, CH_3); 3.25 (br, 1H, OH); 3.83 (m, 1H, CHOH); 4.6 (m, 3H, CHOBn + OCH_2Ph); 7.34 (m, 6H, C_6H_5, + 5-H_{Th}); 7.78 (d, 1H, J = 3.2 Hz, 4-H_{Th}).

MS: m/z (%) = 249 (M^+, 5); 205 (20); 143 (35); 125 (60); 114 (85); 91 (100).

(2S,3R)-1,3-Dibenzyloxy-3-(2-thiazolyl)-1,2,3-propanetriol (13):
Benzyl alcohol (0.21 mL, 2 mmol) is added to a suspension of neutral Al_2O_3 (2 g) in ether (20 mL). After stirring for 15 min, a solution of the epoxide **11** (0.1 g, 0.4 mmol) in ether (5 mL) is added. After additional stirring for 2 h, the suspension is filtered off and the Al_2O_3 washed with MeOH (10 mL). The solvent is removed *in vacuo* and the residue is chromatographed on silica gel (eluent: CH_2Cl_2/EtOAc; 8:2) to give the alcohol **13**; yield: 0.106 g (75%); oil; $[\alpha]_D^{25}$ +15.4° (c = 0.55, $CHCl_3$).

$C_{20}H_{21}NO_3S$	calc.	C 67.59	H 5.96	N 3.94
(355.5)	found	67.61	5.94	3.96

^{1}H-NMR ($CDCl_3/D_2O$): δ = 3.4 (m, 2H, CH_2OBn); 3.81 (m, 1H, CHOD); 4.44 (AB quartet, 2H, OCH_2Ph); 4.51 (s, 2H, OCH_2Ph); 4.77 (d, 1H, J = 4.6 Hz, CHOBn); 7.12 (m, 11H, 2 × C_6H_5 + 5-H_{Th}); 7.59 (d, 1H, J = 3.2 Hz, 4-H_{Th}).

MS: m/z (%) = 355 (M^+, 6); 264 (10); 235 (20); 205 (30); 155 (62); 128 (53); 114 (85); 108 (65); 91 (100).

Synthesis of 12 via the *O*-Tosylate 14:
Step 1:
A solution of Et_3N (1.43 mL, 9.9 mmol) in CH_2Cl_2 (20 mL) is added dropwise to a stirred solution of the diol **7** (1.05 g, 3.96 mmol) and TsCl (0.9 g, 4.32 mmol) in the same solvent (50 mL). After 24 h, the mixture is worked up as above for the mesyl derivative **6** (Typical Procedure). Chromatography of the residue on silica gel (eluent: CH_2Cl_2/EtOAc, 7:3) gives the *O*-tosylate **14**; yield: 0.6 g (36%); mp 63–65°C (from ethyl acetate/*n*-hexane).

14:

$C_{20}H_{21}NO_5S_2$	calc.	C 57.28	H 5.05	N 3.34
(419.5)	found	57.31	5.03	3.36

^{1}H-NMR: δ = 2.4 (s, 3H, CH_3); 3.52 (br, 1H, OH); 4.2 (m, 3H, CH_2O + CHOH); 4.6 (AB quartet, 2H, OCH_2Ph); 4.77 (d, 1H, J = 6.2 Hz, CHOBn); 7.15–7.9 (m, 11H, 9H_{arom} + 5-H_{Th} + 4-H_{Th}).

Step 2:
The reduction of **14** (0.1 g, 0.24 mmol) with $LiAlH_4$ (18 mg, 0.48 mmol) in THF (5 mL) is carried out as described above for the reductive opening of the epoxide **9** and **11**. Usual work-up and chromatography affords **12**; yield: 36 mg (60%).

(1R,2R)-1-Benzyloxy-1-(2-thiazolyl)-2-tosyloxy-1,2-propanediol (15):
A solution of the alcohol **12** (0.2 g, 0.8 mmol), TsCl (0.23 g, 1.2 mmol) in pyridine (2 mL) is stirred overnight. The solvent is removed *in vacuo* and the residue is chromatographed on silica gel (eluent: petroleum ether/EtOAc, 8:2) to give **15**; yield: 0.27 g (83%); oil.

$C_{20}H_{21}NO_4S_2$	calc.	C 59.55	H 5.25	N 3.47
(403.5)	found	59.51	5.23	3.49

^{1}H-NMR ($CDCl_3$): δ = 1.25 (d, 3H, J = 6.4 Hz, CH_3); 2.39 (s, 3H, Ar–CH_3); 4.6 (s, 2H, OCH_2Ph); 4.84 (d, 1H, J = 3.4 Hz, CHOBn); 5.04 (m, 1H, CHOTs); 7.2–7.9 (m, 11H, 9H_{arom} + 5-H_{Th} + 4-H_{Th}).

(1R,2S)-2-Azido-1-benzyloxy-1-(2-thiazolyl)-propanol (16):
A solution of the *O*-tosylate **15** (0.2 g, 0.5 mmol) and NaN_3 (0.1 g, 1.5 mmol) in DMF (3 mL) is heated at 80°C for 1 h. The mixture is diluted with water (20 mL) and extracted with ether (2 × 30 mL). The organic layer is dried (Na_2SO_4), the solvent removed under vacuum. Chromatography of the residue on silica gel (eluent: petroleum ether/EtOAc, 8:2) gives the azido derivative **16**: yield: 96 mg (70%); oil; $[\alpha]_D^{25}$ +109.1° (c = 0.74, $CHCl_3$).

$C_{13}H_{14}N_4OS$	calc.	C 56.93	H 5.15	N 20.43
(274.4)	found	56.97	5.13	20.46

IR (film): ν = 2110 cm^{-1}.

^{1}H-NMR ($CDCl_3$): δ = 1.17 (d, 3H, J = 6.7 Hz, CH_3); 3.77 (m, 1H, CHN_3); 4.58 (AB quartet, 2H, OCH_2Ph); 4.70 (d, 1H, J = 5.8 Hz, CHOBn); 7.35 (m, 6H, C_6H_5 + 5-H_{Th}); 7.80 (d, 1H, J = 3.3 Hz, 4-H_{Th}).
MS: m/z (%) = 274 (M^+, 7); 204 (63); 183 (41); 168 (55); 91 (100).

(2R,3R)-3-*O*-Benzyloxycarbonyl-1,2-*O*-isopropylidene-3-(2-thiazolyl)-1,2,3-propanetriol (18):
To **3b** (3 g, 13.9 mmol) in THF (30 mL) is added portionwise NaH 50% (0.73 g, 15.3 mmol) at room temperature. The mixture is gently refluxed for 20 min and then benzyl chloroformate (3.06 g, 18.0 mmol) in THF (20 mL) is added. After 12 h at room temperature, the solvent is concentrated at reduced pressure, sat. $NaHCO_3$ (20 mL) is added and the mixture is extracted with CH_2Cl_2 (2 × 30 mL). After drying (Na_2SO_4), the solvent is removed *in vacuo* and the residue is chromatographed on silica gel (eluent: cyclohexane/EtOAc, 8:2) giving the *O*-benzyloxycarbonyl derivative **18**; yield: 4.57 g (96%); oil.

$C_{17}H_{19}NO_5S$	calc.	C 58.45	H 5.48	N 4.01
(349.4)	found	58.49	5.50	3.99

^{1}H-NMR ($CDCl_3$): δ = 1.33 (s, 6H, Me_2C), 4.07 (m, 2H, CH_2O), 4.67 (m, 1H, CHO), 5.15 (s, 2H, OCH_2Ph), 6.04 (d, 1H, J = 4.8 Hz, $CHOCO_2$), 7.28 (m, 6H, C_6H_5 + 5-H_{Th}), 7.73 (d, 1H, J = 3.3 Hz, 4-H_{Th}).

(2R,3R)-1-*tert*-Butyldimethylsilyloxy-2-methylsulfonyloxy-3-(2-thiazolyl)-1,2,3-propanetriol (21):
Step 1:
Ring opening of the 1,3-dioxolane ring is carried out as described for the diol **7** (Typical Procedure). Starting from **18** (3 g, 8.7 mmol), CF_3CO_2H (12 mL), and water (1.2 mL), usual work-up and chromatography of the residue on silica gel (eluent: EtOAc/cyclohexane, 7:3) gives the crude glycol; yield: 2.2 g (83%).

^{1}H-NMR ($CDCl_3/D_2O$): δ = 3.73 (d, 2H, CH_2OD); 4.2 (m, 1H, CHOD); 5.15 (s, 2H, OCH_2Ph); 5.98 (d, 1H, J = 6.4 Hz, $CHOCO_2$); 7.3 (m, 6H, C_6H_5 + 5-H_{Th}); 7.7 (d, 1H, J = 3.2 Hz, 4-H_{Th}).

Step 2:
Silylation and mesylation of this product (2.2 g, 7.1 mmol) are carried out as described for **8** to give the totally protected triol; overall yield: 2.74 g (77%); oil.

^{1}H-NMR ($CDCl_3$): δ = 0.05 (s, 3H, Me_2Si); 0.062 (s, 3H, Me_2Si); 0.88 (s, 9H, *t*-Bu); 2.95 (s, 3H, CH_3SO_2); 3.87 (m, 2H, CH_2OSi); 5.15 (m, 3H, OCH_2Ph + CHOMs), 6.22 (d, 1H, J = 4 Hz, $CHOCO_2$), 7.3 (m, 6H, C_6H_5 + 5-H_{Th}); 7.74 (d, 1H, J = 3.2 Hz, 4-H_{Th}).

Step 3:
A solution of the above product (1.8 g, 3.6 mmol) in EtOH (150 mL) is hydrogenated (24 h) over 10% Pd/C (0.2 g). The catalyst is filtered off and the solvent removed *in vacuo*. The residue is chromatographed on silica gel (eluent: CH_2Cl_2/Et_2O, 9:1) to give the alcohol **21**; yield: 0.8 g (61%); oil.

$C_{13}H_{25}NO_5SiS_2$	calc.	C 42.48	H 6.85	N 3.81
(367.6)	found	42.51	6.83	3.79

^{1}H-NMR ($CDCl_3$): δ = 0.04 (s, 3H, Me_2Si); 0.062 (s, 3H, Me_2Si) 0.88 (s, 9H, *t*-Bu); 3.02 (s, 3H, CH_3SO_2); 3.88 (d, 2H, J = 4.6 Hz, CH_2OSi); 4.36 (d, 1H, J = 6.4 Hz, OH); 5.02 (m, 1H, CHOMs); 5.3 (dd, 1H, J = 4 Hz, J = 6.4 Hz, CHOH); 7.28 (d, 1H, J = 3.3 Hz, 5-H_{Th}); 7.70 (d, 1H, J = 3.3 Hz, 4-H_{Th}).

(2R,3R)-1-*tert*-Butyldimethylsilyloxy-2,3-epoxy-3-(2-thiazolyl)propanol (23):
The reaction is carried out by the same procedure for the synthesis of **9**

and **11**. Starting from **21** (0.2 g, 0.5 mmol) and NaOMe (0.32 mg, 0.6 mmol) in MeOH (10 mL), chromatography affords the epoxide **23**; yield: 0.11 g (81%); oil; $[\alpha]_D^{25} - 39.7°$ ($c = 5.5$, $CHCl_3$).

$C_{12}H_{21}NO_2SiS$	calc.	C 53.09	H 7.80	N 5.16
(271.5)	found	53.05	7.82	5.13

^{1}H-NMR ($CDCl_3$): $\delta = 0.1$ (s, 6H, Me_2Si); 0.9 (s, 9H, *t*-Bu); 3.34 (m, 1H, CHO); 3.9 (m, 2H, CH_2OSi); 4.22 (d, 1H, $J = 2$ Hz, CHO); 7.23 (d, 1H, $J = 3.3$ Hz, 5-H_{Th}); 7.66 (d, 1H, $J = 3.3$ Hz, 4-H_{Th}).

(2*R*,3*S*)-3-Azido-1,2-*O*-isopropylidene-3-(2-thiazolyl)-1,2-propanediol (20):

Step 1:

The reaction is carried out as described above for **14** starting from **3b** (0.6 g, 2.8 mmol), TsCl (1 g, 5.6 mmol) in pyridine (3 mL). Chromatography on silica gel (eluent: petroleum ether/EtOAc, 1:1) gives the *O*-tosylate derivative **17**; yield: 0.85 g (83%); mp 84–85°C (from ether/petroleum ether).

$C_{16}H_{19}NO_5S_2$	calc.	C 52.03	H 5.19	N 3.79
(369.5)	found	52.01	5.21	3.77

^{1}H-NMR ($CDCl_3$): $\delta = 1.29$ (s, 6H, Me_2C); 2.36 (s, 3H, $ArCH_3$); 4.02 (d, 2H, $J = 6.4$ Hz, CH_2O); 4.6 (m, 1H, CHO); 5.8 (d, 1H, $J = 5.2$ Hz, CHOTs); 7.2–7.75 (m, 6H, 4 H_{arom} + 4-H_{Th} + 5-H_{Th}).

Step 2:

A solution of the *O*-tosylate **17** (0.3 g, 0.79 mmol) and NaN_3 (0.16 g, 24 mmol) in DMF (3 mL) at 80°C for 40 min gives after work-up (see preparation of **15**) and chromatography on silica gel (eluent: petroleum ether/EtOAc, 1:1) the azide **20**; yield: 0.16 g (84%); oil; $[\alpha]_D^{25} - 44.2°$ ($c = 1.74$, $CHCl_3$).

$C_9H_{12}N_4SO_2$	calc.	C 45.00	H 5.04	N 23.33
(240.3)	found	45.03	5.01	23.35

IR (film): $\nu = 2120\ cm^{-1}$.

^{1}H-NMR ($CDCl_3$): $\delta = 1.40$ (s, 3H, Me_2C); 1.50 (s, 3H, Me_2C); 4.07 (m, 2H, CH_2O); 4.51 (m, 1H, CHO); 4.08 (d, 1H, $J = 7.6$ Hz, CHN_3); 7.38 (d, 1H, $J = 3.2$ Hz, 5-H_{Th}); 7.78 (d, 1H, $J = 3.2$ Hz, 4-H_{Th}).

MS: *m/z* (%) = 240 (M^+, 3); 225 (73); 137 (50); 112 (100); 101 (57); 74 (91).

(*R*)-1,2-*O*-Isopropylidene-3-(2-thiazolyl)-1,2-propanediol (19):

A solution of the alcohol **3b** (2 g, 9.3 mmol) and thiocarbonyldiimidazole (3.3 g, 18.6 mmol) in THF (50 mL) is refluxed for 5 h. The solvent is removed under vacuum and the residue is chromatographed on silica gel (eluent: EtOAc/cyclohexane, 7:3) to give the corresponding thiocarbonate; yield: 3 g (99%). This is dissolved in toluene (100 mL) and slowly added (2 h) to a refluxing solution of Bu_3SnH (3.66 mL, 13.8 mmol) in the same solvent (300 mL). After refluxing for 4 h, the solution is cooled and concentrated *in vacuo*. The residue is extracted with hot MeCN (3 × 50 mL) and the combined extract is washed with hexane (4 × 50 mL) to remove tin-containing compounds. After concentration of the acetonitrile layer *in vacuo*, the crude product is chromatographed on silica gel (eluent: EtOAc/cyclohexane, 1:1) to give the deoxy alcohol **19**; yield: 1.46 g (81%); oil.

$C_9H_{13}NO_2S$	calc.	C 54.26	H 6.58	N 7.03
(199.2)	found	54.29	6.60	7.00

^{1}H-NMR ($CDCl_3$): $\delta = 1.37$ (s, 3H, Me_2C); 1.43 (s, 3H, Me_2C); 3.31 (dd, 2H, $J = 2$ Hz, $J = 6.4$ Hz, CH_2); 3.72 (dd, 1H, $J = 6.4$ Hz, $J = 8.8$ Hz, CH_2O); 4.10 (dd, 1H, $J = 6$ Hz, $J = 8.8$ Hz, CH_2O); 4.47 (m, 1H, CHO); 7.21 (d, 1H, $J = 3.2$ Hz, 5-H_{Th}); 7.69 (d, 1H, $J = 3.2$ Hz, 4-H_{Th}).

2-Deoxy-1,2-*O*-isopropylidene-D-erythrose (22):

A solution of the thiazole-erythrose **19** (1.46 g, 7.3 mmol) and MeI (10.36 g, 73 mmol) in MeCN (25 mL) is heated under reflux until the starting material is totally consumed (12 h). After distillation of the solvent and excess MeI under reduced pressure, the crude thiazolium iodide is dissolved in dry MeOH (20 mL) and treated with $NaBH_4$ (0.41 g, 11 mmol) at −10°C. After 30 min, acetone (2 mL) is added, the solvent is removed by distillation and the residue treated with brine (30 mL). After extraction with EtOAc (3 × 30 mL), the organic layer is dried (Na_2SO_4). Distillation of the solvent furnishes the crude thiazolidine, which is dissolved in MeCN (3 mL) and slowly added to a solution of $HgCl_2$ (2.38 mg, 8.8 mmol) in 4:1 MeCN/water (30 mL). The mixture is stirred for 30 min and then filtered. The filtrate is evaporated to dryness and the residue treated with water (30 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The solvent is evaporated and the residue chromatographed on silica gel (eluent: Et_2O/cyclohexane; 7:3) to give the deoxy-D-erythrose **22**; yield: 0.63 g (60%); oil; $[\alpha]_D^{25} - 3.1°$ ($c = 1.25$, $CHCl_3$).

$C_7H_{12}O_3$	calc.	C 58.31	H 8.39	
(144.2)	found	58.35	8.37	

IR (film): $\nu = 1735\ cm^{-1}$.

^{1}H-NMR ($CDCl_3$): $\delta = 1.35$ (s, 3H, Me_2C); 1.42 (s, 3H, Me_2C); 2.73 (m, 2H, CH_2); 3.57 (dd, 1H, $J = 6.4$ Hz, $J = 8$ Hz, CH_2O); 4.16 (dd, 1H, $J = 6$ Hz, $J = 8$ Hz, CH_2O); 4.45 (m, 1H, CHO); 9.77 (t, 1H, $J = 1.6$ Hz, CHO).

MS: *m/z* (%) = 144 (M^+, 5); 129 (17); 83 (25); 69 (100).

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