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Another mode of heterocyclization of an enantiopure C_2-symmetric bis-epoxide leading to the symmetric dialkyl sulfide

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ABSTRACT

Reexamination of heterocyclization of an enantiopure C_2-symmetric bis-epoxide (**7**) with sodium sulfide is described. In addition to the reported processes leading to thiane (**4a**) and thiepane (**6**), another mode of cyclization was found to occur to a considerable extent, affording a symmetric dialkyl sulfide (**5**), and the structure of the main product reported (**4a**) has been revised. Conditions for the chemoselective formation of **6** were established, and effective transformation of **6** into **4** was accomplished by the modification of the processes.

1. Introduction

Sugars including intracyclic hetero atom possess unique physicochemical properties and exhibit remarkable biological activities.[1] For example, these sugar-mimics that inhibit glycosidases or glycotransferases may find therapeutic applications to treat various diseases as diabetes, cancer, and viral infections.[1c–e]

A number of synthetic methods utilizing the stereochemistry of sugars, i.e., transformations starting from appropriate sugars, have been reported.[2] Another prominent approach is the base catalyzed heterocyclization of enantiomerically pure bis-epoxides.[3] Among them, Le Merrer et al. reported the preparation of enantiomerically pure sugar-mimics by employing the heterocyclization of C_2-symmetric bis-epoxides. In the reaction, it is reported that three different evolutions occurred after opening of the first epoxide moiety at a minor substituted site as illustrated in Scheme 1.[4] As a continuing study on the structure–activity relationship (SAR) of salacinol,[5,6] a potent α-glucosidase inhibitor bearing the thiosugar moiety, the authors could have synthesized deoxynojirimycin (**2**) efficiently by employing this method, and led **2** to a salacinol aza-analog (**3**).[6g] However, attempts to synthesize the corresponding thio-analog 1,5-dideoxy-1,5-epithio-D-glucitol (**4b**), according to their protocol[4b,c] revealed that structure of the main product reported (**4a**) was incorrect, the product being found to be a symmetrical dimeric isomer, 1,1′-thiobis(2,5-anhydro-3,4-di-*O*-benzyl-D-glucitol) (**5**), via another mode of ring opening process. In this paper is described the rigorous study on this multi-directional reaction including the structure revision of the main product. Optimization of the reaction conditions to improve the chemoselectivity leading to 3,4-di-*O*-benzyl-1,6-dideoxy-1,6-epithio-L-iditol (**6**), and modification of the process to convert thiepane (**6**) into the target thiane (**4b**) are also described (Fig. 1).

2. Results and discussion

Thus, according to the procedure reported,[4b,c] bis-epoxide, 1,2:5,6-dianhydro-3,4-bis-*O*-benzyl-L-iditol[4d] (**7**) was treated with sodium sulfide. Work-up and purification of the products afforded two major compounds in a ratio of ca. 2:1 (Table 1, run 1). ^{1}H and ^{13}C NMR spectroscopic properties of the major product were consistent with those of the compound assigned as **4a** by Le Merrer et al.[4c] The Birch reduction of the product gave the corresponding debenzylated product, the NMR spectroscopic properties of which were also in accord with those of the compound assigned as **4b**.[4c]

An alternative synthesis of thiosugar (**4b**) had already been reported by Yuasa et al.[7a] and its ^{13}C NMR data were listed in Table 2. Szczepina et al. reported the synthesis of **4b**, providing with ^{1}H NMR data assigned also in Table 2.[7b] With respect to these ^{1}H and

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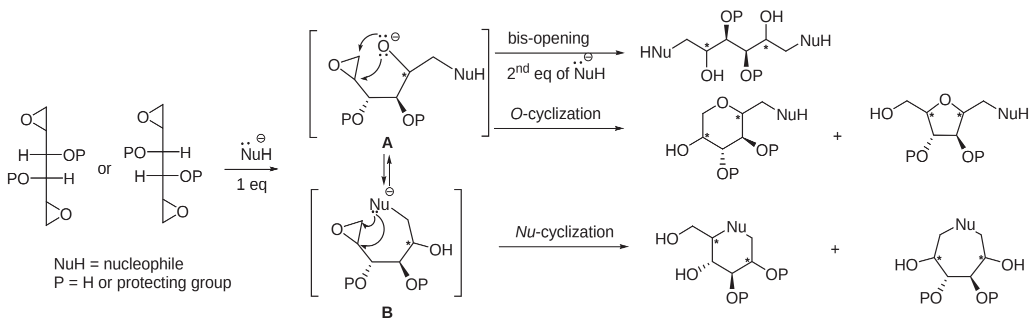


Scheme 1.

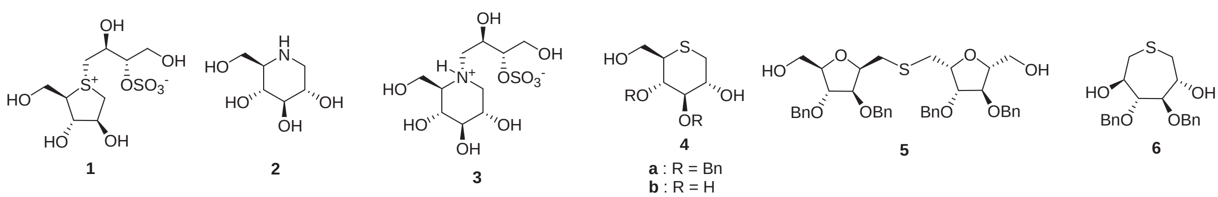


Figure 1.

Table 1
Thiocyclization of epoxide **7** with Na_2S

Run	Solvent	Concentration of **7** (mM)	Time (h)	Product distribution **5**/**6**
1	EtOH	223	<0.5	**5**: 43,[a] **6**: 24[a]
2	EtOH	25	0.5	ca. 1/12[b]
3	MeCN	25	5	Trace/1[b]
4	MeCN–H_2O	22	0.5	**6**: 94[a]

[a] Isolated yield (%).
[b] Product distributions were determined on the basis of ^1H NMR spectrum.

experiments indicated the presence of a carbon chain comprised of six carbons. On the basis of intensive two-dimensional NMR spectroscopic studies, structure of the product was elucidated to be **5** as shown in Scheme 2.

The relative stereo-structure was clarified by ROESY experiments, in which NOE correlations were observed between the proton pairs as shown in Scheme 2. On the basis of above evidences, the absolute stereo-structure of the product was elucidated to be **5**. Thus, signals at δ_C 84.7 and δ_C 81.6 were reasonably assigned as α-carbons to the oxygen in the tetrahydrofuran ring. Small coupling constants between H-2 and H-3 in the ^1H NMR spectrum were also well interpreted.

Table 2
^1H and ^{13}C NMR data for compound **4b** (δ in ppm and J in Hz)

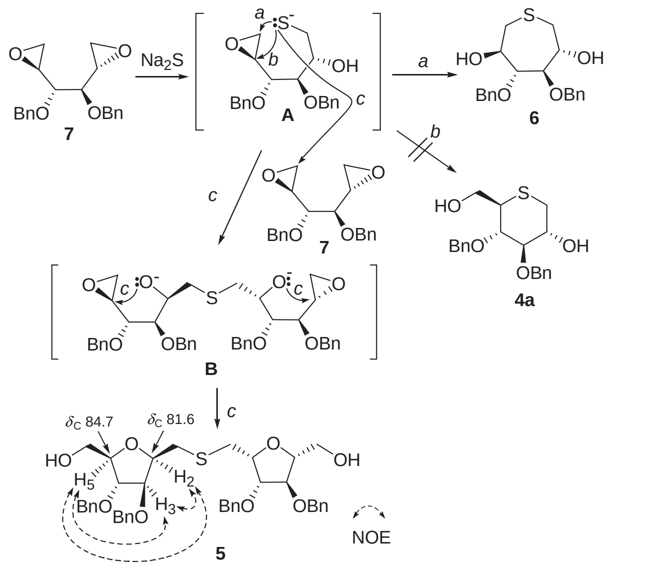
	Le Merrer's data[4c]	Szczepina's data[7b]		Le Merrer's data[4c]	Yuasa's data [7a]
	δ_H[a]	δ_H[b]		δ_C[a]	δ_C[b]
H-1ax	2.86 (dd, J=15.4, 7.2)	2.62 (dd, J=13.3, 11.0)	C-1	31.6	32.4
H-1eq	3.00 (dd, J=15.4, 6.8)	2.71 (dd, J=13.3, 4.6)			
H-2	4.12 (ddd, J=7.2, 6.8, 3.2)	3.64 (m)	C-2	80.2	74.2[c]
H-3	3.88–3.96 (m)	3.19 (t, J=9.1)	C-3	87.8	79.7[c]
H-4	3.88–3.96 (m)	3.48 (dd, J=10.2, 9.1)	C-4	82.9	74.7[c]
H-5	3.97 (ddd, J=5.2, 4.1, 2.8)	2.88 (m)	C-5	78.4	49.4
H-6a	3.62–3.68 (dd, J=11.6, 5.2)	3.75 (dd, J=11.9, 6.4)	C-6	63.6	61.8
H-6b	3.62–3.682 (dd, J=11.6, 4.1)	3.90 (dd, J=11.9, 3.2)			

[a] In CD_3OD.
[b] In D_2O.
[c] Assigned in the present study.

^{13}C NMR spectroscopic data, there appeared apparent discrepancies between Le Merrer's results[4c] and those by the other two groups. Le Merrer et al. reported that the molecular formula of the cyclization product was $C_{20}H_{24}O_4S$ on the basis of both the CIMS measurement and the elemental analysis. However, in our careful reexamination of FABMS measurements, the compound showed peaks at m/z 685 and 687 corresponding to $[M-H]^-$ and $[M+H]^+$ ions, run in negative- and positive-ion modes, respectively. By the HR-FABMS analysis, its molecular formula was elucidated to be $C_{40}H_{46}O_8S$. Almost doubled molecular formula and far less ^{13}C NMR signals compared to the number of carbons involved in the molecule suggested that the major product was symmetric. ^1H–^1H COSY

The formation of **5** would be ascribed to predominant attack of an initially formed sulfide ion (intermediate **A**) to the reactant (**7**) (route c), followed by another mode of cyclization via the intermediate **B** as shown in Scheme 2.

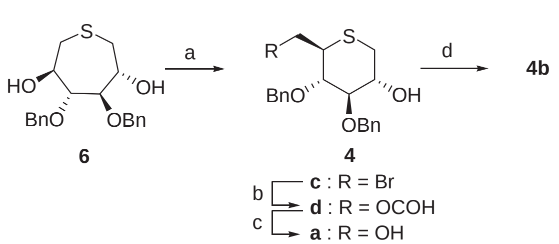
Next, reaction conditions of this multi-mode reaction were examined to increase the chemoselectivity. Firstly, in order to reduce the attack of the intermediate **A** to bis-epoxide (**7**), the reaction was carried out under diluted conditions (25 mM, Table 1, run 2), where predominant 7-*endo-tet* *S*-cyclization (route a) occurred, giving **6** as the major product (**5**/**6**=ca. 1/12). When



Scheme 2.

acetonitrile was used as the solvent, **6** was obtained as almost the sole product, although longer reaction time (5 h) was required owning probably to the less solubility of sodium sulfide in acetonitrile (run 3). Aqueous acetonitrile was found to be more effective, thiepane (**6**) being obtained in 94% yield in a shorter reaction time (run 4).

The thiepane (**6**) thus obtained was subjected to the ring contraction reaction by treatment with a mixture of Ph_3P and CBr_4 to give 3,4-di-*O*-benzyl-6-bromo-1,5,6-trideoxy-1,5-epithio-D-glucitol[4c] (**4c**) as the main product. However, **4c** was found to be labile and decomposed while purification through column chromatography, the yield being limited to around up to 30%.[4c] Therefore, the crude bromide (**4c**) was converted to the corresponding formate, 3,4-di-*O*-benzyl-1,5-dideoxy-1,5-epithio-D-glucitol 6-formate (**4d**) by treatment with sodium formate, and by the subsequent hydrolysis of **4d**, the desired thiane (**4a**) was obtained in 78% overall yield from **6**. Finally, the Birch reduction of **4a** gave the desired **4b** in 91% yield. Thus the overall yield of this sequence via four steps from **6** was improved up to 71%, an efficient and practical alternative route to **4b** being developed (Scheme 3).



Scheme 3. Reagents and conditions: (a) Ph_3P, CBr_4, MeCN, 60 °C; (b) 4.5% aq HCO_2Na, 60 °C; (c) 20% aq NaOH, MeOH, rt; (d) Na, liq. NH_3, −60 °C.

3. Conclusion

As the result, the third mode of cyclization leading to the symmetrical dialkyl sulfide (**5**) was found to occur in the thiocyclization of bis-epoxide (**7**) by sodium sulfide, and the structure of the main product was revised. The reaction proceeded in a highly chemoselctive manner under diluted conditions to afford the 7-*endo-tet S*-cyclization product (**6**) in excellent yield. The yield of transformation of thiepane (**6**) into the target thiane (**4b**) was improved up to 71% by modification of the processes.

4. Experimental

4.1. General

Mps were determined on a Yanagimoto MP-3S micromelting point apparatus, and mps and bps are uncorrected. IR spectra were measured on either a Shimadzu IR-435 grating spectrophotometer or a Shimadzu FTIR-8600PC spectrophotometer. NMR spectra were recorded on a JEOL JNM-GSX 270 (270 MHz ^{1}H, 67.5 MHz ^{13}C), a JEOL AL 400 (400 MHz ^{1}H, 100 MHz ^{13}C), a JEOL JNM-ECA 500 (500 MHz ^{1}H, 125 MHz ^{13}C), a JEOL JNM-ECA 600 (600 MHz ^{1}H, 150 MHz ^{13}C) or a JEOL JNM-ECA 700 (700 MHz ^{1}H, 175 MHz ^{13}C) spectrometer. Chemical shifts (δ) and coupling constants (J) are given in parts per million and hertz, respectively. Low-resolution and high-resolution mass spectra were recorded on a JEOL JMS-HX 100 spectrometer. Optical rotations were determined with a JASCODIP-370 digital polarimeter. Column chromatography was effected over Fuji Silysia Chemical silica gel BW-200. All the organic extracts were dried over anhydrous sodium sulfate prior to evaporation.

4.2. Thiocyclization of bis-epoxide (7)

4.2.1. Method A (in EtOH, concentration of **7***: 223 mM).* According to the literature,[4c] a mixture of bis-epoxide (**7**, 290 mg, 0.89 mmol), $Na_2S\cdot9H_2O$ (427 mg, 1.8 mmol), and EtOH (4 ml) was heated under reflux for 30 min. The mixture was poured into ice-water (25 ml) and extracted with Et_2O. The extract was washed with brine and evaporated to give a pale brown oil (291 mg), which on column chromatography (*n*-hexane–acetone, 25:1) gave 1,1′-thiobis(2,5-anhydro-3,4-di-*O*-benzyl-D-glucitol) (**5**, 131 mg, 43%) and 3,4-di-*O*-benzyl-1,6-dideoxy-1,6-epithio-L-iditol (**6**, 77 mg, 24%).

4.2.1.1. Compound **5**. Colorless oil. $[\alpha]_D^{26}$ +75.6 (*c* 0.68, CH_2Cl_2), lit.[4c] +76 (*c* 0.585, CH_2Cl_2). IR (neat): 3423, 1497, 1454, 1396, 1353, 1207, 1100, 1053 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ: 2.76 (2H, dd, J=13.4, 6.7, H-1a), 2.81 (2H, dd, J=13.4, 7.2, H-1b), 3.38 (2H, ddd, J=11.0, 6.7, 5.7, H-6a), 3.44 (2H, ddd, J=11.0, 5.7, 5.7, H-6b), 3.79 (2H, ddd, J=6.7, 5.7, 2.6, H-5), 3.94 (2H, d, J=3.6, H-3), 3.96 (2H, d, J=2.6, H-4), 4.02 (2H, ddd, J=7.2, 6.7, 3.6, H-2), 4.42/4.57 (each 2H, d, J=12.0, PhCH_2), 4.54 (4H, s-like, PhCH_2), 4.82 (2H, t, J=5.7, OH), 4.25–7.37 (20H. m, arom.). ^{13}C NMR (150 MHz, DMSO-d_6) δ: 30.8 (C-1), 62.2 (C-6), 70.76/70.84 (PhCH_2), 81.1 (C-2), 82.3 (C-3), 83.2 (C-4), 85.0 (C-5), 127.6/127.7/128.4 (d, arom), 138.2/138.37 (s, arom.). FABMS m/z: 687 $[M+H]^+$ (Pos.), 685 $[M-H]^-$ (Neg.). FABHRMS m/z: 687.3001 ($C_{40}H_{47}O_8S$ requires 687.2992). The ^{1}H and ^{13}C NMR spectral data in $CDCl_3$ were in good accordance with those reported by Le Merrer[4c] as were summarized in Table 3 and 4, respectively.

Table 3
^{1}H NMR data of **5** in $CDCl_3$

	δ Observed (600 MHz)	δ Lit.[4c] (250 MHz)
H-1a	2.82 (dd, J=13.7, 6.2)	2.8 (dd, J=13.5, 6.3)
H-1b	3.02 (dd, J=13.7, 7.0)	3.00 (dd, J=13.5, 7)
H-2	4.22 (ddd, J=7.0, 6.3, 3.7)	4.19 (ddd, J=7, 6.3, 3.7)
H-3	3.96 (dd, J=3.7, 0.8)	3.94 (d, J=3.7)
H-4	4.02 (m)	4.02 (m)
H-5	4.03 (m)	4.02 (m)
H-6a	3.61 (br ddd-like, J=11.6, 6.0, 3.2)	3.6 (m)
H-6b	3.75 (br ddd-like, J=11.6, 3.2, 3.2)	3.73 (m)
OH	2.51 (br, dd-like, J=6.0, 3.2)	—
PhCH_2	4.43/4.58 (d, J=11.5), 4.50/4.54 (d, J=12.0)	4.59–4.89 (J=11.7)
arom.	7.28–7.38 (m)	7.29 (m)

Table 4
^{13}C NMR data of **5** in $CDCl_3$

	δ Observed (150 MHz)	δ lit.[4c] (63 MHz)
C-1	30.8	30.8
C-2	81.7	81.6
C-3	82.5	82.5
C-4	82.6	82.5
C-5	84.7	84.7
C-6	62.8	62.8
$PhCH_2$	71.7/71.9	71.6/71.8
arom.	127.6/127.9/127.98/128.00/ 128.50/128.54 (d) 137.3/137.5(s)	127.5/127.8/128.4(d) 137.3/ 137.5 (s)

*4.2.1.2. Compound **6**.* Colorless needles (from *n*-hexane–AcOEt). Mp 100–101.5, lit.[4c] 98 °C. $[\alpha]_D^{25}$ +123.6 (*c* 0.84, CH_2Cl_2), lit.[4c] +124 (*c* 0.91, CH_2Cl_2). ^{1}H and ^{13}C NMR spectral properties of **6** were in accordance with those reported.[4c]

*4.2.2. Method B (in EtOH, concentration of **7**: 25 mM).* Following the method A, a mixture of 7 (100 mg, 0.31 mmol), $Na_2S\cdot 9H_2O$ (144 mg, 0.6 mmol), and EtOH (12 ml) was heated under reflux for 30 min. Work-up gave a mixture of **5** and **6** as a pale yellow solid (95.4 mg, 5/6=ca. 1/12).

*4.2.3. Method C (in MeCN, concentration of **7**: 25 mM).* Following the method B, a mixture of **7** (100 mg, 0.31 mmol), $Na_2S\cdot 9H_2O$ (144 mg, 0.6 mmol), and MeCN (12 ml) was heated under reflux for 5 h. Work-up gave a mixture of **5** and **6** as a pale yellow solid (103 mg), ^{1}H NMR spectrum of the crude mixture showed the formation of trace amount of **5**.

*4.2.4. Method D (in aq MeCN, concentration of **7**: 22 mM).* Following the method B, a mixture of **7** (100 mg, 0.31 mmol), $Na_2S\cdot 9H_2O$ (144 mg, 0.6 mmol), MeCN (12 ml), and water (2 ml) was heated under reflux for 30 min. Work-up gave a pale yellow solid (115 mg), which on column chromatography (benzene–acetone, 10:1) gave **6** (103 mg, 94%) as a colorless solid.

4.3. Modification of reaction conditions to convert thiepane (6) into thiane (4b)

*4.3.1. 3,4-Di-O-benzyl-1,5-dideoxy-1,5-epithio-D-glucitol 6-O-Formate (**4d**).* To a solution of CBr_4 (9.02 g, 27.2 mmol) in MeCN (180 ml) were added successively triphenylphosphine (7.13 g, 27.1 mmol) and **6** (4.9 g, ca. 13.7 mmol), and the reaction mixture was heated at 60 °C for 9 h. Deposited solids were filtered and washed with MeCN. To a mixture of the filtrate and washings containing the corresponding bromide, 3,4-di-*O*-benzyl-6-bromo-1,5,6-trideoxy-1,5-epithio-D-glucitol (**4c**), was added aqueous solution (100 ml) of sodium formate (4.63 g, 68 mmol). After being heated at 80 °C for 1 h, the reaction mixture was concentrated in vacuo, and the residue was dissolved in Et_2O (300 ml) and washed with brine. The organic phase was evaporated to give the title formate (**4d**) as a pale brown oil (12.8 g), which was used in the next step without purification. Analytical sample of **4d** was obtained by means of PTLC (*n*-hexane–AcOEt=1:1).

*4.3.1.1. Compound **4d**.* Colorless oil. $[\alpha]_D^{24}$ +72.1 (*c* 1.35, $CHCl_3$). IR (neat): 3339, 1719, 1306, 1168, 1093, 1076, 1024 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.56 (1H, dd, *J*=13.5, 9.7, H-1ax), 2.78 (br s, OH), 2.84 (1H, dd, *J*=13.5, 3.8, H-1eq), 3.06 (1H, ddd, *J*=8.8, 5.9, 3.9, H-5), 3.33 (1H, t, *J*=8.1, H-3), 3.70 (1H, dd, *J*=8.8, 8.1, H-4), 3.83 (1H, ddd, *J*=9.7, 8.1, 3.8, H-2), 4.43 (1H, dd, *J*=11.5, 5.9, H-6a), 4.5 (1H, dd, *J*=11.5, 3.9, H-6b), 4,62/4,85 (each 1H, d, *J*=11.2, $PhCH_2$), 4,67/4,93 (each 1H, d, *J*=11.5, $PhCH_2$), 7.28–7.40 (10H, m, arom.), 8.02 (1H, s, OCO*H*). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 31.0 (C-1), 44.5 (C-5), 62.3 (C-6), 71.7 (C-2), 74.9/75.4 ($PhCH_2$), 79.8 (C-4), 85.7 (C-3), 127.6/127.9/128.1/128.1/128.6/128.8 (d, arom.), 137.3/137.9 (s, arom.), 160.5 (OCHO). MS *m*/*z* (%): 388 (M^+, 0.11), 191 (21.9), 91 (100). HRMS *m*/*z*: 388.1358 ($C_{21}H_{24}O_5S$ requires 388.1344).

*4.3.2. 3,4-Di-O-benzyl-1,5-dideoxy-1,5-epithio-D-glucitol (**4a**).* To a solution of crude formate **4d** (12.8 g) in MeOH (160 ml) was added dropwise 20% aqueous solution of sodium hydroxide (15 ml) at 0 °C. After being stirred at room temperature for 1 h, the reaction mixture was concentrated in vacuo. The residue was diluted with AcOEt (300 ml), and the resulting mixture was washed with brine. The washings were re-extracted with AcOEt, and the combined extracts were evaporated to give a pale brown oil (11.8 g), which on column chromatography (*n*-hexane–AcOEt, 5:1) gave the title compound **4a** as a colorless solid (3.8 g, 78% from **6**). Mp 123.5–125 °C. $[\alpha]_D^{26}$ +56.3 (*c* 1.09, $CHCl_3$). IR (KBr): 3356, 1107, 1054, 1045 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.90 (1H, dd, *J*=6.6, 5.6, OH), 2.57 (1H, dd, *J*=13.5, 9.7, H-1ax), 2.82 (1H, d, *J*=4.0, OH), 2.85 (1H, dd, *J*=13.5, 4.0, H-1eq), 2.93 (1H, ddd, *J*=8.9, 5.5, 4.3, H-5), 3.32 (1H, dd, *J*=8.0, 8.0, H-3), 3.74 (1H, dd, *J*=8.9, 8.0, H-4), 3.81 (1H, ddd-like, *J*=9.7, 8.0, 4.0, H-2), 3.81 (1H, ddd-like, *J*=12.0, 5.6, 4.3, H-6a), 3.90 (1H, ddd, *J*=12.0, 6.6, 5.5, H-6b), 4.68/4.93 (each 1H, d, *J*=11.5, $PhCH_2$), 4.72/4.86 (each 1H, d, *J*=11.2, $PhCH_2$), 7.29–7.39 (10H, m, arom.). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 30.8 (C-1), 48.0 (C-5), 61.9 (C-6), 71.8 (C-2), 74.8/75.4 ($PhCH_2$), 80.7 (C-4), 85.8 (C-3), 127.8/128.0/128.1/128.6/128.7 (d, arom.), 137.6/138.0 (s, arom.). MS *m*/*z* (%): 360 (M^+, 0.06), 269 (7), 163 (20), 91 (100). HRMS *m*/*z*: 360.1389 ($C_{20}H_{24}O_4S$ requires 360.1395).

*4.3.3. 1,5-Dideoxy-1,5-epithio-D-glucitol (**4b**).* To a mixture of **4a** (2.4 g, 6.7 mmol), THF (50 ml), and liquid ammonia (ca. 100 ml) was added sodium (790 mg, 34.3 mg-atom) in small portions at −70 °C, and the mixture was stirred at −60 °C for 3 h. After addition of MeOH (30 ml) to the mixture, ammonia was gradually removed by increasing the temperature of the mixture, and the resulting mixture was neutralized with concd hydrochloric acid. The resulting precipitates were filtered and washed with MeOH. The combined filtrate and washings were evaporated in vacuo. The residue (2.93 g) was purified on column chromatography ($CHCl_3$–MeOH, 10:1) to give the title compound **4b** (1.09 g, 91%) as a colorless solid. Mp 131.5–132.5 °C, lit.[7a] 132–134 °C, lit.[7b] 110–115 °C. $[\alpha]_D^{24}$ +25.9 (*c* 1.25, CH_3OH), lit.[7b] +27.4, (*c* 1.2, CH_3OH). ^{1}H NMR (500 MHz, D_2O) δ: 2.63 (1H, dd, *J*=13.2, 11.2, H-1ax), 2.72 (1H, dd, *J*=13.2, 4.6, H-1eq), 2.90 (1H, ddd, *J*=10.6, 6.6, 3.2, H-5), 3.20 (1H, dd, *J*=9.2, 9.2, H-3), 3.49 (1H, dd, *J*=10.4, 9.2, H-4), 3.65 (1H, ddd, *J*=11.2, 9.2, 4.6, H-2), 3.76 (1H, dd, *J*=11.8, 6.6, H-6a), 3.91 (1H, dd, *J*=11.8, 3.2, H-6b). ^{13}C NMR (125 MHz, D_2O) δ: 33.8 (C-1), 50.8 (C-5), 63.2 (C-6), 75.6 (C-2), 76.1 (C-4), 81.1 (C-3).

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Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2010.07.064.

References and notes

1. (a) Recent review relevant to the present work: George, A. O. *J. Am. Chem. Soc.* **2008**, *130*, 6651; (b) Greinel, P.; Spreitz, J.; Sprenger, F. K.; Stutz, A. E.; Wrodnigg, T. M. *Org. Chem. Sugars* **2006**, 383; (c) Zbigniew, J. W.; James, M. C. *Appl.*

Microbiol. Biotechnol. **2005**, *69*, 237; (d) Borges de Melo, E.; da Silveira Gomes, A.; Carvalho, I. *Tetrahedron* **2006**, *62*, 10277; (e) Philippe, C.; Vinvent, C.; Olivier, R. M. *Tetrahedron: Asymmetry* **2009**, *20*, 672; (f) Yuasa, H.; Izumi, M.; Hashimoto, H. *Curr. Top. Med. Chem.* **2009**, *9*, 76; (g) Uenishi, J.; Ohmiya, H. *Tetrahedron* **2003**, 7011; (h) Witczak, J. Z. *Curr. Med. Chem.* **1999**, *6*, 165; (i) Robina, I.; Vogel, P.; Witczak, J. Z. *Curr. Org. Chem.* **2001**, *5*, 1177; (j) Robina, I.; Vogel, P. *Curr. Org. Chem.* **2002**, *6*, 471; (k) Yuasa, H.; Kajimoto, T.; Wong, C. H. *Tetrahedron Lett.* **1994**, *35*, 8243 and references cited therein.

2. (a) Driguez, H.; Henrissat, B. *Tetrahedron Lett.* **1981**, 5061; (b) AL-Masoudi, N. A. L.; Hughes, N. *Carbohydr. Res.* **1986**, *148*, 25; (c) Bozó, É.; Boros, S.; Kuszmann, J.; Gács-Baitz, E. *Carbohydr. Res.* **1996**, *290*, 159; (d) Izquierdo, C. I.; Plaza, L. M. T.; Asenjo, A. R.; Ramírez, F. A. *Carbohydr. Lett.* **1999**, *3*, 323 and references cited therein.
3. (a) Poitout, L.; Le Merrer, Y.; Depezay, J.-C. *Tetrahedron Lett.* **1995**, *36*, 6887; (b) Le Merrer, Y.; Saniere, M.; McCort, I.; Dupuy, C.; Depezay, J.-C. *Tetrahedron Lett.* **2001**, *42*, 2661; (c) Saladino, R.; Ciambecchini, U.; Hanessian, S. *Eur. J. Org. Chem.* **2003**, 4401; (d) Busca, P.; McCort, I.; Prange, T.; Le Merrer, Y. *Eur. J. Org. Chem.* **2006**, 2403.
4. (a) Le Merrer, Y.; Gravier-Pelletier, C.; Depezay, J.-C. *Recent Res. Devel. Org. Chem.* **2001**, *5*, 257; (b) Fuzier, M.; Le Merrer, Y.; Depezay, J.-C. *Tetrahedron Lett.* **1995**, *3*, 6443; (c) Le Merrer, Y.; Fuzier, M.; Dosbaa, I.; Foglietti, M.-J.; Depezay, J.-C. *Tetrahedron* **1997**, *53*, 16731; (d) Poitout, L.; Le Merrer, Y.; Depezay, J.-C. *Tetrahedron Lett.* **1994**, *35*, 3293; (e) Le Merrer, Y.; Poitout, L.; Depezay, J.-C.; Dosbaa, I.; Geoffroy, S.; Foglietti, M. J. *Bioorg. Med. Chem.* **1997**, *5*, 519 and references cited therein.
5. (a) Yoshikawa, M.; Murakami, T.; Shimada, H.; Matsuda, H.; Yamahara, J.; Tanabe, G.; Muraoka, O. *Tetrahedron Lett.* **1997**, *38*, 8367; (b) Yoshikawa, M.; Morikawa, T.; Matsuda, H.; Tanabe, G.; Muraoka, O. *Bioorg. Med. Chem.* **2002**, *10*, 1547.
6. (a) Recent review relevant to the present work: Mohan, S.; Pinto, B. M. *Carbohydr. Res.* **2007**, *342*, 1551; (b) Nasi, R.; Patrick, B. O.; Sim, L.; Rose, D. R.; Pinto, B. M. *J. Org. Chem.* **2008**, *73*, 6172; (c) Muraoka, O.; Xie, W.; Tanabe, G.; Amer, M. F. A.; Minematsu, T.; Yoshikawa, M. *Tetrahedron Lett.* **2008**, *49*, 7315; (d) Yoshikawa, M.; Xu, F.; Nakamura, S.; Wang, T.; Matsuda, H.; Tanabe, G.; Muraoka, O. *Heterocycles* **2008**, *75*, 1397; (e) Jayakanthan, K.; Mohan, S.; Pinto, B. M. *J. Am. Chem. Soc.* **2009**, *131*, 5621; (f) Tanabe, G.; Xie, W.; Ogawa, A.; Minematsu, T.; Yoshikawa, M.; Muraoka, O. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 2195; (g) Tanabe, G.; Hatanaka, T.; Minematsu, T.; Matsuda, H.; Yoshikawa, M.; Muraoka, O. *Heterocycles* **2009**, *79*, 1093; (h) Sim, L.; Jayakanthan, K.; Mohan, S.; Nasi, R.; Johnston, B. D.; Pinto, B. M.; Rose, D. R. *Biochemistry* **2010**, *49*, 443; (i) Mohan, S.; Jayakanthan, K.; Nasi, R.; Kuntz, D. A.; Rose, D. R.; Pinto, B. M. *Org. Lett.* **2010**, *12*, 1088; (j) Eskandari, R.; Kuntz, D. A.; Rose, D. R.; Pinto, B. M. *Org. Lett.* **2010**, *12*, 1632.
7. (a) Yuasa, H.; Nakano, Y.; Hashimoto, H. *Carbohydr. Lett.* **1996**, *2*, 23; (b) Szczepina, M. G.; Johnston, B. D.; Yuan, Y.; Svensson, B.; Pinto, B. M. *J. Am. Chem. Soc.* **2004**, *126*, 12458.