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Synthesis of methyl 4,6-*O*-benzylidene-2,3-dideoxy-5-thio-β-DL-*threo*-hex-2-enopyranoside via hetero-Diels–Alder reaction and unusual stabilities of 1,5-anhydro-4,6-*O*-benzylidene 2,3-dideoxy-5-thio-DL-*threo*-hex-2-enitol

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ABSTRACT

The title compound was prepared via hetero-Diels–Alder reaction of 1-acetoxy-1,3-butadiene and thioaldehyde, followed by Pummerer rearrangement. Different from the corresponding sugar and 5a-carba sugar, C-inside isomer of 1,5-anhydro-4,6-*O*-benzylidene-2,3-dideoxy-5-thio-DL-*thero*-hex-2-enitol was found to be thermodynamically more stable than the corresponding O-inside one and these thermodynamic stabilities were corroborated by ab initio calculations.

1. Introduction

5-Thiosugars having a sulfur atom instead of a ring oxygen atom are known to have several useful bioactivities. For example, 5-thio-D-glucose **1** (Fig. 1) showed weak α-glycosidase inhibitor,[1] and some 5-thioglycosides have anti-thrombotic effect[2] and other useful medical properties.[3] In 1987, 5-thio-D-mannose **2** was found in a sort of marine sponge.[4] Many 5-thiosugars were synthesized from sugars,[5] however, not only these methods generally required long steps, but also did not apply for preparation of 2,3-unsaturated 5-thiosugars. We have interest in preparation of 5-thiosugar derivatives not only for bioactivities but also theoretical interest such as anomeric effect[6] and conformational analysis.

For this purpose 1,4-di-*O*-acetyl-5-thio-2-enopyranuronate **3** is attractive, because its 2,3-double bond should be reactive to several reagents, for example, oxidation of **3** with OsO_4 gave *cis*-diol (Scheme 1).[7] However, preparation of 1,4-diacetoxy-1,3-butadiene requires equimolar amount of environmentally unfriendly $Hg(OAc)_2$,[8] otherwise specific apparatus for flash vacuum pyrolysis.[9]

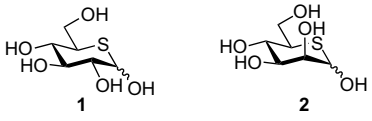
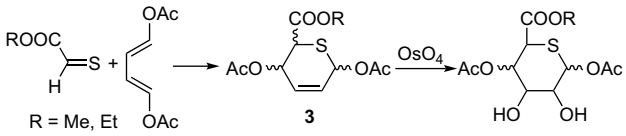


Figure 1. Examples of 5-thiosugars.



Scheme 1. Example of hetero-Diels–Alder reaction of thioaldehyde.

Therefore, we planned to prepare methyl 5-thio-2-enopyranoside **4** by the use of hetero-Diels–Alder reaction[10] of ethyl thioxoacetate and 1-acetoxy-1,3-butadiene,[11] followed by reduction of the ethoxycarbonyl group, benzylidenation, and then Pummerer rearrangement (Scheme 2).

According to the route we have prepared methyl 5-thio-β-DL-2-enopyranoside **4** and 5-thio-DL-2-enitol **5**, and performed optical resolution of 1,5-anhydro-5-thio-DL-*threo*-hex-2-enitol **6**. Furthermore we found unusual thermodynamic stabilities of 4,6-*O*-benzylidene-DL-*threo*-2-enitol **5** compared with the corresponding sugar and 5a-carba sugar and these thermodynamic differences were corroborated by ab initio calculations.

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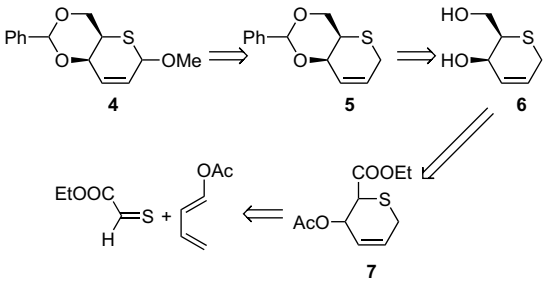


Scheme 2. Strategy for preparation of 5-thio-DL-2-enopyranoside **4**.

2. Results and discussion

2.1. Ab initio calculation for dienophiles

When an unsymmetrical diene is employed, it is enough possible to generate regioisomers. Our desired product is 4-acetoxyl derivative because introduction of oxygen atom at anomeric center should be achieved by Pummerer rearrangement.[12] In this context, the reaction of 1-acetoxy-1,3-butadiene and methyl (diisopropylphosphono) dithioformate, which afforded 3,6-dihydro-2*H*-thiopyran having the acetoxy group at the 5-position[10a] was promising. Concerned with regioselectivity of hetero-Diels–Alder reaction between thioaldehydes and 1,3-butadiene derivatives, ab initio calculations[13] agreed with experimental results.[10a,10b] However, regioselectivity is not determined experimentally or theoretically by the use of thioxoacetyl ester. Firstly we calculated ethyl thioxoacetate at B3LYP/6-31+G* level.[14] Contribution of the sulfur atom to $\pi^*_{C=S}$ was larger than that of the carbon atom as judged from the figure of LUMO drawn by Gauss View. To confirm the reliability of the result, we then calculated ethyl acrylate and ethyl glyoxylate. As expected from experimental data,[15] contribution of the carbon atom (C-3) to $\pi^*_{C=C}$ was apparently larger than that of C-2 in ethyl acrylate. Contribution of the carbon atom to $\pi^*_{C=O}$ is known to be larger than that of the oxygen atom, which was reproduced in the case of ethyl glyoxylate (Fig. 2). Encouraged to these results, we performed the hetero-Diels–Alder reaction.

2.2. Hetero-Diels–Alder reaction

Treatment of 1-acetoxy-1,3-butadiene with ethyl thioxoacetate derived in situ from ethyl thioglycolate[10c] gave an inseparable mixture of *threo*- and *erythro*-isomers **8** in 68% yield.

As expected from the calculation, evidence for formation of the regioisomer, introduction of the acetoxyl group at C-1, was not obtained. After reduction with $LiAlH_4$, the mixture was separated by column chromatography to give 4,6-dihydroxyl sugar **9** (DL-*threo*) in 56% yield and **10** (DL-*erythro*) in 28% yield (Scheme 3).

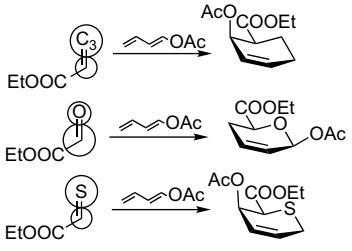
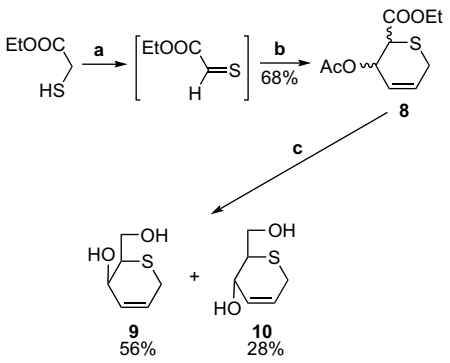


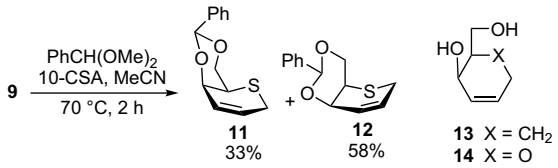
Figure 2. Schematic diagram of LUMO of dienophiles derived by ab initio calculations (B3LYP/6-31+G*) and expected regioselectivity.



Scheme 3. Hetero-Diels–Alder reaction. Reagents and conditions: (a) NCS, toluene, rt, 2 h; (b) 1-OAc-1,3-butadiene, MeOH, toluene, 0 °C, 2 h; (c) $LiAlH_4$, distd THF, 0 °C, 1 h.

2.3. Benzylidenation of 9 and conformational analysis

Conventional acidic benzylidenation of *threo*-enitol **9** afforded two products **11** and **12** (Scheme 4). $^{S}H_5$ conformation (O-inside) for **11** was suggested by small coupling constants of $J_{5,6a}$ 3.2 Hz (Fig. 3) and confirmed by correlation between the methine proton on acetal carbon (H-7) and both H-4 and H-6a in NOESY spectrum. On the other hand, compound **12** was assigned to occupy $^{5}H_S$ conformation (C-inside) by large coupling constant, $J_{5,6a}$ 11.6 Hz (Fig. 3) and correlation between H-6a and H-1a as well as between H-7 and H-3 in NOESY spectrum. These two compounds are generated by chirality at the benzylidene methine carbon atom (C-7).



Scheme 4. Benzylidenation of 5-thiosugar **9**.

Although compounds **11** and **12** are DL mixture, C-inside isomer **12** has *R* configuration and *O*-isomer **11** has *S* one, if we choose the D-series and hereafter structural formulas of D-series products were written. In general conventional acidic benzylidenation is thermodynamically controlled to give a more stable O-inside isomer as a major product.

This is reasonable because in C-inside isomer the more bulky hydroxymethyl group (*A*-value:[16] 1.76) occupies the axial position

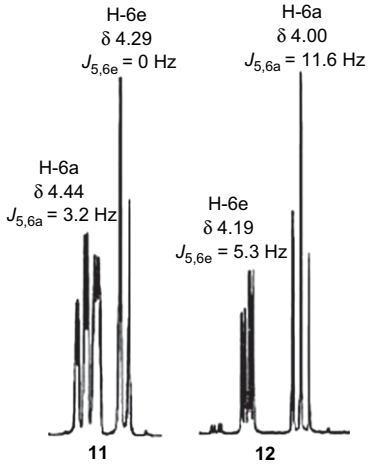
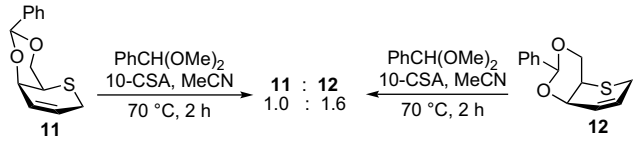


Figure 3. Part of ^{1}H NMR spectra of **11** and **12** around H-6.

and less bulky hydroxyl group (*A*-value:[16] 0.60) the equatorial one. In fact similar benzylidenation of the corresponding 5a-carbasugar **13** and sugar **14** had afforded almost exclusively O-inside isomer.[17] However, to our surprise, benzylidenation of 5-thiosugar **9** exceptionally gave the C-inside isomer as a major product in spite of the *A*-values. When O-inside **11** was treated under the conditions employed for the preparation of **11** and **12** (at 343 K), 1.0:1.6 mixture of **11** and **12** was formed (Scheme 5). The same equilibrium mixture was obtained from C-inside **12**. These results revealed that C-inside isomer **12** is more stable than O-inside **11** by 0.32 kcal/mol. Therefore, we performed ab initio calculations whether or not the thermodynamic stabilities of these benzylidene derivatives were corroborated by experimental results as will be described in Section 2.6.



Scheme 5. Equilibration of **11** and **12**.

2.4. Introduction of oxygen atom at C-1 by Pummerer rearrangement

Although Pummerer rearrangement is widely used for organic synthesis,[18] its application to carbohydrate chemistry seems to be limited to 5-thiohexose and 4-thiopentoses.[12,19,20] This reaction is believed to proceed via a cationic intermediate, followed by addition of a nucleophile.[18b] Undoubtedly cationic intermediate **17** generated at C-1 is much more stable than an alternative **18** formed at C-5 (Scheme 6), because the former is stabilized by the double bond, whereas the latter is destabilized by deformation of the dioxane ring due to the change of hybridization of C-5 from sp^3 to sp^2.

Treatment of **12** with *m*-CPBA afforded sulfoxides **15** and **16** due to the chirality at the sulfur atom in 46% and 38% yields, respectively. Chirality at sulfur atom was determined by NMR data. Chemical shift of gauche proton to S=O bond moves lower field than that of antiperiplanar proton.[21] As shown in Figure 4, both protons at C-1 of **15** shift lower field than those of precursor sulfide **12**, whereas one proton shift to lower field, but an alternative one does not for **16**. Thus sulfoxides **15** and **16** were assigned to have equatorial and axial oxygen atoms, respectively. This assignment is supported by geminal coupling constant of methylene group adjacent to the sulfoxide. It is reported that axial sulfoxide has larger geminal coupling constant than equatorial sulfoxide.[19] In fact axial sulfoxide **16** has larger geminal coupling constant ($J_{1a,1e}$ 17.4 Hz) than equatorial one **15** ($J_{1a,1e}$ 15.4 Hz). Chemical shift of C-1 was not conflict with the report,[21] in which carbon signals adjacent

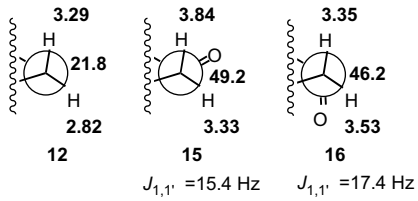
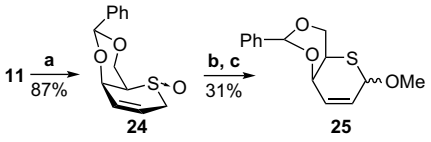


Figure 4. Newman projection of **12**, **15**, **16** view from C-1 to S-5. Chemical shift (δ) of H-1a and H-1e as well as that of C-1 (δ) were shown.

to the sulfur atom having axial oxygen atom appeared at higher field than those having equatorial one.

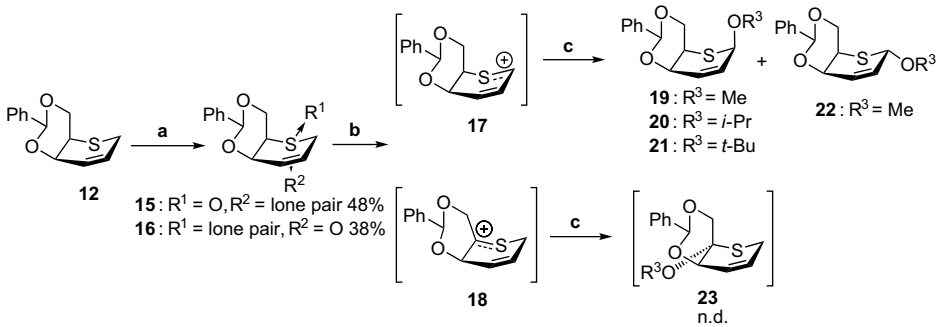
Different from the case of C-inside **12**, similar oxidation of O-inside **11** with *m*-CPBA afforded only one sulfoxide **24** in 87% yield (Scheme 7). Equatorial occupation of the oxygen atom for **24** was tentatively assigned by the following speculation. Both anomeric protons of sulfoxide **24** appeared at lower field than those of sulfide **11**: H-1a (δ 4.01) and H-1e (δ 3.35) of **24** versus H-1a (δ 3.50) and H-1e (δ 3.06) of **11**. Apparently an alternative isomer is sterically unfavorable due to 1,3-diaxial repulsion between both O-4 and O-6 and oxygen atom at the sulfur atom.



Scheme 7. Pummerer rearrangement **24**. Reagents and conditions: (a) *m*-CPBA, CH_2Cl_2, 0 °C, 30 min; (b) TFAA, pyridine, 0 °C, 30 min; (c) MeOH, PPTS, rt, 48 h.

Treatment of sulfoxide **15** with trifluoroacetic anhydride followed by addition of methanol gave a mixture of methyl 4,6-*O*-benzylidene-5-thio-α-and-β-DL-*threo*-2-enopyranoside **19** and **22** in 66% yield, in which β-anomer **19** became a major product. Similar result was obtained from **16**. Addition of *iso*-PrOH and *tert*-BuOH instead of MeOH afforded the β-anomer **20** in moderate and **21** in low yield, respectively. Regioisomer **23** formed from cationic intermediate **18** was not detected in these reactions (Table 1). As expected from anomeric effect β-anomers **19**–**21** occupied C-inside conformation as judged from NMR data.

Similar Pummerer reaction of sulfoxide **24** derived from O-inside isomer **11** afforded complicated mixture, from which an inseparable mixture of methyl α- and β-DL-2-enopyranoside **25** (α:β=~6:1) was obtained in 31% yield (Scheme 7). Thus stereoselectivities were different between C-insides and O-inside. This should be explained as follows. It is known that glycosidation of 5-thiosugar gave α-anomer with high stereoselectivity probably due to anomeric effect.[22] If this is the case, β-anomer should be predominantly obtained from C-insides **15** and **16**, because in this



Scheme 6. Pummerer rearrangement of **15** and **16**. Reagents and conditions: (a) *m*-CPBA, CH_2Cl_2, 0 °C, 30 min; (b) TFAA, pyridine, 0 °C, 30 min; (c) R^3OH, PPTS, rt, 48 h.

Table 1
Pummerer rearrangement and introduction of alkoxyl group at C-1

Entry	R^3OH	Sulfoxide	Yield[a] (%)	
			α-anomer	β-anomer
1	MeOH	**15**	9	57
2	MeOH	**16**	11	54
3	*iso*-PrOH	**15**	n.d.[b]	47
4	*iso*-PrOH	**16**	n.d.	45
5	*tert*-BuOH	**15**	n.d.	18
6	*tert*-BuOH	**16**	n.d.	18

[a] Isolated yield.
[b] n.d. means not detected.

conformation, different from the O-inside **24**, β-anomer enjoys anomeric effect. Thus C-inside isomers **15** and **16** were found to be useful precursors for preparation of β-anomer (not readily available by conventional method), although the yields were not high.

2.5. Optical resolution of 9

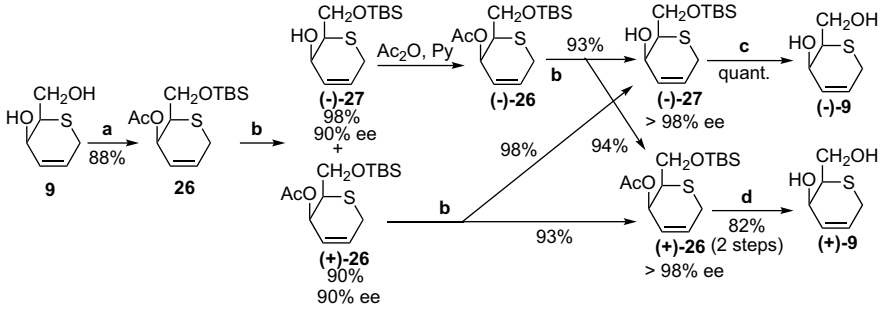
To test bioactivities of 5-thio sugars, optical resolution is desirable. To our best knowledge, however, only one paper reported optical resolution of cyclic adduct derived by hetero-Diels–Alder reactions of thioaldehyde.[7] Although treatment of 4,6-di-*O*-acetate of **9** with several kinds of lipase resulted in deacetylation regardless of the chirality. We succeeded optical resolution by the use of Lipase PS to 4-*O*-acetyl-6-*O*-*tert*-butyldimethylsilyl derivative **26** (Scheme 8). Treatment of **9** with *tert*-butyldimethylsilyl chloride, followed by acetylation with Ac_2O gave **26**. Selective deacetylation of **26** with Lipase PS in buffer suspension occurred to give crude (−)-**27** and (+)-**26**. The mixture was readily separated by column chromatography. Optical yield was around 90%ee. When thus isolated acetate mainly consisted of (+)-**26** as well as acetate derived by acetylation of crude (−)-**27** was again similarly treated with Lipase PS, optical yield reached up to >98%ee.

2.6. Ab initio calculation of benzylidene derivatives

Thus C-inside isomer **12** was found to be slightly more stable than O-inside one **11**, different from the prediction based on *A*-values. This is characteristic for 5-thio sugar **9**, because benzylidenation of the corresponding 5a-carba sugar **13** and sugar **14** almost exclusively gave O-inside isomers. To examine whether or not the interesting results agreed with ab initio calculation, we have calculated these compounds at B3LYP/6-31+G* level. Furthermore *threo* isomer should be conformationally flexible, we firstly calculated several conformers of **12** to confirm that C-inside conformation was most stable as indicated by NMR data. For this purpose three possible conformers, C-inside, O-inside having the axial phenyl group, and O-inside having a twist boat form of the dioxane ring were calculated. Furthermore eclipsed and bisected forms between the phenyl plane and C7–H7 bond were calculated for these three conformers: dihedral angle of H7C7C1′C2′ (the phenyl ring) was 0° and 180°.

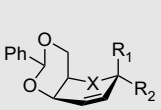
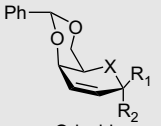
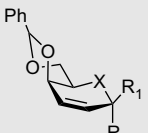
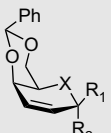
Stabilities of these conformer decrease along with the sequence of C-inside (0.0 kcal/mol)<O-inside having the axial phenyl group (4.0 kcal/mol)<O-inside having twisted boat form (4.2 kcal/mol) (Table 2, entry 1). Thus occupation of C-inside conformation for **12** revealed by NMR data was in good agreement with the calculations.

Secondly we calculated the *S*-isomer **11** having O-inside conformation. The *R*-isomer **12** with C-inside conformation was more stable than the *S*-isomer **11** having O-inside one by 1.8 kcal/mol: the calculations qualitatively agreed with the experimental data (Table 2, entry 1). As had been mentioned, the corresponding 5a-carba sugar **13** and sugar **14** almost exclusively afforded 4,6-*O*-benzylidene derivatives having O-inside conformation, indicating that the O-inside isomer is more stable than the C-inside isomer. In fact calculations of 4,6-*O*-benzylidene derivatives of 5a-carba sugar



Scheme 8. Optical resolution of **9**. Reagents and conditions: (a) TBSCl, imidazole, DMAP, CH_2Cl_2, 0 °C, 1 h, then Ac_2O, pyridine, 0 °C, 3 h; (b) Lipase PS Amano SD, pH 7.0 buffer; (c) TBAF·$3H_2O$, distd THF, rt, 30 min; (d) TBAF·$3H_2O$, distd THF, rt, 30 min, then MeONa, MeOH, rt, 1 h.

Table 2
Stabilities of conformers of benzylidene derivatives calculated at B3LYP/6-31+G* level and energy differences are shown (kcal/mol)

Entry		 C-inside	 O-inside axial phenyl group	 O-inside twisted dioxan ring	 O-inside equatorial phenyl group
1	X=S, R_1=R_2=H	0.0	4.0	4.2	1.8
2	X=S, R_1=OMe, R_2=H	0.0	6.5	6.4	4.4
3	X=S, R_1=H, R_2=OMe	1.3	2.1	2.8	0.0
4	X=CH_2, R_1=R_2=H	1.5	2.5	3.4	0.0
5	X=O, R_1=R_2=H	1.9	2.5	3.5	0.0

13 and sugar **14** having O-inside conformation were more stable than C-inside ones by 1.5 and 1.9 kcal/mol, respectively (Table 2, entries 4 and 5). Thus predominance of C-inside isomer observed herewith is characteristic for 5-thiosugar (Scheme 4).

Ab initio calculation of several conformers of methyl β-anomer **19** showed that C-inside form was most stable (Table 2, entry 2). Compared with entry 1 and 2 in Table 2, energy difference between C-inside and other conformers in **19** (entry 2) is larger than those of 1,5-anhydro-2-enitol **12** (entry 1) by 2.2–2.5 kcal/mol: this is predictable by anomeric effect. It is noteworthy that in spite of anomeric effect α-anomer **22** occupies C-inside conformation as judged from NMR data: $J_{5,6a}$ 10.9 Hz and observation of correlations between H-6a and H-1 as well as H-7 and H-3 in NOESY spectrum. Occupation of C-inside conformation for **22** again agreed with ab initio calculation (Table 2, entry 3).

3. Conclusion

We developed a facile synthetic route for 2,3-unsaturated 5-thiosugars via hetero-Diels–Alder reaction. Optical resolution of **9** was performed by the use of Lipase PS. Different from the cases of corresponding 5a-carba sugar **13** and sugar **14**, benzylidenation of 5-thiosugar **9** gave C-inside isomer as a major product. This unusual behavior of 5-thiosugar **9** and NMR data of **12**, **19**, and **22** were corroborated by ab initio calculations.

4. Experimental

4.1. General methods

Melting points are uncorrected. Optical rotations were determined with a Horiba High Sensitive Polarimeter (SEPA-200). Most of reactions were monitored by TLC using silica gel coated on glass. Products were purified by flash column chromatography and recrystallized if necessary. NMR spectra were measured by Bruker AVANCE 400 (400 MHz/^{1}H, 100 MHz/^{13}C) with TMS as an internal standard. Some signals were assigned by the use of COSY, HMQC, HMBC, and/or NOESY. IR spectra were recorded for KBr pellets on a Perkin–Elmer Spectrum One FT-IR spectrometer. Silica gel {C-60 (Kanto) or 40–63 μm (MERCK)} was used for column chromatography.

4.2. Ethyl 4-*O*-acetyl-1,5-anhydro-2,3-dideoxy-DL-5-thio-hex-2-enopyranuronate (8)

Ethylthioglycolate (10 g, 83.3 mmol) was added dropwise to a suspension of *N*-chlorosuccinimide (11.4 g, 85.4 mmol) in toluene (100 mL) at 0 °C. After stirring for 2 h during that time the mixture turned yellow, it was filtered to remove solid material. The filtrate was added dropwise to solution of 1-acetoxy-1,3-butadiene (6.4 g, 66.7 mmol) and triethylamine (8.6 g, 85.1 mmol) in toluene (50 mL) and MeOH (50 mL) at room temperature. After stirring for 2 h, 5% aq $NaHCO_3$ solution was added and then the mixture was stirred for 30 min and extracted with AcOEt for three times. Aqueous layer was extracted with AcOEt for three times. Organic layers thus obtained were combined and washed with brine solution, dried over $MgSO_4$ and evaporated in vacuo. The residue was purified by silica gel column chromatography (AcOEt/hexane=1:5) to give 10.5 g (68%) of **8** consisted of *erythro* and *threo*-enitols, of which separation was failed.

4.3. Reduction of 8 with lithium aluminum hydride

Solution of **8** (3 g, 13.04 mmol) in dry THF (20 mL) was added dropwise to a suspension of $LiAlH_4$ (1.49 g, 39.12 mmol) in distd THF (50 mL) at 0 °C. After stirring for 2 h at room temperature, the mixture was cooled to 0 °C and AcOEt (20 mL) was added dropwise at 0 °C and then 1 M HCl was added. AcOEt (100 mL) was added and stirred 10 min and gray pulp residue was removed by decantation, and residue was washed with AcOEt for three times. Organic layer combined was evaporated in vacuo. The residue was purified by silica gel column chromatography (MeOH/$CHCl_3$=1:30) to give 1.02 g of *threo* **9** (56%) and 572 mg of *erythro* **10** isomers (28%).

4.3.1. 1,5-Anhydro-2,3-dideoxy-5-thio-DL-threo-hex-2-enitol (*9*)

Colorless solid. Mp 53–55 °C (recrystallized from EtOH). ^{1}H NMR (pyridine-d_5): δ 3.14 (ddd, 1H, $J_{1,1'}$ 17.8 Hz, $J_{1,2}$ 3.8 Hz, $J_{1,3}$ 1.9 Hz, H-1), 3.09 (ddd, 1H, $J_{1',2}$ 3.8 Hz, $J_{1',3}$ 1.6 Hz, H-1′), 5.92–5.87 (m, 1H, H-2), 6.12 (dddd, 1H, $J_{2,3}$ 10.7 Hz, $J_{3,4}$ 2.1 Hz, H-3), 4.86 (br s, 1H, H-4), 3.45 (ddd, 1H, $J_{4,5}$ 3.0 Hz, $J_{5,6}$ 3.8 Hz, $J_{5,6'}$ 3.8 Hz, H-5), 4.53 (ddd, 1H, $J_{6,6'}$ 12.0 Hz, $J_{6,OH}$ 5.2 Hz, H-6), 4.21 (ddd, 1H, $J_{6',OH}$ 5.2 Hz, H-6′), 6.57 (d, 1H, $J_{4,OH}$ 7.0 Hz, 4-OH), 6.35 (dd, 1H, 6-OH). ^{13}C NMR (pyridine-d_5): δ 25.1 (C-1), 126.6 (C-2), 132.6 (C-3), 64.7 (C-4), 47.5 (C-5), 62.1 (C-6). IR (KBr): ν 3306, 1655, 1412 cm^{-1}. Anal. Calcd for $C_6H_{10}O_2S$: C, 49.29; H, 6.89; S, 21.93. Found: C, 49.07; H, 6.61; S, 21.97.

4.3.2. 1,5-Anhyro-2,3-dideoxy-5-thio-DL-erythro-hex-2-enitol (*10*)

Colorless solid. Mp 82–83 °C (recrystallized from EtOH). ^{1}H NMR($CDCl_3$): δ 3.20 (ddd, 1H, $J_{1,1'}$ 17.9 Hz, $J_{1,2}$ 3.6 Hz, $J_{1,3}$ 2.2 Hz, H-1), 3.04 (ddd, 1H, $J_{1',2}$ 3.8 Hz, $J_{1',3}$ 1.9 Hz, H-1), 5.93 (ddd, 1H, $J_{2,3}$ 9.2 Hz, H-2), 5.81 (ddd, 1H, $J_{3,4}$ 0.8 Hz, H-3), 4.26 (br s, 1H, H-4), 2.92 (dt, 1H, $J_{4,5}$ 6.6 Hz, $J_{5,6}$ 6.5 Hz, H-5), 3.84–3.77 (m, 2H, H-6), 3.57 (d, 1H, $J_{4,OH}$ 7.3 Hz, 4-OH), 3.38 (t, 1H, $J_{6,OH}$ 5.6 Hz, 6-OH). ^{13}C NMR ($CDCl_3$): δ 24.5 (C-1), 126.4 (C-2), 131.1 (C-3), 66.3 (C-4), 46.2 (C-5), 63.4 (C-6). IR (KBr): ν 3393, 3305, 1655, 1411 cm^{-1}. Anal. Calcd for $C_6H_{10}O_2S$: C, 49.29; H, 6.89; S, 21.93. Found: C, 49.39; H, 6.61; S, 22.03.

4.4. 1,5-Anhyro-4,6-*O*-benzylidene-2,3-dideoxy-5-thio-DL-*threo*-hex-2-enitol

10-Camphorsulfonic acid (10-CSA) (30 mg, 0.13 mmol) was added to a solution of **9** (200 mg, 1.37 mmol) and benzaldehyde dimethylacetal (300 mg, 2.0 mmol) in MeCN (10 mL) at 70 °C. The mixture was stirred for 30 min at the same temperature. After addition of Et_3N (1 mL), the mixture was extracted with AcOEt and the aqueous layer was extracted with AcOEt for three times. The organic layer combined was washed with brine solution, dried over $MgSO_4$, and evaporated in vacuo. The residue was purified by silica gel column chromatography (toluene) to give 106 mg of O-inside **11** (33%) and 186 mg of C-inside **12** (58%).

4.4.1. Physical data of O-inside isomer *11*

Colorless solid. Mp 117–118 °C (recrystallized from EtOH and hexane). ^{1}H NMR ($CDCl_3$): δ 3.50 (ddd, 1H, $J_{1qa,1qe}$ 17.7 Hz, $J_{1qa,2}$ 4.2 Hz, $J_{1qa,3}$ 2.0 Hz, H-1qa), 3.06 (br dd, 1H, $J_{1qe,2}$ 6.2 Hz, H-1qe), 6.20 (ddd, 1H, $J_{2,3}$ 9.8 Hz, 1H, H-2), 5.97–5.93 (m, 1H, H-3), 4.40–4.39 (m, 1H, H-4), 3.00 (br s, 1H, H-5), 4.44 (dd, 1H, $J_{5,6a}$ 3.2 Hz, $J_{6a,6e}$ 12.5 Hz, H-6a), 4.29 (br d, 1H, $J_{5,6e}$ 0 Hz, H-6e), 7.54–7.32 (m, 5H,–Ph), 5.61 (s, 1H, Ph*CH*–). ^{13}C NMR ($CDCl_3$): δ 27.6 (C-1), 129.4 (C-2), 130.7 (C-3), 70.7 (C-4), 39.1 (C-5), 69.6 (C-6), 138.4, 128.7, 127.4, 126.8 (–Ph), 102.4 (–Ph*CH*). IR (KBr): ν 1655, 1499, 1384 cm^{-1}. Anal. Calcd for $C_{11}H_{18}O_2S$: C, 66.64; H, 6.02; S, 13.68. Found: C, 66.47; H, 5.99; S, 13.42.

4.4.2. Physical data of C-inside isomer *12*

Colorless solid. Mp 78–79 °C (recrystallized from EtOH and hexane). ^{1}H NMR ($CDCl_3$): δ 3.32–3.26 (m, 2H, H-1a, H-5), 2.82 (ddd, 1H, $J_{1qa,1qe}$ 18.2 Hz, $J_{1qe,2}$ 2.2 Hz, $J_{1qe,3}$ 2.1 Hz, H-1qe), 6.12 (ddd, 1H, $J_{2,3}$ 11.2 Hz, H-2), 5.90 (dddd, 1H, $J_{3,4}$ 2.6 Hz, H-3), 4.96 (dd, 1H, $J_{4,5}$ 2.7 Hz, H-4), 4.19 (ddd, 1H, $J_{5,6e}$ 5.3 Hz, $J_{6a,6e}$ 11.3 Hz, H-6e), 4.00 (dd, 1H, $J_{5,6a}$ 11.6 Hz, H-6a), 7.48–7.34 (m,5H, –Ph), 5.61 (s, 1H, Ph*CH*–). ^{13}C NMR ($CDCl_3$): δ 21.8 (C-1), 129.7 (C-2), 128.7 (C-3), 70.5 (C-4),

32.7 (C-5), 67.0(C-6), 138.8, 129.1, 128.8, 126.8 (Ph), 95.4 (Ph*CH*–). IR (KBr): ν 1657, 1496, 1392 cm^{-1}. Anal. Calcd for $C_{11}H_{18}O_2S$: C, 66.64; H, 6.02; S, 13.68. Found: C, 66.85; H, 6.18; S, 13.42.

4.5. Experiment for equilibration

A solution of 4,6-*O*-acetal **11** (20 mg) in distd MeCN (3 mL) and benzaldehyde dimethyl acetal (1.0 equiv) was warmed to reflux under Ar atmosphere, to which 10-CSA (0.1 equiv) was added and the mixture kept for 2 h at 70 °C. After addition of triethylamine (1 mL), water was added and the mixture was extracted with AcOEt. Extracts were washed water, dried over $MgSO_4$, and evaporated. ^1H NMR spectrum of the residue showed it is a 1.0:1.6 mixture of **11** and **12**.

The same treatment of **12** (20 mg) again gave a 1.0:1.6 mixture of **11** and **12**.

4.6. Oxidation of 12

Powder of *m*-CPBA (175 mg, 1.0 mmol) was gradually added to a solution of **12** (234 mg, 1.0 mmol) in CH_2Cl_2 (5 mL) at 0 °C until TLC spot of **12** had been disappeared. The reaction mixture was quenched with 10% aq $Na_2S_2O_3$, and poured into saturated aq $NaHCO_3$, the mixture was extracted with AcOEt for three times and combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated in vacuo. The residue was chromatographed silica gel column with AcOEt to give 115 mg of **15** (46%) and 95 mg of **16** (38%).

4.6.1. Physical data of *15*

Colorless solid. Mp 212–213 °C. ^1H NMR ($CDCl_3$): δ 3.84 (dd, 1H, $J_{1qa,1qe}$ 15.4 Hz, $J_{1qa,2}$ 6.0 Hz, H-1qa), 3.33 (ddd, 1H, $J_{1qe,2}$ 3.2 Hz, $J_{1qe,3}$ 1.9 Hz, H-1qe), 5.95 (ddd, 1H, $J_{2,3}$ 10.9 Hz, H-2), 6.04–6.01 (m, 1H, H-3), 4.94 (br s, 1H, H-4), 4.07 (ddd, 1H, $J_{4,5}$ 2.4 Hz, $J_{5,6e}$ 4.1 Hz, $J_{5,6a}$ 11.4 Hz, H-5), 4.66 (dd, 1H, $J_{6a,6e}$ 11.5 Hz, H-6e), 4.21 (dd, 1H, H-6a), 7.49–7.37 (m, 5H, –Ph), 5.58 (s, 1H, Ph*CH*–). ^{13}C NMR ($CDCl_3$): δ 49.2 (C-1), 122.2 (C-2), 130.2 (C-3), 70.3 (C-4), 44.3 (C-5), 61.6 (C-6), 137.7, 129.7, 128.8, 126.5 (–Ph), 96.8 (Ph*CH*–). IR (KBr): ν 1651 cm^{-1}. Anal. Calcd for $C_{13}H_{14}O_3S$: C, 62.38; H, 5.64; S, 12.81. Found: C, 62.16; H, 5.52; S, 12.91.

4.6.2. Physical data of *16*

Colorless solid. Mp 224–225 °C. ^1H NMR ($CDCl_3$): δ 3.35 (dd, 1H, $J_{1qa,1qe}$ 17.4 Hz, $J_{1qa,2}$ 4.2 Hz, H-1qa), 3.53 (ddd, 1H, $J_{1qe,2}$ 4.5 Hz, $J_{1qe,3}$ 1.9 Hz, H-1qe), 6.07 (ddd, 1H, $J_{2,3}$ 10.8 Hz, H-2), 5.98–5.91 (m, 1H, H-3), 5.04 (br s, 1H, H-4), 3.42 (ddd, 1H, $J_{4,5}$ 2.0 Hz, $J_{5,6e}$ 4.1 Hz, $J_{5,6a}$ 7.8 Hz, H-5), 4.28 (dd, 1H, $J_{6a,6e}$ 11.8 Hz, H-6e), 4.09 (dd, 1H, H-6a), 7.50–7.37 (m, 5H, –Ph), 5.94 (s, 1H, Ph*CH*–). ^{13}C NMR ($CDCl_3$): δ 46.2 (C-1), 122.1 (C-2), 129.7 (C-3), 66.4 (C-4), 54.5 (C-5), 60.3 (C-6), 137.3, 129.3, 129.2, 127.0 (–Ph), 97.4 (Ph*CH*–). IR (KBr): ν 1654 cm^{-1}. Anal. Calcd for $C_{13}H_{14}O_3S$: C, 62.38; H, 5.64; S, 12.81. Found: C, 62.46; H, 5.60; S, 13.05.

4.7. Pummerer rearrangement of sulfoxides 15 and 16 in the presence of methanol

To a solution of sulfoxide **15** (200 mg, 0.80 mmol) in pyridine (5 mL), TFAA (200 μL, 1.42 mmol) was added dropwise at 0 °C. After the mixture was stirred for 30 min, MeOH (3 mL) and PPTS (10 mg) were added and the solution was stirred for 48 h at room temperature and then poured into saturated aq $NaHCO_3$ and extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and then concentrated in vacuo. The residue was chromatographed with silica gel column eluting with AcOEt to give 120 mg of **19** (57%) and 20 mg of **22** (9%).

Similar reaction of **16** gave 114 mg of **19** (54%) and 24 mg of **22** (11%).

4.7.1. Physical data of β-anomer *19*

Colorless solid. Mp 70–72 °C. ^1H NMR ($CDCl_3$): δ 4.56 (dd, 1H, $J_{1,2}$ 4.5 Hz, $J_{1,3}$ 1.5 Hz, H-1), 6.15 (dd, 1H, $J_{2,3}$ 11.1 Hz, H-2), 5.97 (ddd, 1H, $J_{3,4}$ 1.5 Hz, H-3), 4.95 (dd, 1H, $J_{4,5}$ 3.3 Hz, H-4), 3.33 (ddd, 1H, $J_{5,6a}$ 11.7 Hz, $J_{5,6e}$ 4.6 Hz, H-5), 4.43 (dd, 1H, $J_{6a,6e}$ 11.8 Hz, H-6a), 4.07 (dd, 1H, H-6e), 7.48–7.34 (m, 5H, –Ph), 5.70 (s, 1H, Ph*CH*–), 4.06 (s, 3H, –OMe). ^{13}C NMR ($CDCl_3$): δ 75.5 (C-1), 129.5 (C-2), 131.1 (C-3), 71.2 (C-4), 32.2 (C-5), 67.7 (C-6), 138.4, 129.4, 128.8, 126.5 (–Ph), 95.9 (Ph*CH*–), 57.5 (–OMe). IR (KBr): ν 1667, 1462 cm^{-1}. Anal. Calcd for $C_{14}H_{16}O_3S$: C, 63.61; H, 6.10; S, 12.13. Found: C, 63.44; H, 6.01; S, 12.33.

4.7.2. Physical data of α-anomer *22*

Colorless solid. Mp 69–71 °C (recrystallized from Et_2O). ^1H NMR ($CDCl_3$): δ 5.24 (d, 1H, $J_{1,2}$ 3.3 Hz, H-1), 6.13 (dd, 1H, $J_{2,3}$ 11.2 Hz, H-2), 6.07 (dd, 1H, $J_{3,4}$ 2.2 Hz, H-3), 4.95 (br d, 1H, H-4), 3.51–3.45 (m, 1H, H-5), 3.96 (dd, 1H, $J_{5,6a}$ 10.9 Hz, $J_{6a,6e}$ 11.2 Hz, H-6a), 4.20 (dd, 1H, $J_{5,6e}$ 5.1 Hz, H-6e), 7.48–7.34 (m, 5H, –Ph), 5.73 (s, 1H, Ph*CH*–), 3.40 (s, 3H, –OMe). ^{13}C NMR ($CDCl_3$): δ 75.8 (C-1), 130.9 (C-2), 131.6 (C-3), 69.2 (C-4), 37.7 (C-5), 67.1 (C-6), 138.0, 129.4, 128.9 126.6 (–Ph), 95.9 (Ph*CH*–), 55.7 (–OMe). IR (KBr): ν 1659, 1498 cm^{-1}. Anal. Calcd for $C_{14}H_{16}O_3S$: C, 63.61; H, 6.10; S, 12.13. Found: C, 63.42; H, 6.38; S, 12.11.

4.8. Pummerer rearrangement of sulfoxides 15 and 16 in the presence of *iso*-propanol

Similar Pummerer rearrangement of **15** (200 mg, 0.80 mmol) except replacement of MeOH to *iso*-PrOH (3 mL) gave 110 mg of **20** (47%).

Similar reaction of **16** gave 105 mg of **20** (45%).

4.8.1. Physical data of *20*

Colorless solid. Mp 55–56 °C. ^1H NMR ($CDCl_3$): δ 4.78 (dd, 1H, $J_{1,2}$ 4.4 Hz, $J_{1,3}$ 2.2 Hz, H-1), 6.10 (dd, 1H, $J_{2,3}$ 11.0 Hz, H-2), 5.96 (ddd, 1H, $J_{3,4}$ 2.3 Hz, H-3), 4.78 (dd, 1H, $J_{4,5}$ 3.4, H-4), 3.35 (ddd, 1H, $J_{5,6a}$ 11.7 Hz, $J_{5,6e}$ 4.4 Hz, H-5), 4.54 (dd, 1H, $J_{6a,6e}$ 12.0 Hz, H-6a), 4.08 (dd, 1H, H-6e), 7.45–7.34 (m, 5H, –Ph), 5.72 (s, 1H, Ph*CH*–), 3.94–3.90 (m, 1H, –*i*-Pr), 1.22, 1.16 (each 3H, *J* 6.3 Hz, –*i*-Pr). ^{13}C NMR ($CDCl_3$): δ 71.2 (C-1), 130.8 (C-2), 130.2 (C-3), 71.0 (C-4), 32.3 (C-5), 67.7 (C-6), 138.4, 129.3, 128.7, 126.4 (–Ph), 95.8 (Ph*CH*–), 70.5, 23.5, 20.9 (–O*i*-Pr). IR (KBr): ν 1661, 1457 cm^{-1}. Anal. Calcd for $C_{16}H_{20}O_3S$: C, 65.72; H, 6.89; S, 10.97; Found: C, 65.66; H, 7.18; S, 10.95.

4.9. Pummerer rearrangement of sulfoxides 15 and 16 in the presence of *tert*-butanol

Similar Pummerer rearrangement of **15** (200 mg, 0.80 mmol) except replacement of MeOH to *tert*-BuOH (3 mL) gave 44 mg of **21** (18%).

Similar reaction of **16** gave 45 mg of **21** (18%), respectively.

4.9.1. Physical data of *21*

Pale yellow solid. Mp 73–75 °C. ^1H NMR ($CDCl_3$): δ 4.90–4.87 (m, 2H, H-1, H-4), 6.00 (dd, 1H, $J_{1,2}$ 4.4 Hz, $J_{2,3}$ 10.1 Hz, H-2), 5.89 (dd, 1H, $J_{3,4}$ 1.5 Hz, H-3), 3.35 (ddd, 1H, $J_{4,5}$ 0 Hz,, $J_{5,6a}$ 11.9 Hz, $J_{5,6e}$ 5.0 Hz, H-5), 4.52 (dd, 1H, $J_{6a,6e}$ 11.9 Hz, H-6a), 4.12 (dd, 1H, H-6e), 7.49–7.33 (m, 5H, –Ph), 5.75 (s, 1H, Ph*CH*–), 1.26 (s, 9H, –*t*-Bu). ^{13}C NMR ($CDCl_3$): δ 70.8 (C-1), 132.0 (C-2), 129.8 (C-3), 66.6 (C-4), 32.8 (C-5), 76.2 (C-6), 138.6, 129.3, 128.7, 126.5 (–Ph), 95.7 (Ph*CH*–), 68.0, 28.5 (–*t*-Bu). IR (KBr): ν 1650, 1464 cm^{-1}. Anal. Calcd for $C_{17}H_{22}O_3S$: C, 66.63; H, 7.24; S, 10.46. Found: C, 66.63; H, 7.47; S, 10.45.

4.10. Oxidation of 11

Powder of *m*-CPBA (88 mg, 0.5 mmol) was gradually added to a solution of **11** (117 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) at 0 °C until TLC spot of **11** had been disappeared. The reaction mixture was quenched with 10% aq $Na_2S_2O_3$, and poured into saturated aq $NaHCO_3$, the mixture was extracted with AcOEt for three times and combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated in vacuo. The residue was chromatographed with silica gel column with AcOEt to give 109 mg of **24** (87%).

Physical data of **24**. Colorless solid. Mp 187–190 °C. ^{1}H NMR ($CDCl_3$): δ 4.01 (dd, 1H, $J_{1qa,1qe}$ 15.7 Hz, $J_{1qa,2}$ 6.0 Hz, H-1qa), 3.35 (ddd, 1H, $J_{1qe,2}$ 2.5 Hz, $J_{1qe,3}$ 2.1 Hz, H-1qe), 5.82 (dddd, 1H, $J_{2,3}$ 10.3H, $J_{2,4}$ 1.3 Hz, H-2), 5.96 (ddd, 1H, $J_{3,4}$ 4.3 Hz, H-3), 4.86 (br dd, 1H, $J_{4,5}$ 3.5 Hz, H-4), 2.88 (br s, 1H, H-5), 4.97 (br d, 1H, $J_{6a,6e}$ 13.1 Hz, H-6e), 4.26 (dd, 1H, $J_{5,6a}$ 1.2 Hz, H-6a), 7.50–7.36 (m, 5H, –Ph), 5.66 (s, 1H, Ph*CH*–). ^{13}C NMR ($CDCl_3$): δ 50.5 (C-1), 123.1 (C-2), 129.2 (C-3), 7 3.9 (C-4), 60.3 (C-5), 63.5 (C-6), 137.8, 129.7, 129.2, 126.6 (–Ph), 102.7 (Ph*CH*). IR (KBr): ν 1649, 1497 cm^{-1}. Anal. Calcd for $C_{13}H_{14}O_3S$: C, 62.38; H, 5.64; S, 12.81. Found: C, 62.02; H, 5.47; S, 13.15.

4.11. Pummerer rearrangement of 24 in the presence of methanol

Similar Pummerer rearrangement of **24** (200 mg, 0.80 mmol) gave inseparable ~6:1 mixture of α- and β-anomer **25** (66 mg 31%), assuming that anomeric proton of α-anomer appears lower field than that of β-anomer.

4.12. Optical resolution of 9

*4.12.1. 4-O-Acetyl-1,5-anhyro-2,3-dideoxy-6-O-(tert-butyldimethyl)silyl-5-thio-DL-erythro-hex-2-enitol (**26**)*

To a solution of **9** (300 mg, 2.05 mmol) and imidazole (210 mg, 3.08 mol) in CH_2Cl_2 (10 mL) was added TBSCl (310 mg, 2.06 mmol) and the solution was stirred at room temperature for 1 h. The mixture was washed with water and organic layer was dried over $MgSO_4$, and evaporated in vacuo. To the residue was added pyridine (5 mL) and Ac_2O (1 mL) and the mixture was stirred for 3 h at 0 °C. The mixture was poured into saturated aq $NaHCO_3$ and extracted with AcOEt for three times. The combined extracts were washed with brine, dried over $MgSO_4$, and evaporated in vacuo. The residue was purified by silica gel column chromatography (AcOEt/hexane=1:10) to give **26** (544 mg, 88%).

Physical data of **26**. Colorless syrup. ^{1}H NMR ($CDCl_3$): δ 3.30 (dd, 1H, $J_{1,1'}$ 17.9 Hz, $J_{1,2}$ 3.4 Hz, H-1), 3.09 (dd, 1H, $J_{1',2}$ 2.2 Hz, H-1′), 6.09 (ddd, 1H, $J_{2,3}$ 10.6 Hz, H-2), 5.93 (dd, 1H, $J_{3,4}$ 2.3 Hz, H-3), 5.47 (br s, 1H, H-4), 3.19 (ddd, 1H, $J_{4,5}$ 1.7 Hz, $J_{5,6}$ 3.0 Hz, $J_{5,6'}$ 3.4 Hz, H-5), 3.77–3.73 (m, 2H, H-6), 2.09 (s, 3H, –OAc), 0.89 (s, 9H, *t*-Bu–), 0.06, 0.05 (each s, 3H, Si*Me*$_2$). ^{13}C NMR($CDCl_3$): δ 25.7 (C-1), 129.5 (C-2), 126.9 (C-3), 64.9 (C-4), 43.7 (C-5), 62.1 (C-6), 170.8, 18.6 (–OAc), 26.2, 18.6, −5.1, −5.1 (–OTBS). IR (KBr): ν 1741, 1657, 1235 cm^{-1}. Anal. Calcd for $C_{14}H_{26}O_3SSi$: C, 55.59; H, 8.66; S, 10.60. Found: C, 55.69; H, 8.72; S, 10.31.

*4.12.2. Deacetylation of **26** with Lipase PS*

A suspension of **26** (200 mg, 0.66 mmol) in phosphate buffer (HANNA® instruments HI7007, pH 7.01) (30 mL) in the presence of Lipase PS Amano SD (200 mg) was stirred at room temperature for 12 h. The mixture was filtered by Celite® and the filtrate was extracted with AcOEt for three times, the extracts were dried over $MgSO_4$, and evaporated in vacuo. The residue was purified by silica gel column chromatography (AcOEt/hexane=1:20) to give optically crude (+)-**26** (78 mg, yield 90%, 90%ee) and (−)-**27** (98 mg, yield 98%, 90%ee). Acetylation of crude (−)-**27** with Ac_2O in pyridine and gave crude (−)-**26**. Similar treatment of crude (+)-**26** and (−)-**26** with Lipase PS Amano SD gave deacetylated pure (−)-**27** and recovered (+)-**26**, respectively. Optical rotation of thus isolated (+)-**26** and (−)-**26** was $[\alpha]_D^{20}$ +132.2 and $[\alpha]_D^{20}$ −132.2.

4.13. (−)-1,5-Anhyro-2,3-dideoxy-6-*O*-(*tert*-butyldimethyl)silyl-5-thio-*threo*-hex-2-enitol ((−)-27)

Colorless syrup. $[\alpha]_D^{20}$ −91.5 (*c* 0.95, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 3.26 (dd, 1H, $J_{1,1'}$ 15.7 Hz, $J_{1,2}$ 2.1 Hz, H-1), 2.97 (dd, 1H, $J_{1',2}$ 4.6 Hz, H-1′), 5.98–5.94 (m, 2H, H-2, H-3), 4.30 (br d, 1H, $J_{4,OH}$ 9.9 Hz, H-4), 3.13 (ddd, 1H, $J_{4,5}$ 2.9 Hz, $J_{5,6}$ 9.0 Hz, $J_{5,6'}$ 5.4 Hz, H-5), 3.92 (dd, $J_{6,6'}$ 10.1 Hz, 1H, H-6), 3.81 (dd, 1H, H-6′), 2.85 (br d, 1H, -OH), 0.91 (s, 9H, *t*-Bu–), 0.09, 0.08 (each s, 3H, Si*Me*$_2$). ^{13}C NMR ($CDCl_3$): δ 25.9 (C-1), 131.6 (C-2), 126.6 (C-3), 63.7 (C-4), 45.3 (C-5), 63.5 (C-6), 26.2, 18.6, −5.1, −5.0 (–OTBS). IR (KBr): ν 3452, 1653, 1256 cm^{-1}. Anal. Calcd for $C_{12}H_{24}O_2SSi$: C, 55.33; H, 9.29; S, 12.29. Found: C, 55.39; H, 9.58; S, 12.33.

*4.13.1. Deprotection of (−)-**27***

A solution of (−)-**27** (100 mg, 0.38 mmol) in distd THF (5 mL) was stirred with TBAF·$3H_2O$ (142 mg, 0.45 mmol) at room temperature for 30 min. Reaction mixture was evaporated in vacuo. The residue was purified by silica gel column chromatography ($CHCl_3$/MeOH=30:1) to give (−)-**9** (54 mg, 97%). $[\alpha]_D^{20}$ −174.2 (*c* 1.05, $CHCl_3$).

*4.13.2. Deprotection of (+)-**26***

Compound (+)-**26** (100 mg, 0.33 mmol) was added to a solution of MeONa (10 mg, 0.19 mmol) in MeOH (10 mL) at room temperature. After stirring for 1 h, the mixture was neutralized with Amberlite® IR-120 (plus) and Amberlite® was removed by filtration. The filtrate was evaporated in vacuo, and similar treatment of the residue gave (+)-**9** (40 mg, 83%). $[\alpha]_D^{20}$ +174.2 (*c* 0.95, $CHCl_3$).

Supplementary data

^{1}H and ^{13}C NMR spectra of all new compounds and NOESY spectra for conformationally interesting compounds as well as optimized structure of all compounds in Table 2 and LUMO figure of three compounds in Section 2.1. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.11.025.

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