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(2S,3S)-1-Phenylthio-2,3-butanediol. A Useful Chiral Building Block for a Simple Syntheses of (4R,5S)-5-Hydroxyhexan-4-olide and (4R,5S)-5-Hydroxy-2-hexen-4-olide

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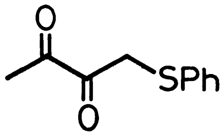
(4R,5S)-5-Hydroxyhexan-4-olide and (4R,5S)-5-hydroxy-2-hexen-4-olide were easily synthesized from (2S,3S)-1-phenylthio-2,3-butanediol, obtained by the bakers' yeast reduction of 1-phenylthio-2,3-butanedione.

Microorganism-mediated reaction of synthetic substrates provides a useful method for the preparation of chiral building blocks in natural products synthesis. We have recently demonstrated that introduction of a sulfur functional group to ketones is an effective way both for the stereocontrol in the asymmetric reduction with bakers' yeast and for further manipulation of the reduction product to natural products.[1] Herein we wish to present a new chiral building block, (2S,3S)-1-phenylthio-2,3-butanediol (**2**), prepared by the bakers' yeast-mediated reduction of 1-phenylthio-2,3-butanedione (**1**), and its application to the enantioselective syntheses of (4R,5S)-5-hydroxyhexan-4-olide (**3**) and (4R,5S)-5-hydroxy-2-hexen-4-olide (**4**), isolated from an antifeeding-active plant (*Osmunda japonica*) against the larvae of the yellow butterfly (*Eurema hecabe mandarian*).[2] The former lactone **3** has been also known as an important constituent of various wines[3] and a precursor of L-amicetose.[4]

The starting material, diketone **1**, was easily prepared by the reaction of 1-bromo-2,3-butanedione[5] with benzenethiol in the presence of triethylamine in methanol and used for the bakers' yeast reduction without further purification after aqueous workup. Diketone **1** (18.2 mmol) was reduced by bakesr' yeast (100 g)(Oriental Yeast Co.) and glucose (120 g) in H_2O (800 ml) for 3 d to give a mixture of *anti*-(2S,3S)-1-phenylthio-2,3-butanediol (**2**) and its *syn*-isomer with a ratio of 86 : 14 in 66% yield from 1-bromo-2,3-butanedione. The absolute configuration of **2** was confirmed by converting into (S)-4-phenylthio-2-butanol (**5**), $[\alpha]^{23}_{D}$ -28.3°(c 0.12, $CHCl_3$),[6] and (S)-1-phenylthio-2-butanol (**6**), $[\alpha]^{23}_{D}$ +53.7° (c 0.78, $CHCl_3$), lit.[7] $[\alpha]^{23}_{D}$ +63.9° (c 1.186, $CHCl_3$), *via* monotosylation of **2** and subsequent reduction with $LiAlH_4$. Recrystallization of **2** from hexane-ether gave optically pure **2**, mp 61 °C, $[\alpha]^{23}_{D}$ +80.9°(c 1.0, MeOH) in 55 - 60% yield.

Diol **2**, utilizing the sulfenyl group, was converted into (2R,3S)-1,2-epoxy-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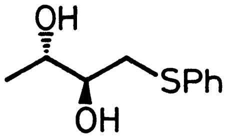
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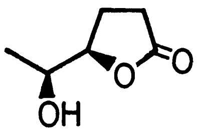
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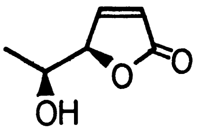
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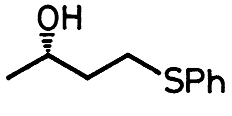

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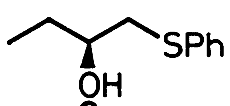

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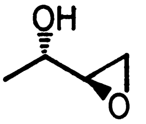

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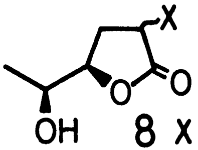

8 X = SPh
9 X = SePh

3-butanol (**7**) in 63% yield by treatment with trimethyloxonium fluoroborate (1.5 equiv) and then with a methanol solution of KOH (2.0 M), $[\alpha]^{23}_{D}$ +16.9° (c 0.2, MeOH), lit.8) $[\alpha]^{26}_{D}$ -17.9° (c 1.16, MeOH) for (2S,3R)-**7**. Ring opening reaction9) of **7** with 2.5 equiv of the lithio derivative of phenylthioacetic acid in THF at -70 °C to room temperature over 9 h and then at room temperature for 14 h, followed by lactonization in dichloromethane in the presence of cat. p-TsOH and anhydrous sodium sulfate at room temperature for 40 h, gave a 1 : 1 diastereomeric mixture of lactone **8** in 91% yield. Oxidation of **8** with m-chloroperbenzoic acid at -50 °C in dichloromethane and reduction with Al-Hg gave the desired **3** in 93% yield, $[\alpha]^{23}_{D}$ -10.2° (c 1.5, $CHCl_3$), lit.2,4) $[\alpha]^{22}_{D}$ -9.23° (c 0.79, $CHCl_3$). Elimination of the sulfoxide of **8** afforded the hexenolide **4**, however, along with a considerable amount of (4S,5S)-isomer, due to the epimerization at C_4 at the reflux temperature of toluene. For milder conditions at the elimination step, phenylsulfoxide group was replaced with phenylselenoxide group. Thus, the similar treatment of **7** with the dianion of phenylselenoacetic acid10) and lactonization gave **9** in 97% yield. Oxidation of **9** with H_2O_2 at 0 °C furnished **4** in 46% yield, $[\alpha]^{23}_{D}$ +88.8° (c 0.472, $CHCl_3$), lit.2) $[\alpha]^{22}_{D}$ +87.7° (c 1.37, $CHCl_3$).

Thus, the bakers' yeast mediated reduction of 1-phenylthio-2,3-butanedione provides a useful chiral building block for the synthesis of natural products having *anti*-1,2-diol structure.

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