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Preparation of Chiral 1,2-Alkanediols with Baker's Yeast-Mediated Oxidation

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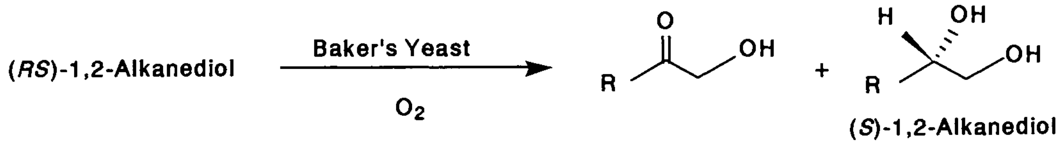
(*S*)-1,2-Alkanediols, which were the opposite configuration to those produced by baker's yeast-mediated bioreduction of corresponding 1-hydroxy-2-alkanones, were prepared by baker's yeast-mediated oxidation. Treatment of racemic 1,2-alkanediols with baker's yeast under the aerobic condition followed by removal of the corresponding 1-hydroxy-2-alkanones, which were produced by enantioselective oxidation of (*R*)-1,2-alkanediols, afforded (*S*)-1,2-alkanediols.

Baker's yeast has been used as a reagent in organic synthesis and a large number of scientific works were devoted to the yeast-mediated bioreductions for preparing chiral compounds in enantiomerically pure form.[1] By the procedure, one enantiomer can be conveniently produced and, however, the formation of the other isomer is essentially impossible. Here, we would like to describe an enantioselective oxidation mediated by baker's yeast and a consequent preparation of the latter enantiomer.

In the course of our study on baker's yeast-mediated transformations, we found that (*R*)-1,2-alkanediol, which was produced by baker's yeast-mediated bioreduction of the corresponding 1-hydroxy-2-alkanone,[2] was enantioselectively oxidized to the starting ketone by treatment with baker's yeast. This reaction would accompany with reduction of NAD^+, and the reduced co-enzyme would be continuously regenerated as NAD^+ through respiratory chain in the cells. Thus, treatment of (*RS*)-1,2-alkanediol with baker's yeast in the presence of oxygen afforded a mixture of (*S*)-1,2-alkanediol and 1-hydroxy-2-alkanone, which were easily separated.



Typical procedure is as follows. A suspension of baker's yeast (56 g), (*RS*)-1,2-propanediol (5 g, 66 mmol), and water (0.5 dm^3) in a 3-dm^3 Erlenmeyer flask was vigorously shaken at 30 °C. The reaction proceeded as shown in Fig. 1 (monitored by GLC). After 24 h, the yeast cells were filtered using Celite and the filtrate was concentrated by means of an evaporator at less than 40 °C. In this condition, acetol evaporated with water. The resultant oil was distilled *in vacuo* to give (*S*)-(+)-1,2-propanediol (2.55 g, 51%). The optical rotation and the purity were $[\alpha]_D^{23}$ +15.1° (neat) and 82.3% ee, respectively. The (*S*)-1,2-propanediol (2.0 g, 26 mmol) was treated with baker's yeast (22.4 g) in water (0.2 dm^3) again. The optical purity of the product (1.42 g, 71%) was enriched through the treatment to 98.0% ee.

Preparations of (*S*)–1,2–alkanediols by this procedure are summarized in Table 1. Though microbial resolutions of 1,2–hexanediol and 1,2–phenylethanediol were not effectively achieved, propane–, butane–, and pentane–1,2–diols with *S*–form were prepared in high optical purity.

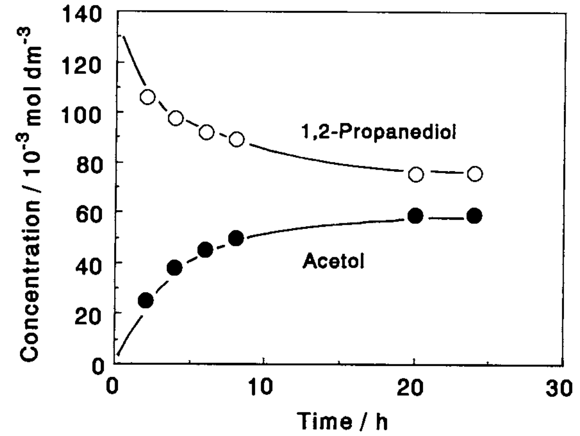


Fig. 1. Time courses of baker's yeast-mediated oxidation of (*RS*)-1,2-propanediol.

Table 1. Preparation of (*S*)-RCH(OH)CH_2OH by baker's yeast-mediated oxidation

1,2-Alkanediol R	First treatment			Second treatment[a]		
	$[\alpha]_D^{23}$/° (*c*)	ee / %	yield / %[b]	$[\alpha]_D^{23}$/° (*c*)	ee / %	yield / %[b]
CH_3	+15.1 (neat)	82.3[c]	51	+17.0 (neat)	98.0[c]	71
C_2H_5	-13.1 (2.02)[d]	86.8[c]	43	-14.2 (2.04)[d]	98.9[c]	86
n-C_3H_7	-18.0 (2.05)[d]	88.5[c]	43	-19.2 (2.00)[d]	99.4[c]	84
n-C_4H_9	-7.4 (2.02)[d]	39.2[c]	61	-11.4 (2.08)[d]	62.4[c]	75
phenyl	+7.3 (0.99)[e]	9.4[f]	76	+11.2 (1.01)[e]	19.9[f]	80

a) Treatment of the product obtained by the first treatment with baker's yeast. b) Isolated yield. c) Determined by HPLC analysis of each mono (*R*)-(+)-MTPA ester [Nomura Develosil 100-3, hexane-ether (9 : 1 - 19 : 1), 1 ml/min, 254 nm]. d) Measured in EtOH. e) Measured in $CHCl_3$. f) Determined by HPLC analysis [Daicel Chiralcel OB, hexane-isopropanol (9: 1), 0.5 ml/min, 254 nm].

In the asymmetric reduction of acetol to (*R*)–1,2–propanediol, oxidoreductases catalyze the transformation using NADH, which is an actual reducing agent, and the resulting NAD^+ is immediately converted into NADH in the yeast cells using some energy source such as ethanol.[3] The oxidoreductases would catalyze the oxidation of (*R*)–1,2–propanediol using NAD^+ as a co–enzyme and the resulting NADH would be converted into NAD^+ through respiratory chain in the cells. This is consistent with the fact that the yeast–mediated oxidation did not proceed under the anaerobic condition. The microbial resolution of the racemic other alkanediols would also proceed in the same manner.

As oxidations mediated by baker's yeast have scarcely been described, this is the first report on its use for preparing chiral alcohols. This procedure is very simple and easy to follow on a laboratory–scale.

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