Baker's Yeast Mediated Reduction of Optically Active Diketone

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Abstract: Baker's Yeast mediated reduction of optically active diketone has been described.

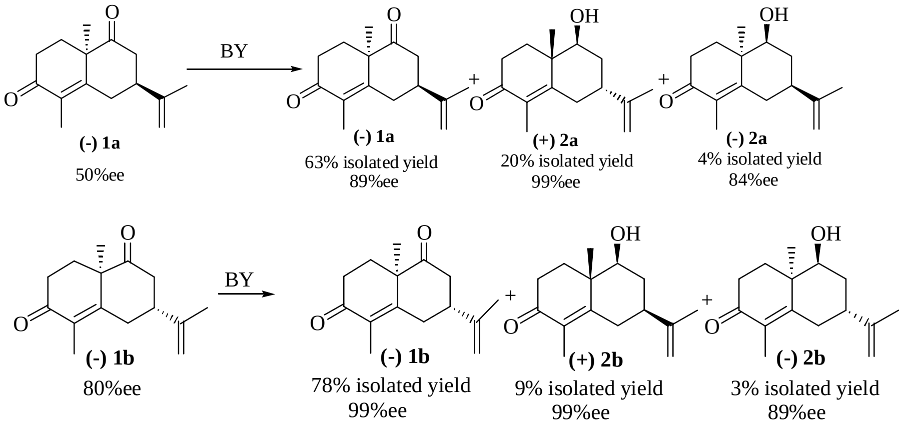
Keywords: Baker's yeast, reduction, optically active, diketone.

Baker's yeast (BY) mediated reduction of synthetic substrate is a useful method for preparing chiral intermediate in synthesis chemistry[1,2], because it is readily available and inexpensive. The selectivity is generally predicted by Prelog rule[3], that is, a hydride is transferred to the *re* face of the prochiral ketone.

The baker's yeast mediated reduction of bicyclic diketones was previously reported by several groups[4-6], but to our knowledge, no application of this reduction to sesquiterpene-type diketone. 9-Oxo-epi-cyperone **1a** and its isomer **1b** were prepared according to the literature method[7]. **1a** was reduced by BY which was incubated at 35°C in phosphate buffer solution with addition of glucose at intervals (**Scheme 1**). Product **(+) 2a** (99% *ee*) was obtained in 20% yield along with **(-) 1a** (89% *ee*) in 63% yield recovered. There is a little amount of **(-) 2a** (84% *ee*) produced at the same time. The absolute configuration of **(+) 2a** and **(-) 2a** can be elucidated by comparison of the spectra data with those for compound which is reduced by $NaBH_4$ from **(-) 1a.** Extension of the reaction time leads to the presence of the diol but not the enhancement of the reaction yield. Similarly, we apply this BY mediated reduction to compound **1b**, nearly all of the compound **(+) 1b** and a little (-) **1b** were reduced to afford **(+) 2b** (99% *ee*) and **(-) 2b** (89% *ee*) in 9% and 3% yield respectively. Optically pure (-) **2b** (99% *ee*) was recovered in 78% yield[8].

The BY mediated reduction proceeded in a highly enatiomerically selective manner according to Prelog rule. It achieved the kinetic resolution of the asymmetric diketones and therefore afforded highly optically active key intermediates smoothly.

Scheme 1



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References and Notes

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8. Spectra data of **(+) 2a** (99% ee): $[\alpha]_D^{25}$ + 94.2 (c 1.4, $CDCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$, δ ppm) 1.16 (s, 3H, 10-Me), 1.71 (s, 3H, 11-Me),179 (s, 3H, 4-Me), 2.81-2.89 (m, 1H, 7-CH), 3.50 (dd, 1H, 9-CH, J = 11.1Hz, J = 5.3Hz), 4.53, 4.74 (each br s, 2H, 12-CH_2); Spectra data of **(-) 2a** (84% ee): $[\alpha]_D^{25}$ – 73.3 (c 1.4, $CDCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$, δ ppm) 121 (s, 3H, 10-Me), 1.82 (s, 3H, 11-Me),184 (s, 3H, 4-Me), 2.86-2.80 (m, 1H, 7-CH), 3.50 (d, 1H, 9-CH, J = 4.8Hz), 4.83, 4.84 (each br s, 2H, 12-CH_2); Spectra data of **(+) 2b** (99% ee): $[\alpha]_D^{25}$ +67.2 (c 1.4, $CDCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$, δ ppm), 1.16 (s, 3H, 10-Me), 1.75 (s, 3H, 11-Me), 176 (s, 3H, 4-Me), 2.64-2.67 (m,1H, 7-CH), 3.43 (dd, 1H, 9-CH, J = 11.6Hz, J = 4.3Hz), 4.74 (br s, 2H, 12-CH_2); Spectra data of **(-) 2b** (89% ee): $[\alpha]_D^{25}$ -57.4 (c 1.2, $CDCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$, δ ppm) 1.23 (s, 3H,10-Me), 1.79 (s, 3H, 11-Me), 1.81 (s, 3H, 4-Me), 2.75-2.79 (m,1H, 7-CH), 3.69 (t, 1H, 9-CH, J = 2.5Hz), 4.82 (s, 2H, 12-CH_2).

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