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Bioreduction of Ethyl 3-Oxobutanoate with Immobilized Baker's Yeast in Organic-Water Solvent Systems[1)]

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Immobilized baker's yeast entrapped in calcium alginate beads has been active in some organic-water solvent systems and reduced ethyl 3-oxobutanoate to ethyl (S)-3-hydroxybutanoate of high enantiomeric purity (95-97% ee's) in good chemical yields.

Although many investigations have been done concerning the use of baker's yeast (Saccharomyces cerevisiae) in water solvent systems in the field of organic synthesis,[2)] there have been few reports on the use of the biocatalyst in organic solvent systems.[3)] Recently, we have prepared immobilized baker's yeast (IBY) entrapped in carrageenan or calcium alginate beads and employed the IBY's in aqueous solutions for transforming several kinds of keto acids and keto esters to alcohol products of high ee.[4,5)] As a continuation of our works on the use of IBY in organic synthesis, we made an investigation of asymmetric bioreductions with IBY in some organic-water solvent systems.

Table 1 exemplifies the bioreductions of ethyl 3-oxobutanoate (**1**) in hexane-, acetonitrile-, and ethyl acetate-water solvent systems employing IBY entrapped in calcium alginate beads of 1-1.5 mm diameter.[5)] For organic (100 mL)-water (900 mL) solvent systems, the repetitive use of the IBY in hexane-water (HW) and in acetonitrile-water (AW) gave the (S)-enantiomer of ethyl 3-hydroxybutanoate (**2**) in 5-47% yields and 96-97% ee's and in 6-57% yields and 97% ee, respectively. However, in ethyl acetate-water (EW) system the bioreduction of **1** did not progress. When organic (500 mL)-water (500 mL) solvent systems were examined, the reduction of **1** proceeded only in HW system to provide (S)-**2** in 33-51% yields, which showed an optical purity of 97% ee. In 1000 mL of hexane, the bioreduction of 2 g of **1** with the IBY catalyst gave (S)-**2** with 96% ee in a maximum yield of 32%. Further, similar bioreduction of 10 g of **1** went more smoothly and (S)-**2**, having an optical purity of 95% ee, was formed in a 53% yield.

In summary, of the three organic media examined hexane was found to be the best solvent, and the bioreduction of **1** with the present IBY in a hexane system yielded (S)-**2** with a high ee on a gram scale.

References

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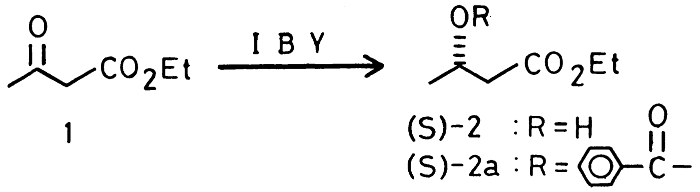
2) R. MacLeod, H. Prosser, L. Fikentscher, J. Lanyi, and H. S. Mosher,

Table 1. Asymmetric Reduction of Ethyl 3-Oxobutanoate (**1**) with IBY in Organic-Water Solvent Systems



Reuse number	% yield[a)] HW	% yield[a)] AW	% yield[a)] EW	% ee[b)] HW	% ee[b)] AW	% ee[b)] EW
A. organic 100 mL-water 900 mL[c)]						
1	47	57	0	96	97	-
2	33	33		96	97	
3	5	6		97	-	
B. organic 500 mL-water 500 mL[c)]						
1	51	0	0	97	-	-
2	38			97		
3	33			97		

Reuse number	% yield[a)]	% ee[b)]
C. hexane 1000 mL[c)]		
1	32	96
2	14	96
3	2	-
1[d)]	53	95[e)]

a) Purified by a combination of column chromatography and micro-vacuum distillation. b) Determined by HPLC analysis of each benzoate ester (S)-**2a**.[5)] c) All experiments were done using **1** (2 g) and IBY prepared from baker's yeast (50 g).[4,5)] Amounts of water in IBY were not examined. d) Use of 10 g of **1**. e) $[\alpha]_D^{22}$ +40.47° (c 0.1738, $CHCl_3$).

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