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ENZYME MEDIATED SYNTHESIS OF OPTICALLY ACTIVE ω-ARENESULFINYLALKANOIC ESTERS

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Incubation of methyl arenesulfinylacetates and methyl α-benzenesulphinylpropionate with *Corynebacterium equi* IFO 3730 afforded the corresponding chiral sulfoxides of high optical purities in moderate to good chemical yields.

Optically active sulfoxides, especially α-sulfinylacetates, have been used as versatile chiral synthons in asymmetric synthesis.[1-3] Availability of this chiral sulfoxides is thus the key for effective synthetic routes. The most general procedure for obtaining chiral α-sulfinylacetates involves the resolution of diasteromeric *l*-menthyl arenesulfinates, followed by the reaction with certain carbanions.[3]

In the course of our studies on microbial transformations of organic molecules,[4] we have found that *Corynebacterium equi* IFO 3730 has an esterase activity which can be applied to enantio-differentiating hydrolysis of sulfinyl esters. This system presents a convenient method for obtaining optically active sulfinylacetates and propionate.

Methyl benzenesulfinylacetate (100 mg) and a suspension of *C. equi* (5 ml) were added to a 45 ml medium containing inorganic salts and 0.5% of 1,2-propanediol as the sole carbon source,[5] and the mixture was shaken at 30 °C. The rate of consumption of the starting ester was revealed to fall down remarkably when about a half of the ester was hydrolyzed.[6] Extraction with ethyl acetate and purification by preparative TLC on silica gel resulted in recovery of the starting material

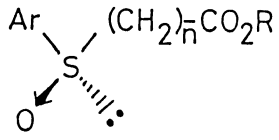

Table 1. Asymmetric Hydrolysis of Arenesulfinyl-Substituted Alkanoates[a]

	Ar	R	n	Recovery/%	$[\alpha]_D^{b)}$/°	Optical purity/%
1	C_6H_5	CH_3	1	43	+155	90
2	p-$CH_3C_6H_4$	CH_3	1	30	+181	90
3	p-ClC_6H_4	CH_3	1	30	+193	97
4	C_6H_5	C_8H_{17}	1	31	+20	42
5	C_6H_5	$C_{11}H_{22}$	1	90	0	0
6	C_6H_5	CH_3	2	22	+87	96
7	C_6H_5	CH_3	3	0	-	-

a) Incubation was carried out at 30 °C for 24 h.
b) As measured in ethanol (c=1-2) at room temperature.

in a yield of 43%. Thus, it is estimated that the rates of enzymatic hydrolysis of (*R*)- and (*S*)-sulfinyl esters are different from each other. In fact, measurement of specific rotation of recovered esters revealed that they are optically active and assumed to have (*R*) absolute configuration from the sign of the rotation.[2] The optical purities of resulting sulfinyl esters were determined by 400 MHz ^{1}H-NMR analysis (methoxy group) using Eu(tfc)$_3$ as chiral shift reagent. The results are summerized in Table 1.

Enzymatic hydrolysis of methyl arenesulfinylacetates uniformly gave high optical yields without regard to the substituent on the aromatic rings. On the other hand, the alkyl group of alcohol moiety seriously effected the rate of hydrolysis (columns 1, 4 and 5). Interesting is the case of methyl β-benzenesulfinylpropionate. In spite of the fact that this substrate has two methylene groups between the ester moiety and the asymmetric center, the enzyme system nicely distinguished the chirality of the substrate, resulting in the recovery of 22% of unhydrolyzed ester in over 95% optical purity (cf. columns 1, 6 and 7). The effect of the number of methylene on the recognition of chirality is well correlate to the results reported by Sih *et al.* in the hydrolysis of diethyl-3-hydroxyglutarate by the same strain.[7]

It will be worthy to mention that acetone-dried cells of this bacterium also catalyzed the enantioselective hydrolysis of benzenesulfinylacetate. Moreover, the dried cells can be stored in a refrigerator without depression of the enzyme activity for at least 2 weeks. Thus, the present method will provide a convenient way for preparing optically active arenesulphinylacetates and propionates.

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6) The presence of a small amount of hydrolyzed free acid in the broth was confirmed by TLC and ^{1}H-NMR. The most part of the acid is supposed to be metabolized by the bacterium. Although, benzenesulfonylacetic acid or ester was estimated as the intermediate, it was not detected in reaction mixture.
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