**Note**

**Enantiomeric Resolution of 1-Phenyl-2-propanol by *Pseudomonas cepacia***

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*Pseudomonas cepacia* hydrolyzed rac-1-phenyl-2-propyl acetate and propionate asymmetrically, affording R(-)-1-phenyl-2-propa- 

and the ester of S(+)1-phenyl-2-propanol.

Sterespecific reactions by enzymes or microorganisms are useful in the preparation of a variety of optically active compounds. 

Especially in the preparation of chiral synthon, optical resolution of racemic compounds by microorganisms is so useful that many 

investigations have been reported.1,2

In the course of our investigation on the biotransformation of organic compounds by *Pseudomonas cepacia*, we have already 

reported that representative antiseptics, parabens,3 and a commonly used pesticide, carbaryl,4 were degraded by the 

bacterium. We also reported the regioselective hydroxylation of 

benzyl alcohol to salicyl alcohol by the bacterium.5 This paper 

reports the results of asymmetric hydrolysis of rac-1-phenyl-2- 

propyl acetate and propionate by *Pseudomonas cepacia*. It is 

interesting that asymmetric hydrolysis occurs under simple 

conditions, in only water solutions of substrates by the 

bacterium.

1-Phenyl-2-propanol, an important chiral synthon, was resolved optically by asymmetric hydrolysis of its acetate and 

propionate by *Pseudomonas cepacia*. After rac-1-phenyl-2-propyl 

acetate or propionate was incubated for a week with *Pseudomonas cepacia*, the S(+)-ester and R(-)-free alcohol were found to be 

almost at equal amounts; about 50% toward the initial 

concentration of rac-compounds, suggesting no other reactions 

occur without hydrolysis. Optical purities of S(+)3-esters and 

R(-)-free alcohols were 60-80% e.e. measured by HPLC. On 

the other hand, rac-1-phenyl-1-propanol was similarly resolved 

optically, though the optical purities were low. In addition, 

rac-1-phenyl-1-ethanol was also resolved optically only when its 

propionate was used as the substrate. When its acetate was 

used as the substrate, however, rac-1-phenyl-1-ethanol was not resolved 

optically. The numbers of the bacteria were found to increase 

gradually during the biocconversion period, measured by the OD660 

of the culture liquid. For instance, the OD660 of the culture liquid 

increased from 0.05 to 0.15 during the biocconversion period.

*Pseudomonas cepacia* (IFO 15124) used in this experiment was 

given us by the IFO (Institute for Fermentation, Osaka). 

Rac-1-phenyl-2-propanol, rac-1-phenyl-1-propanol and rac-1- 

phenyl-1-ethanol, and their R3-isomers (e.e. >99) were 

purchased from Fluka Fine Chemicals. [x]D50 of R3-isomers were 

as follows; R-1-phenyl-2-propanol, -41.0°; S-1-phenyl-2-propanol, 

+41.1°; R-1-phenyl-1-propanol, +46.9°; S-3-phenyl-1- 

propanol, -46.8°; R-1-phenyl-1-ethanol, +44.8°; S-1-phenyl-1- 

ethanol, -44.9°. Acetylation and propionylation were done by 

treating the chemicals with acetic anhydride or propionic anhydride in pyridine, respectively. The products were extracted 

with ethyl acetate and purified by preparative TLC on silica gel 

(Merk, Art 5715 Kiesel gel 60 F254) with a solvent system of 

hexane-ethyl acetate (8:2). The esterified products were almost 

50% R-isomer and almost 50% S-isomer by HPLC. 

In each case, a number of 500-ml Erlenmeyer flasks containing 

250 ml of water were autoclaved for 20 min, then ester was added. 

A 200 µg/ml solution of esters was used as a culture medium. A 

few loops of bacteria, cultured on SCD (soybean casein digest) 

agar medium, containing 1.5% peptone, 0.5% soybean peptone, 

0.5% NaCl, and 1.5% agar, were inoculated into flasks, which 

were left for about seven days at 30°C.

After culture for a week, when almost half the esters were 

hydrolyzed, the incubated solution with cells was extracted 

with ethyl acetate. Evaporation of the solvent gave yellow 

materials, which were separated by preparative TLC on silica gel (Merk, 

Art 5715 Kieselgel 60 F254) with a solvent system of hexane-

ethyl acetate (8:2). A well-separated band, Rf 0.8, was collected 

and stripped with methanol, then put on HPLC to measure the 

optical purity. Another well-separated band, Rf 0.3, was collected 

and stripped with methanol, which was esterified with acetic 

anhydride. The reaction product was dissolved in methanol and 

was put on HPLC to measure the optical purity. No change in 

the concentration of esters and ratios of R-isomers and S-isomers 

were observed under the same conditions in the blank test.

For HPLC analysis, the mobile phase, 0.01M NH4H2PO4 

(adjusted to pH 2.5 with H3PO4)-CH2CN (6:4) was used. The 

**Table I. Retention Times of R,S-1-Phenyl-2-propyl, R,S-1-Phenyl-1- 

propyl, and R,S-1-Phenyl-1-ethyl Acetate and Propionate**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Retention time of S-isomer (min)</th>
<th>Retention time of R-isomer (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-Phenyl-2-propyl-acetate</td>
<td>4.5</td>
<td>5.0</td>
</tr>
<tr>
<td>1-Phenyl-2-propyl-propionate</td>
<td>4.4</td>
<td>5.0</td>
</tr>
<tr>
<td>1-Phenyl-1-propyl-acetate</td>
<td>7.0</td>
<td>8.5</td>
</tr>
<tr>
<td>1-Phenyl-1-propyl-propionate</td>
<td>6.9</td>
<td>8.5</td>
</tr>
<tr>
<td>1-Phenyl-1-ethyl-acetate</td>
<td>5.0</td>
<td>6.0</td>
</tr>
<tr>
<td>1-Phenyl-1-ethyl-propionate</td>
<td>4.6</td>
<td>5.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Hydrolysis ratio (%)</th>
<th>e.e. (%) of (R)-Free alcohol</th>
<th>e.e. (%) of (S)-Ester</th>
</tr>
</thead>
<tbody>
<tr>
<td>rac-1-Phenyl-2-propyl-acetate</td>
<td>50.1</td>
<td>78.3</td>
<td>70.7</td>
</tr>
<tr>
<td>rac-1-Phenyl-2-propyl-propionate</td>
<td>46.9</td>
<td>64.0</td>
<td>78.9</td>
</tr>
<tr>
<td>rac-1-Phenyl-1-propyl-acetate</td>
<td>56.0</td>
<td>25.4</td>
<td>44.3</td>
</tr>
<tr>
<td>rac-1-Phenyl-1-propyl-propionate</td>
<td>50.8</td>
<td>Not measured</td>
<td>14.8</td>
</tr>
<tr>
<td>rac-1-Phenyl-1-ethyl-propionate</td>
<td>45.4</td>
<td>80.3</td>
<td>79.6</td>
</tr>
</tbody>
</table>

* Molar ratio of free alcohol to initial rac-ester.
column used was Shiseido Capcell Pak C_{18} SG-120 (150 mm x 6.0 mm i.d.) commercially packed with reversed-phase octadecysilica, through which the above mobile phase was run at a flow-rate of 1.0 ml/min. The detection was done at 254 nm and samples of 10 μl were injected onto the column. The concentrations of the compounds were measured by the internal standard method.

HPLC for measurement of optical purity was done as follows. As the mobile phase, methanol was used. The column used was a Shiseido Ceramospher Chiral RU-1 (250 mm x 4.6 mm i.d.), commonly used for the separation of rac-compounds, through which methanol was run at a flow-rate of 1.0 ml/min. The detection was done at 254 nm and samples of 10 μl were injected on to the column. The optical purities were measured by the peak area ratio. Retention times of R-isomers and S-isomers are shown in Table I.

rac-1-Phenyl-2-propyl acetate and propionate were resolved optically to R(-)-1-phenyl-2-propanol and S(+)1-phenyl-2-propyl acetate or S(+)1-phenyl-2-propyl propionate. Similarly, rac-1-phenyl-1-propyl acetate and propionate were resolved optically to R(+)-1-phenyl-1-propanol and S(-)-1-phenyl-1-propyl acetate or S(-)1-phenyl-1-propyl propionate. On the other hand, rac-1-phenyl-1-ethyl propionate was resolved optically to R(+)-1-phenyl-1-ethanol and S(-)-1-phenyl-1-ethyl propionate, while rac-1-phenyl-1-ethyl acetate was not resolved optically. Hydrolysis ratios and optical purities are shown in Table II.

Esterase produced by Pseudomonas cepacia was found to hydrolyze R-isomers of esters stereoselectively. In the case of rac-1-phenyl-1-ethanol acetate, however, stereoselective hydrolysis did not occur.

References