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A convenient chemoenzymatic synthesis of chiral 1-benzyl-5-(hydroxymethyl)-2-piperidone enabled by lipase AK desymmetrization of prochiral 1,3-diol and its diacetate

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Dimethyl 2-(3-(benzylamino)-3-oxopropyl)malonate 10
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N-Benzyl-5-acetoxy-4-(acetoxymethyl)pentanamide 5
5-(benzylamino)-2-(hydroxymethyl)-5-oxopentyl acetate 3

\[
\begin{align*}
\text{AcO} & \quad \text{CONHBn} \\
\end{align*}
\]
(R)-1-benzyl-4-(hydroxymethyl)piperidin-2-one 1
HPLC diagrams of racemic-, (R)- and (S)- of monoacetate 3

**racemic-3**

Retention time: 45.3 min
Area ratio: 58.07

Retention time: 49.9 min
Area ratio: 48.92

**(R)-3: ee = 96.7% – 3.3% ≈ 93%**

Retention time: 48.1 min
Area ratio: 95.7%

Retention time: 49.8 min
Area ratio: 3.9%

**(S)-3  ee = 96.4% – 3.6% ≈ 93%**

Retention time: 49.1 min
Area ratio: 96.43%

Retention time: 49.5 min
Area ratio: 3.57%