SYNFACTS

Highlights in Current
Synthetic Organic
Chemistry

REPRINT



Thieme

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Use of a Robust Dehydrogenase from an Archael Hyperthermophile in Asymmetric Catalysis – Dynamic Kinetic Resolution Entry into (*S*)-Profens

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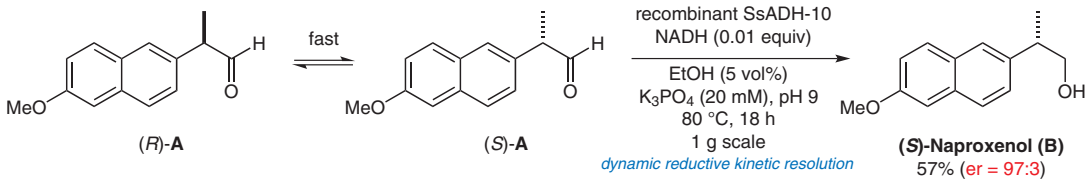
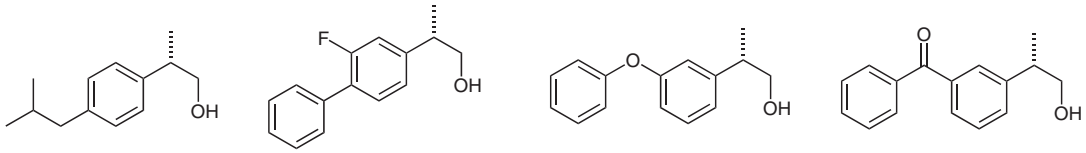
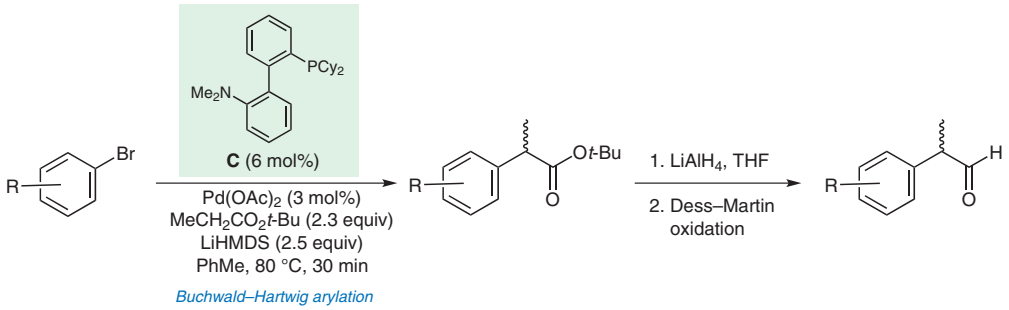
# Synthesis of (*S*)-Profens




**The following (*S*)-profenols were similarly prepared:**




**Synthesis of the starting racemic 2-arylpropanals:**




**Significance:** Recombinant alcohol dehydrogenase-10 from the hyperthermophile *Solfolobus solfataricus* (SsADH-10) effects efficient dynamic reductive kinetic resolution of 2-arylpropanals. The reaction is performed at 80 °C using NADH as the catalytic reductant and 5% EtOH as the stoichiometric reductant. Success depends on the rapid equilibration of the 2-arylpropanal substrates (e.g. **A**) under the basic reaction conditions (pH 9). Only one of twelve substrates examined failed to react. The yields ranged from 55–99% and the er was generally >95:5.

**Comment:** Oxidation of the profenols (e.g. **B**) to the corresponding carboxylic acids gives commercially significant non-steroidal anti-inflammatory drugs (NSAIDs), such as naproxen, ibuprofen, flurbiprofen, fenoprofen and ketoprofen. The starting racemic 2-arylpropanals were synthesized via Buchwald–Hartwig arylations of the lithium enolate derived from *tert*-butyl propionate.

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**Category**

**Synthesis of Natural Products and Potential Drugs**

**Key words**

**profens**

**dynamic kinetic resolution**

**enzymatic reduction**

**dehydrogenases**

**racemization**