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Synthesis of (S)-Profens

The following (S)-profenols were similarly prepared:

(S)-Ibuprofenol 92% (er > 99:1)
(S)-Flurbiprofenol 77% (er > 98:2)
(S)-Fenoprofenol 85% (er > 97:3)
(S) Ketoprofenol 85% (er > 97:3)

Synthesis of the starting racemic 2-arylpropanals:

Significance: Recombinant alcohol dehydrogenase-10 from the hyperthermophile Sulfolobus 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 alylations of the lithium enolate derived from tert-butyl propionate.

SYNFACTS Contributors: Philip Kocienski
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