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Naproxen-Derivate durch enantioselektive Decarboxylierung

Asymmetric Catalysis, 134 [1]. Naproxen Derivatives by Enantioselective Decarboxylation Henri Brunner und Peter Schmidt

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2-Aryl-substituted propionic acids, such as the important anti-inflammatory agent Naproxen, exist in two enantiomeric forms. The (*S*)-enantiomer of 2-(6-methoxynaphth-2-yl)propionic acid **1** is about 28 times more effective than the (*R*)-enantiomer. A new catalytic method to synthesize Naproxen (*S*)-**1** involves the enantioselective decarboxylation of suitably substituted malonic acid derivatives. Thus, 2-(6-methoxynaphth-2-yl)-2-methylmalonic acid **6** and its monoester **7** were stirred in THF with catalytic amounts of chiral bases, which induced decarboxylation. After work-up, optical inductions up to 39.8% *ee* were found in the resulting products **1** and **9**. The optically active bases may be fully recycled by extraction.