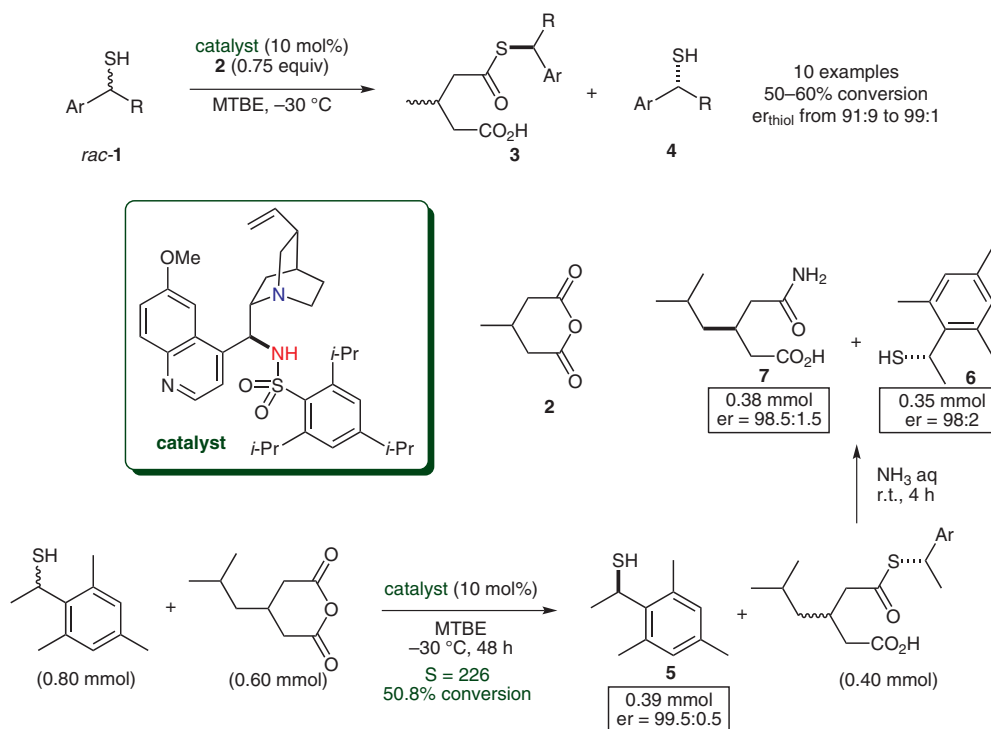


A. PESCHIULLI, B. PROCURANTI, C. J. O'CONNOR, S. J. CONNOR* (THE UNIVERSITY OF DUBLIN, IRELAND)

Synergistic Organocatalysis in the Kinetic Resolution of Secondary Thiols with Concomitant Desymmetrization of an Anhydride

Nat. Chem. **2010**, *2*, 380-384.

Kinetic Resolution of Thiols



Significance: An efficient direct acylative kinetic resolution of racemic secondary thiols **1** was reported by the authors, using a novel sulfonamide catalyst derived from a cinchona alkaloid. Under optimal conditions (10 mol% catalyst loading, -30 °C in MTBE), with **2** as the electrophile, various secondary aromatic thiols can be resolved with high er at ~50% conversion. The selectivity ($S = k_{\text{fast}}/k_{\text{slow}}$) of the resolution is in the range of 50–275. In addition, during the kinetic resolution of the thiols, a simultaneous desymmetrization of a meso-anhydride electrophile (like **2**) also occurred with excellent enantioselectivity.

Comment: Although the kinetic resolution of alcohols is a well-established process, analogous methods for thiols are rare. This organocatalytic transformation involving a kinetic resolution of a racemic thiol and a simultaneous enantioselective desymmetrization of an achiral anhydride, is quite useful and atom-economic. The preparation of the hemiamide **7** [a precursor for (*R*)-pregabalin] shown in the Scheme is a nice demonstration. Both enantiomers (**5** and **6**) of the thiol and the desymmetrization product **7** can be obtained in high yields and high enantiomeric ratios.

SYNFACTS Contributors: Benjamin List, Saihu Liao
Synfacts 2010, 7, 0825-0825 Published online: 22.06.2010
DOI: 10.1055/s-0029-1220116; Reg-No.: B05610SF

2010 © THIEME STUTTGART • NEW YORK

Category

Organo- and Biocatalysis

Key words

kinetic resolution
secondary thiols
desymmetrization

SYNFACTS
of the month