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

**Kinetic Resolution of Thiols**

In the kinetic resolution of racemic secondary thiols (1), a novel sulfonamide organocatalyst derived from a cinchona alkaloid was used. Under optimal conditions (10 mol% catalyst loading, –30 °C in MTBE), with an electrophile (2), various secondary aromatic thiols can be resolved with high enantiomeric ratios (er) at ~50% conversion. The selectivity (S = k_{fast}/k_{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 (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.

**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_{fast}/k_{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.

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