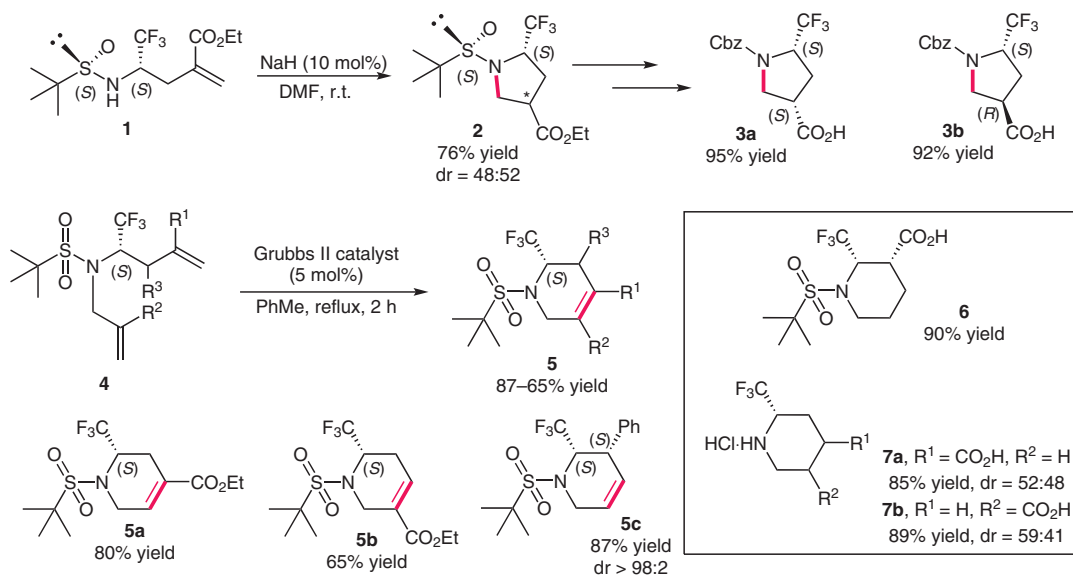


J. HAO, T. MILCENT\*, P. RETAILLEAU, V. A. SOLOSHONOK, S. ONGERI, B. CROUSSE  
(UNIVERSITY OF THE BASQUE COUNTRY, SAN SEBASTIAN, SPAIN; UNIVERSITÉ PARIS-SACLAY, CHÂTENAY-MALABRY AND UNIVERSITÉ PARIS-SUD, FRANCE)

Asymmetric Synthesis of Cyclic Fluorinated Amino Acids

*Eur. J. Org. Chem.* **2018**, 3688–3692.

## Synthesis of Trifluoromethylated Pyrrolidine and Piperidine Amino Acids



**Significance:** The physical and chemical properties of N-heterocycles can be modified by the insertion of fluorine atoms, resulting in great advantages to medicinal chemistry and organocatalysis. In these aspects, fluorine atoms can influence the stability, conformation, basicity, and pharmacokinetic properties of N-heterocycles (see Review below).

**Review:** X.-G. Hu, L. Hunter *Beilstein J. Org. Chem.* **2013**, *9*, 2696–2708.

**Comment:** Reported are the syntheses of the trifluoromethylated  $\beta$ -proline derivatives **2**, **3a**, and **3b** through intramolecular 5-*endo*-trig cyclization of the *N*-homoallylic sulfonamide **1**, and the syntheses of tetrahydropyridines **5** through a ring-closure metathesis (RCM) approach starting from diallylic substrates **4**. Because the diastereomeric mixture **2** could not be separated, the protecting group was replaced with Cbz to permit separation. The products were then separately saponified to give the *N*-Cbz-CF<sub>3</sub>- $\beta$ -prolines **3a** and **3b**. The Grubbs second-generation catalyst was employed in an RCM process to synthesize the tetrahydropyridines **5**. Amino acids **6**, **7a**, and **7b** were prepared from tetrahydropyridines **5** by catalytic hydrogenation/oxidative degradation under Sharpless conditions for compound **6** and by catalytic hydrogenation/cleavage of the protecting group/ester hydrolysis for compounds **7a** and **7b**.

**SYNFACTS Contributors:** Victor Snieckus, Sara Gomes  
Synfacts 2018, 14(10), 1015 Published online: 17.09.2018  
**DOI:** 10.1055/s-0037-1610969; **Reg-No.:** V10418SF

2018 © THIEME STUTTGART • NEW YORK

Category

Synthesis of Heterocycles

Key words

5-*endo*-trig cyclization

ring-closing metathesis

trifluoromethylpyrrolidinecarboxylic acids

trifluoromethylpiperidinecarboxylic acids

Synfact  
of the month

This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.