Enantioselective Addition of Masked Acyl Cyanides to N-Boc Imines

Significance: Yang and Rawal report the enantioselective synthesis of α-amino acid derivatives and peptides starting from N-Boc imines and TBS-protected hydroxyl malononitriles as masked acyl cyanides (MACs). The reaction is catalyzed by an easily accessible quinidine-derived catalyst which generates the desired addition products with good to excellent yields and enantioselectivities under mild reaction conditions. Further derivatization of the primary products to the corresponding esters, amides, and peptides was demonstrated without loss of enantioenrichment.

Comment: In light of the high academic and industrial interest in the synthesis of (protected) amino acids and peptides, the development of new enantioselective approaches to such scaffolds is an attractive research goal. The Rawal group contributes nicely to this area by exploiting the nucleophilic character of the MAC reagent, which enables an umpolung-type bond-forming event (see also: J. Am. Chem. Soc. 2013, 135, 16050; Synfacts 2013, 9, 1348). It is remarkable that even highly sensitive aliphatic N-Boc imines are employed in this methodology.