Enantioselective Michael Addition of Isocynoacetate to Vinyl Selenone: Access to α-Quaternary Amino Acids

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Enantio enriched α-quaternary amino acids are presents in many natural products. Moreover, their resistance against enzymatic degradation and their rigid conformation makes them useful as peptidomimetics.¹

We wish to present our approach towards this key structure through an organocatalyzed Michael addition of α-substituted isocyanoacetate to vinyl selenone. The use of isocyanoacetate as a glycine template is known but only few examples achieved enantioselective transformation without a subsequent cyclization of the isonitrile part. The substitution of the selenoyl group makes this a versatile method to produce α-quaternary amino-acids.

The scalability of this transformation was then illustrated through the enantioselective synthesis of both (+)- and (-)-trigonoliimine A.²

1. For a review on stereoselective synthesis of quaternary α-amino acids see: C. Cativiela, M. D. Díaz-de-Villegas, Tet. Asym. 2007, 18, 569-623.