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BRØNSTED BASE CATALYZED ADDITION OF 2-NITROETHYL SULFONES TO N-BOC IMINES: AN ENTRY TO ALLYLIC AMINES

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Allylic amines appear as common moieties in biologically and pharmacologically active molecules.[1] In addition, their chemical versatility makes them important key intermediates in asymmetric synthesis since transformations based on their use are numerous and usually proceed with excellent stereoinduction. Traditional synthetic approaches for optically active allylic amines are mainly based on either metal catalyzed asymmetric carbon-carbon bond forming reactions or stereoselective reductions.[2] These methods usually provide straightforward routes to non-terminal allylic amines for which certain restrictions related to the substitution patterns apply. In this work, we present a highly efficient organocatalytic methodology for the synthesis of gamma-sulfonyl allyl amines in which the key for success is the use of ureidopeptide based Brønsted base catalysts[3] to promote the reaction of 2-nitroethylsulfones and azomethine groups. The organocatalyzed stereoselective addition, followed by nitrous acid elimination, represents a short and efficient route towards the synthesis of enantiomerically enriched gamma-sulfonyl allyl amines involving a practical formal d3-synthon. Furthermore, the distinct functionality of the resulting gamma-sulfonyl allyl amines gives additional versatility to this procedure since they can be easily transformed into the corresponding enantiomerically enriched allylic amines. [1] For representative examples, see: a) Gram, L.; Larsson, O. M.; Johnsen, A.; Schousboe, A. Br. J. Clin. Pharmacol. 1989, 27, 13S-17S. b) Sheean, G.; Schramm, T.; Anderson, D. S.; Eadie, M. Clin. Exp. Neurol. 1992, 29, 107-116. [2] For a review on the synthesis of chiral allylic amines, see: Cheikh, R. B.; Chaabouni, R.; Laurent, A.; Mison, P.; Nafti, A. Synthesis 1983, 685-700. [3] a) Diosdado, S.; Etxabe, J.; Izquierdo, J.; Landa, A.; Mielgo, A.; Olaizola, I.; López, R.; Palomo, C. Angew. Chem. Int. Ed. 2013, 52, 11846-11851. b) Diosdado, S.; López, R.; Palomo, C. Chem. Eur. J. 2014, 20, 6526-6531. c) Echave, H.; López, R.; Palomo C. Angew. Chem. Int. Ed. 2016, 55, 3364-3368.