Single H-Bond Donor Organocatalytic Enantioselective Pictet-Spengler Reaction of α-Diketones: Development and Application to Facile Access to Natural Product Analogues

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While catalytic enantioselective Pictet-Spengler reaction (PSR) with aldehydes is well-established, the use of ketones as electrophilic partners remains less developed. Thus, we report herein the first example of enantioselective PSR of tryptamines with *α*-diketones using prolyl-urea organocatalysts bearing a single H-bond donor function. A primary kinetic isotope effect (KIE = 2.64) using C2-deteurium-labelled tryptamine indicates that rearomatization of the pentahydro-*β*-carbolinium ion should be the rate- and enantioselectivity-determining step. A concise formal synthesis of (-)-subincanadines A and B was accomplished. After a highly diastereoselective addition on 1-alkyl-1-methoxycarbonyl tetrahydro-β-carbolines (THBCs), a facile access to natural products analogues was achieved.