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Synthesis of All-Carbon, Quaternary Center Containing Cyclohexenones through an Organocatalyzed, Multicomponent Coupling

Enantioselective One-Pot Synthesis of Substituted Cyclohexenones

Significance: The authors report the enantioselective synthesis of substituted cyclohexenones bearing an all-carbon quaternary stereocenter in the C4 position. The corresponding products were obtained in good yields and good to high enantioselectivities. Proline-derived sulfonamide 3 catalyzed the reaction between different enones 1 and α-branched aldehydes 2 only in the presence of benzylamine. Thus, it seems likely that both carbonyl reaction partners have to be activated by means of aminocatalysis. In the proposed mechanism the benzylamine-derived enamine of 2 is reacting with the iminium ion formed from 3 and 1. An alternative mechanism could involve the attack of the 3-derived enamine of 2 to the imine formed by condensation of benzylamine and 1. Both scenarios can be supported by reasonable hydrogen-bonding interactions.

Comment: Organocatalytic multicomponent reactions have attracted considerable attention over the last years, because they allow the construction of complex structures in a simple one-pot operation. The method reported herein gives rapid access to cyclohexenones with two contiguous stereocenters, one of them all-carbon quaternary, in good yields and enantioselectivities. An interesting feature of this reaction is the additional need of benzylamine to promote the desired transformation. However, in this case the amine is not incorporated into the final product as in a related work by the same group (Tetrahedron 2010, 66, 4854). Due to the versatility of the obtained cyclohexenones applications of this method can be expected.