Enantioselective Construction of α,α-Dihaloaldehydes by Tertiary Amine-Catalyzed α-Bromination of α-Chloroaldehydes

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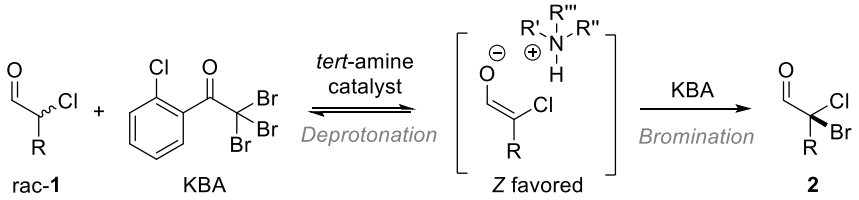
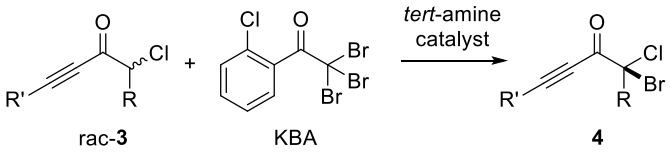
α-Bromocarbonyl compounds can serve as versatile synthetic intermediates in the formation of carbon−carbon bonds as well as various carbon−heteroatom bonds because of the high leaving group ability of the bromine atom. α-Bromination of carbonyl compounds via enamine/enolate intermediates is one of the straightforward synthetic methods for α-bromocarbonyl compounds. Recently, our group has developed the secondary amine-catalyzed asymmetric α-bromination of aldehydes with ketone-based brominating agents (KBA).[1] Although several stereoselective α-bromination of aldehydes have been developed, the enantioselective α-bromination of α-branched aldehydes has proven far more challenging.

Herein, we report a tertiary amine-catalyzed enantioselective α-bromination of α-chloroaldehydes with KBA. A variety of α-bromo-α-chloroaldehydes were obtained with moderate to high yields and enantioselectivities. Mechanistic studies implied that the one enantiomer of α-chloroaldehydes is preferentially deprotonated by the tertiary amine catalyst, leading to *Z*-selective enolate formation.



In addition, alkynyl ketones could also be applied to this reaction system and gave the desired α,α-dihaloketones with high yields and enantioselectivities, while phenyl ketones were not suitable substrates.



1) A. Takeshima, M. Shimogaki, T. Kano, K. Maruoka, *ACS Catal*. **2020**, *10*, 5959.