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Highly stereoselective synthesis of bicyclic α-hydroxy acid derivatives: Co2(CO)8 mediated cyclization of α,α-disubstituted 1,3-dioxolanones.

Highly stereoselective synthesis of bicyclic α-hydroxy acid derivatives via Co2(CO)8 mediated cyclization (Pauson-Khand Reaction) is presented. Formation of cyclopentanone from alkene and alkyne in the presence of Co2(CO)8 is known as Pauson - Khand Reaction.

α-Substituted 1,3-dioxolanone derivatives were used as the starting compounds for the synthesis of bicyclic α-hydroxy acids. These dioxolanones could be easily prepared in the laboratory and also have high synthetic potential in the asymmetric synthesis of α-hydroxy acids. The precursor for the Pausan-Khand cyclization was prepared by propagylating α-allylated 1,3-dioxolane-4-one derivative via its enolate. This reaction was highly stereoselective and only one diastereoisomer was formed in good yield. This stereoselectivity could be rationalized by adopting the conformation of enolate into allylic-strain model (A1,3 strain). The propagylated compound was subjected to Pauson - Khand cyclization in the presence of tertiary amine N-oxide as the promoter. The cyclization was highly selective and desired tricyclic product was isolated as 78:22 mixture of diastereoisomers out of four possible diastereoisomers in 67% yield at room temperature. The two diastereoisomers were seperated by preparative HPLC. The relative stereochemistry of the major diatereoisomer was determined by NMR experiments (NOE difference spectra). This high stereoselectivity could be rationalized by considering steric effect. This methodology is very convenient and could be applied in the synthesis of a wide rang of biologically relavent compounds.