

The Reaction of Cyanohydrins with Epoxides as an Alternative for the Stereoselective Preparation of Aldols

*McGlade, C. A.¹, and Hartel, A.M.²

¹Undergraduate Research Assistant, Department of Chemistry, Winthrop University,

²Professor, Department of Chemistry, Winthrop University
mcgladec2@winthrop.edu

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Abstract: The Aldol addition is one of the most important carbon-carbon bond forming reactions in organic chemistry. The reaction, which occurs between an enolized carbonyl and an aldehyde or ketone, results in the formation of a β -hydroxy carbonyl, or “aldol” product. The reaction can generate up to two new chiral centers, making both enantio- and diastereoselectivity important. We have developed a new method for the stereoselective preparation of aldols exploiting the reaction of O-silylated cyanohydrins with epoxides. The reaction conditions have been optimized and the scope of epoxide substrates has been explored. Current research is focused on investigating the scope of the cyanohydrin component. A series of O-silylated cyanohydrins were synthesized, treated with LiHMDS and the resulting anions reacted with 1,2-epoxybutane to effect alkylation. The crude adduct was then desilylated using TBAF to afford the final aldol product. Overall, variations on the cyanohydrin have been found to be less tolerated than those on the epoxide, however aryl substituents lacking any additional functionality provided the expected aldol in good yield.