アトルバスタチンの短工程合成を目指したβ－アルコキシアルデヒドのシアノメチル化反応

Cyanomethylation of beta-Alkoxyaldehydes: Toward A Short Synthesis of Atorvastatin

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Abstract
In our efforts to develop a short synthesis of atorvastatin, an active pharmaceutical ingredient of Lipitor, cyanomethylation of beta-alkoxyaldehydes has emerged as a convincing transformation. Our initial investigations employed the use of various established catalytic cyanomethylation conditions, but all attempts failed to produce the corresponding products. These elimination-prone aldehydes pose a chemoselectivity issue due to the competing elimination and addition pathways, and there are, indeed, no examples in the literature showing even the racemic addition of acetonitrile using stoichiometric amounts of a Brønsted base. The present work describes a feasibility study of the proposed short synthesis by devising new cyanomethylation conditions. Among Brønsted bases examined, nBuLi effectively promotes the addition of an alpha-cyanocarbanion and suppresses the undesired elimination. The cyanomethylated product can be converted to a known intermediate for the synthesis of atorvastatin, showcasing the synthetic potential of the current transformation.[1]

Reference