SYNLETT
Spotlight 90

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Diazabicyclo[2.2.2]octane – DABCO

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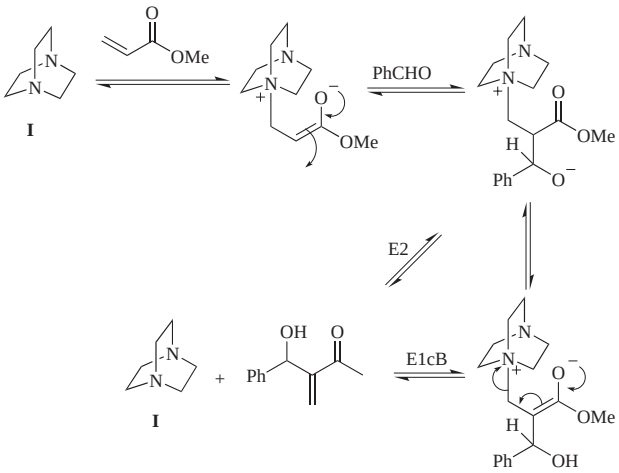
Introduction

Diazabicyclo[2.2.2]octane, DABCO (**I**), is the most commonly used catalyst in the Baylis–Hillman reaction.[1] This important carbon-carbon bond forming reaction has received much attention in recent years because it provides multifunctional molecules with a newly created stereocenter, which are versatile building blocks in organic synthesis.

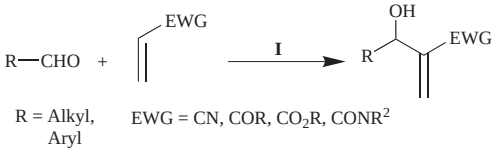
The generally accepted mechanism is illustrated in Scheme 1 for the DABCO-catalyzed Baylis–Hillman reaction of benzaldehyde with methyl acrylate.



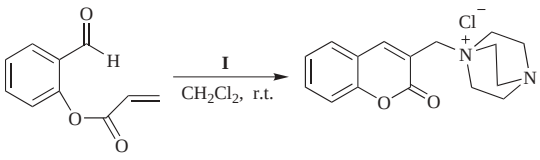
Scheme 1 DABCO catalyzed Baylis–Hillman reaction

Abstracts

(1) In 1972, Anthony Baylis and Melville Hillman[2] described the reaction of an aldehyde with a broad spectrum of activated alkenes under the influence of DABCO (**I**).



(2) Drewes et al.[3] reported the DABCO (**I**)-catalyzed intramolecular Baylis–Hillman reaction of the acrylate ester of salicylaldehyde to afford a crystalline coumarin salt as the major product being in evidence with the proposed mechanism.



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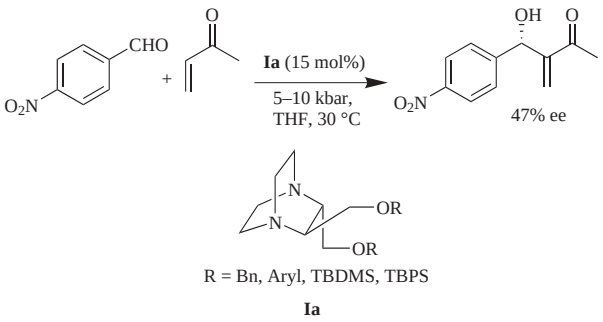
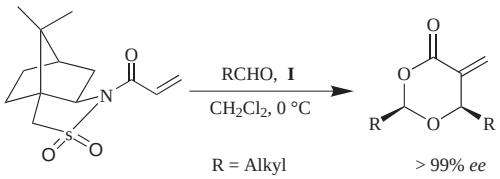
(3) Chiral C_2-symmetric 2,3-disubstituted DABCOs[4] have been effectively utilized for the asymmetric Baylis–Hillman reaction between *p*-nitrobenzaldehyde and methyl vinyl ketone under high pressure (5–10 kbar) to obtain asymmetric induction up to 47% *ee*.

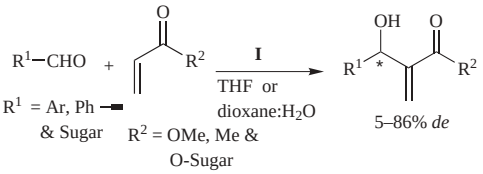


Ia

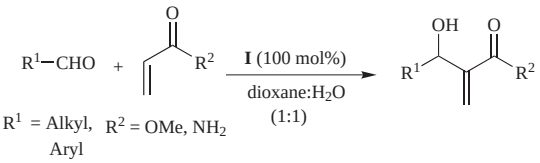
(4) Leahy et al.[5] described the most impressive asymmetric Baylis–Hillman reaction using Oppolzer's sultam as chiral auxiliary and DABCO as catalyst to obtain the chiral dioxanone product in high enantiomeric purity (>99% *ee*). It is noteworthy that the sultam auxiliary was fortuitously cleaved by the addition of a second equivalent of aldehyde.



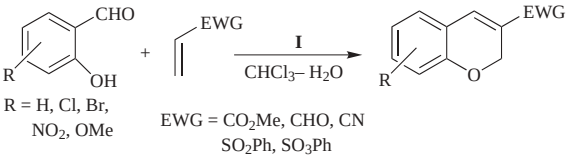
(5) We have recently reported the DABCO-catalyzed diastereoselective Baylis–Hillman reaction using sugar acrylate[6,7] as chiral Michael acceptor and sugar aldehyde[8] as chiral electrophile to achieve moderate to good diastereoselectivities (5–86% *de*).



(6) Recently, Hu and co-workers[9] have shown that the use of stoichiometric base catalyst **I**, in an aqueous medium, accelerates the Baylis–Hillman reaction. Moreover, the less reactive Michael acceptor acrylamide,[10] which normally reacts only under high pressure, also undergoes Baylis–Hillman coupling with reactive electrophiles under these conditions.



(7) The Baylis–Hillman coupling of salicylaldehyde[11,12] with various activated alkenes in the presence of **I** proceeds with regioselective cyclization to afford the corresponding 3-substituted chromene derivatives.



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