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Rate acceleration of Baylis-Hillman reaction

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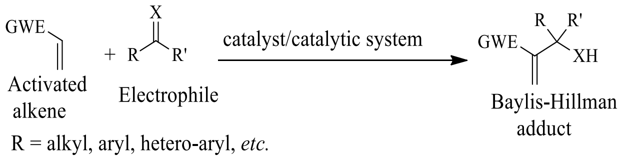
Abstract
In the organic chemistry carbon-carbon bond formations and functional group transformation strategies are very important aspects. The Baylis-Hillman reaction is a carbon-carbon bond forming reaction in the presence of tertiary amine catalyst. This reaction is a coupling at α-position of activated alkenes with electrophiles under the influence of a tertiary amine catalyst to form a densely functionalized molecule (Fig. 1) (essential components are *electrophiles*, *activated alkene* and *catalytic source*). The Baylis-Hillman reaction was discovered by American chemists A. B. Baylis and M. E. D. Hillman in the year 1973.

Keywords: carbon-carbon bond formation, functional group transformation, tertiary amine, electrophiles, activated alkene

Introduction

In the organic chemistry carbon-carbon bond formations and functional group transformation strategies are very important aspects. The Baylis-Hillman reaction [1-3] is a carbon-carbon bond forming reaction in the presence of tertiary amine catalyst. This reaction is a coupling at α-position of activated alkenes with electrophiles under the influence of a tertiary amine catalyst to form a densely functionalized molecule (Fig. 1) (essential components are *electrophiles*, *activated alkene* and *catalytic source*). The Baylis-Hillman reaction [4, 5] was discovered by American chemists A. B. Baylis and M. E. D. Hillman in the year 1973.



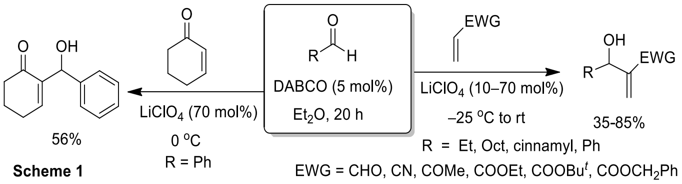
R = alkyl, aryl, hetero-aryl, *etc.*
R' = H, COOR, alkyl, *etc.*
X = O, *N*-Ts, *N*-CO_2R, *N*-$PO(R)_2$, *etc.*
catalyst / catalytic system = *tert*-amines, phosphines, Lewis acids, *etc.*
EWG (Electron Withdrawing Group) = COOR, COR, CHO, CN, $PO(OEt)_2$, SO_2Ph, SO_3Ph, SOPh, *etc.*

Fig 1: General equation

Rate acceleration

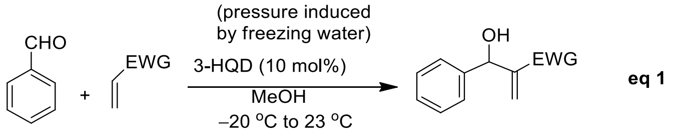
The Baylis–Hillman reaction is a slow reaction which requires a few days to a few weeks for completion. To overcome this problem with respect to all the three essential components electrophiles, activated alkene and catalytic source, a numerous effort has been made by the organic chemists. Use of excess catalyst, concept of hydrogen bonding, aqueous medium, microwave irradiation, reactive activated alkens, reactive electrphiles and high pressures have been examined for accelerating this reaction and considerable success has been achieved in this direction. In addition to the above efforts, recently organic chemists have employed some interesting and innovative strategies for rate acceleration in the Baylis–Hillman reaction

Kamimura and Kobayashi have used lithium perchlorate in diethyl ether as an additive along with a catalytic amount of DABCO for the acceleration of the Baylis–Hillman reaction (Scheme 1) [6].



Scheme 1

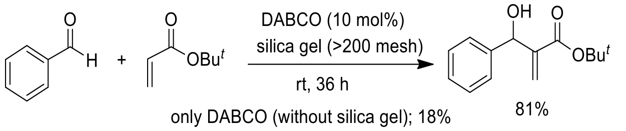
Hayashi and co-workers [7] have observed remarkable rate acceleration in the Baylis–Hillman reaction of benzaldehyde with various activated olefins in the presence of 3-HQD under high pressure induced by freezing water in a sealed autoclave (eq. 1).



eq 1

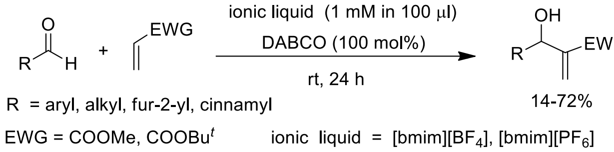
EWG	Pressure (MPa)	Time (h)	Yield (%)
COOMe	0.1	24	40
	200	24	78
$COOBu^t$	0.1	52	52
	200	52	71

Basavaiah research group [8] has observed remarkable rate acceleration in silica gel as a solid phase medium in the Baylis–Hillman reaction. Thus, less reactive activated alkenes like *tert*-butyl acrylate reacts with benzaldehyde to provide the desired adduct in 81% yield in 36 h (eq 2).



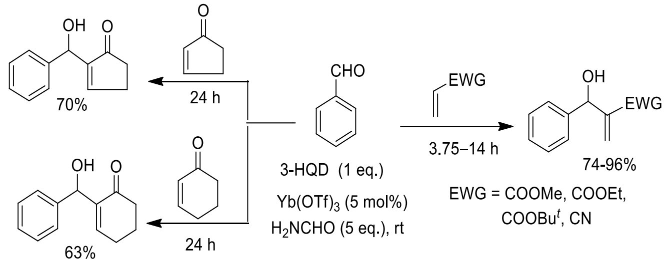
eq 2

Santos *et al.* [9] have found some acceleration in the presence of ionic liquids in the Baylis–Hillman coupling between aldehydes and acrylate esters (eq 3). They have also observed further rate acceleration in the presence of lithium perchlorate as an additive.



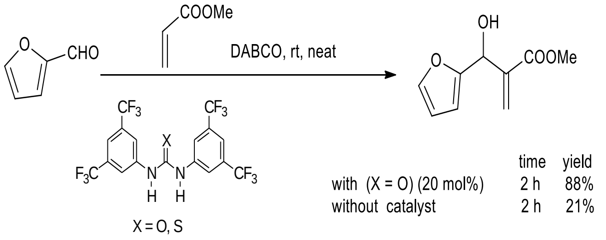
eq 3

Aggarwal and co-workers [10] used protic solvents such as water, formamide in accelerating the Baylis–Hillman reaction and demonstrated the importance of hydrogen bonding for faster reaction. They found that the presence of 5 equivalents of formamide gave better results. Even further acceleration was observed when they use catalytic amount of metal salts such as Yb (OTF)$_3$ (Scheme 2).



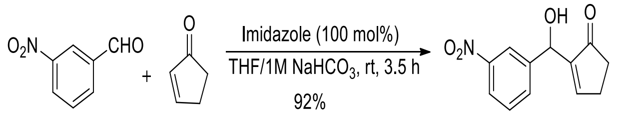
Scheme 2

Connon and co-workers [11] found that catalytic amount of bis-aryl (thio) ureas accelerate the DABCO-promoted Baylis–Hillman reaction between aromatic aldehydes and methyl acrylate in the absence of solvent (eq. 4).



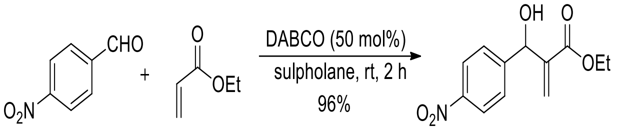
eq. 4

Very recently, Cheng *et al.* [12] have reported a remarkable rate acceleration of imidazole promoted Baylis-Hillman reaction of cyclic enones with aldehydes in basic (NaHCO$_3$) water solution (eq 5).



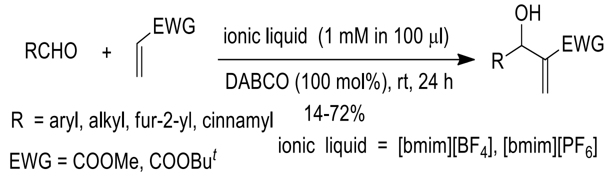
eq 5

Radha Krishna *et al.* [13] have reported a significant rate acceleration of Baylis-Hillman reaction of various aldehydes with different activated alkenes in sulpholane as solvent (eq 6).



eq 6

Santos and co-workers[14] have observed some acceleration in the presence of ionic liquids in the Baylis-Hillman coupling between various aldehydes and alkyl acrylates (eq 7). They have also observed further rate acceleration in the presence of lithium perchlorate as an additive.



eq 7

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