

Green Approach towards Baylis Hillman Reaction using Grinding Technique

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Abstract

A simple and efficient method has been developed for the synthesis of β -hydroxy- α -methylene compounds in Baylis Hillman reactions using grinding technique. The present technique was found to be more efficient than the conventional one in the presence of tertiary amine (DABCO) at room temperature under solvent free conditions. A faster reaction and higher yields were obtained compared to the conventional methods are the advantages of present protocol.

Keywords: Baylis Hillman Reaction, Aldehydes, Olefins, DABCO, Grinding Technique

Introduction:

The adduct β -hydroxy- α -methylene compounds are the multi-functionalized product obtained in Baylis Hillman reactions. As it is commonly known as, an important C-C bond forming reaction between activated olefins and aldehydes in the presence of tertiary amine base catalyst DABCO¹⁻³. This reaction shows a classic example of preserving the atom economy⁴. Beside these significant advantages, the Baylis Hillman reactions have some disadvantages like slow rates and limited substrate scope but due to wide applicability of the β -hydroxy- α -methylene compounds into chemical transformations⁵⁻⁶, continuous efforts have been made to achieve the simple and efficient procedures for the synthesis of these compounds.

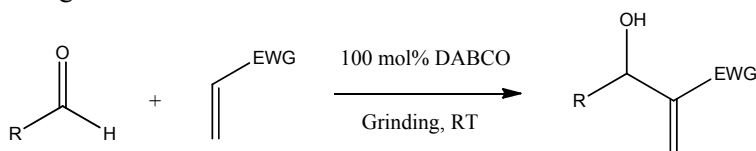
Therefore, several protocols have been proposed to improve their reaction rate, such as use of Ionic Liquids⁷, PEG-400⁸, Sulpholane⁹, supercritical CO₂¹⁰ ultrasound¹¹, high pressure¹², microwave irradiation¹³, aqueous acidic media¹⁴. In this connection some researchers have studied this reaction by using lewis bases such as such as DBU¹⁵, DABCO, Ph₃P¹⁶, Imidazole¹⁷, Quinucidine¹⁸, heterocyclic azoles¹⁹ etc. Very recently, deSouza et al.²⁰ studied this reaction by mixing different solvents along with the effect of stoichiometry of reactants and the catalyst. Some of the above mentioned conditions possess shortcomings, such as slow rates and limited substrate scope and the combination of solvents and long reaction time makes this method environmentally hazardous. Now recently, Saikia et al.²¹ found a remarkable results in terms of rate acceleration and yield enhancement by using solvent free condition. But, still there is need of development of a simple, safe, environmentally benign, and more efficient method for Baylis Hillman reaction is a rewarding challenge.

Recently, the organic chemist has been attracted much attention towards the grindstone technique because of its green and rapid pathway to obtained organic compounds²²⁻²⁴. In grindstone technique, reactions occur through generation of local heat by grinding of crystals of substrate and reagent by mortar and pestle. Reactions are initiated by grinding, with the transfer of very small amount of energy through friction. In continuation to obtained the new methodology for Baylis Hillman reaction. Herein, we report that grindstone technique is more superior than the traditional one since it is eco-friendly,

environmentally benign, high yielding, requires no special apparatus, simple and convenient method for the Baylis Hillman reaction under solvent-free conditions (Scheme 1).

Experimental

All commercial reagents were used as received without purification and all solvents were reagent grade. The reaction was monitored by TLC using 0.25 mm E-Merck silica gel 60 F254 precoated plates, which were visualized with UV light. Melting points were taken in open capillaries. The IR spectra were recorded on a PerkinElmer 257 spectrometer using KBr discs. ^1H NMR spectra were recorded on a VXR-300 MHz instrument using TMS as an internal standard.



Scheme-1

Materials and Method:

General procedure for Baylis Hillman reaction

A mixture of aldehydes (1mmol) and DABCO (100 mol %) were taken in a mortar with a pestle and ground it to make homogenous paste then add activated olefins (3mmol) in the mortar and grind the mixture for 10 minute, then kept the reaction mixture for appropriate time as mentioned in table 2. On completion of reactions by grinding technique as monitored by TLC, the obtained solid mixture was poured into water and extracted with ethyl acetate. Finally the ethyl acetate layer was dried by anhydrous Na_2SO_4 , and the solvent was concentrated under reduced pressure to give the corresponding Baylis Hillman adducts.

Representative spectral data:

3-Hydroxy-2-methylene-3-(4-nitrophenyl) propane nitrile (Entry 3)

^1H -NMR: 400MHz, TMS, CDCl_3 δ : 8.25 (dd, 1H, $J=8.8, 1.8$ Hz, Ar-H); 8.22 (dd, 1H, $J=8.8, 1.8$ Hz, Ar-H), 7.59-7.62 (d, 2H, $J=8.4$ Hz, Ar-H) 6.18- 6.19 (s, 2H, Olefinic H), 6.10 (s, 1H, CH), 2.85 (bs, 1H exchangeable, -OH).

FT- IR (cm^{-1}): 3437, 2854, 2228, 1605, 1519, 1347, 1065, 858, 831 cm^{-1} .

MS (Negative) m/z: 204, (M-1) 203.

3-Hydroxy-2-methylene-3-(2, 4-dichlorophenyl) propane nitrile (Entry 6)

^1H -NMR: 400MHz, TMS, CDCl_3 δ : 7.56-7.59 (d, 1H, $J=8.4, 1.8$ Hz, Ar-H); 7.41-7.42 (d, 1H, $J=, 1.8$ Hz, Ar-H), 7.34 - 7.37 (d, 2H, $J=8.4$ Hz, Ar-H) 6.08 (s, 2H, Olefinic H), 5.72 (s, 1H, CH), 2.62 (bs, 1H exchangeable, -OH).

FT- IR (cm^{-1}): 3434, 2861, 2228, 1608, 1524, 1347, 1185, 859, 789, 731 cm^{-1} .

MS (Negative) m/z : 227, (M-1) 226.

Results and discussion

In order to check the efficiency of this technique, we carried out the reaction of 2-nitrobenzaldehyde and ethyl acrylate was ground in the presence of various basic catalysts such as Imidazole, DBU, and 1,4-diazabicyclo[2.2.2]octane (DABCO) in a mortar by a pestle at room

temperature. Among these catalysts DABCO (100 mol %) was found to be the most efficient catalyst for this reaction (Table 1). The progress of the reaction was checked by thin layer chromatography (TLC) when the reactants were found to have reacted almost completely in 10 minutes but it had to be kept at room temperature for another 20-70 minutes for the completion of the reaction. Optimum conditions of the reaction was achieved by using varying amounts of DABCO and best yields was obtained by using 100 mol% of DABCO to the substituted aldehydes (Table 1).

Table 1. Effect of different basic catalysts on Baylis Hillman reaction in grinding technique^a.

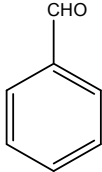



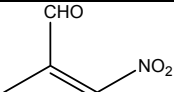

Entry	Catalyst (mol%)	Time (min.)	Yield ^a (%)
1	Imidazole (50)	240	30
2	Imidazole (100)	240	35
3	DBU (50)	120	60
4	DBU(100)	60	65
5	DABCO (50)	50	86
6	DABCO (100)	30	92



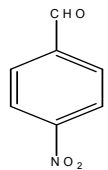



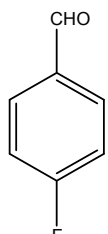



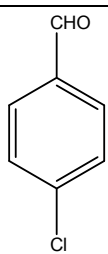



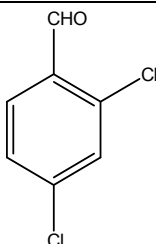



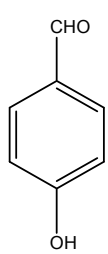



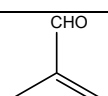

Note: The reaction was performed with 2-nitro benzaldehyde aldehyde (1 mmol) and ethyl acrylate (3 mmol) by grinding at room temperature.



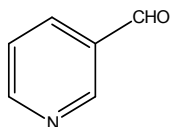



^aIsolated yield.

In order to check scope and generality of this method, a series of β -hydroxy- α -methylene compounds were prepared by reaction of various aldehydes with activated olefins, good yields were obtained as shown in **Table 2**. We have also observed that the electronic effects and nature of substituent's on the aromatic ring shows strong effect in terms of reaction time and yield. When aromatic aldehydes containing electron donating groups (-OMe, -OH) were employed a slightly longer reaction time was required than those reaction encountered with electron withdrawing groups (-NO₂, -X) on aromatic ring. The reaction time and yields of β -hydroxy- α -methylene compounds are summarized in **Table 2**.

Table 2.

Entry	Aldehyde	Activated olefin	Time (min.)	Yield ^a (%)
1			10+30	84
			10+60	86
			10+60	77
2			10+20	96

			10+30	88
			10+40	94
3			10+20	96
			10+30	92
			10+40	94
4			10+30	96
			10+30	92
			10+30	91
5			10+30	92
			10+30	88
			10+30	92
6			10+20	96
			10+30	94
			10+30	93
7			10+40	91
			10+60	88
			10+70	86
8			10+40	92

			10+60	89
			10+70	91
9			10+30	91
			10+40	88
			10+40	92

Note: The reaction was performed with aldehyde (1 mmol) and activated olefins (3 mmol) by grinding for 10 min. then kept for specific period at room temperature mentioned in Table 2.

^aIsolated yield.

It is also consistent with the green chemistry approach because it does not need heating or microwave irradiation. During grinding, the reaction mixture absorbed moisture which was found sufficient to make the reaction mixture homogeneous. The product could be isolated by just adding water and extracted with ethyl acetate. In summary, it can be stated that the present protocol for the Baylis Hillman reaction is highly efficient as it avoids the use of organic solvents at any stage of the reaction

Conclusion

In summary, we have developed a simple, efficient and more eco-friendly methodology for Baylis Hillman reaction at room temperature by using grinding technique. The notable advantages of this method are simple to handle, solvent free, waste free, green and environmentally benign, easy work-up, shorter reaction time, high yields as compared to conventional method.

Acknowledgement:

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