**Short Communication**

**Molecular Iodine: Efficient Catalyst for the Synthesis of Baylis-Hillman Adducts**

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**Abstract:** Baylis-Hillman reaction of aryl aldehydes with methyl and ethyl acrylate has been carried out efficiently in presence of DMSO and molecular iodine.

**Keywords:** Baylis-Hillman reaction; aryl aldehydes; ethyl acrylate; molecular iodine

1. INTRODUCTION

The Baylis-Hillman reaction has roots back in 1968 when Morita described the reaction of an aldehydes with acrylic compounds catalyzed by tricyclohexylphosphine [1]. He named this transformation as a carbinol addition. Great progress has been made in the reaction and first reported in 1972 the reaction of acetaldehyde with ethyl acrylate and acetonitrile in the presence of catalytic amount of DABCO (1,4-diazabicyclo[2.2.2]octane) has been reported and named as Baylis-Hillman reaction and even a catalytic asymmetric synthesis has been obtained from this reaction. This reaction has been developed enormously over the past few years due to its wide applicability towards formation of multifunctional derivatives, heterocycles and natural products [2].

Baylis-Hillman reaction is one of important tool used in carbon-carbon bonds forming organic synthesis. Baylis-Hillman adducts have been widely used in the synthesis of several useful acyclic compounds and cyclic compounds including heterocyclic ones. These reactions suffered from some drawbacks some low reaction rates and difficult work up procedure.

Recently synthesis of Baylis-Hillman adduct by using 4-hydroxy-2-naphthalic acids and benzaldehyde succinimides [1], KCN in DMSO/H₂O₂, AC₂O/amberlyst–15 [3], N-sulfonylimines [4]. The major drawbacks from this reaction are it has been reported relative slowness associated with very low chemical yields (5-10%). To solve this problem various modifications in experimental protocol have been proposed; such as use of microwaves [5] salts and metals [6], ionic liquids [7], an aqueous medium [8] or the use of a Lewis acid, either as catalyst or as promoter [9]. Use of ultrasound also accelerates the rate of these reactions [10]. Baylis-Hillman adducts of catalytic hydrogenation reactions [11], pyrazole carbaldehydes under the influence of DABCO [12], aprotic polar solvents [13], aminomethylbenzotriazoles [14], polystyrene-supported proline as recyclable catalyst in the reaction of arylaldehydes and methyl or ethyl vinyl ketone [15], salicylic N-tosylimine with methyl, ethyl and vinyl ketones [16], bisphenol-based bifunctional organocatalyst [17], pyridinium ionic liquids-accelerated amine-catalyzed [18], chiral bifunctional phosphine amides as catalysts [19, 20], ethyl acetate with methyl and ethyl vinyl ketone [21, 22]. Nevertheless, most of these methods suffer from unsatisfactory products yields, critical product isolation procedures, expensive and detrimental precursors and harsh reaction conditions, which limit

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Numerous advantages for the synthesis of Baylis-Hillman adducts have been explored as a powerful catalyst for various organic transformations. However, there is no example of asymmetric synthesis of hydroxyl compounds using molecular iodine as a catalyst. As part of our ongoing interest, in the use of cheap and eco-friendly materials as catalyst for various organic transformations, we had the opportunity to look into the synthesis of Baylis-Hillman adduct by using molecular iodine.

Here in we report the synthesis Baylis-Hillman adducts in different organic solvents like methanol, ethanol, acetonitrile, toluene, DMF and DMSO. DMSO solvent offered good yield of product in comparison to the other solvent system using catalytic amount of molecular iodine. Whereas, in absence of iodine reaction cannot proceed, even after time period of 24 hrs. We have been demonstrated an efficient and mild protocol for the synthesis of Baylis-Hillman adducts in DMSO using catalytic amount of molecular iodine in excellent yields at room temperature.

2. MATERIAL AND METHODS

TLC routinely checked the purity of the synthesized compounds on silica gel coated plates. IR spectra are recorded in KBr pellets on a Perkin-Elmer FTIR, PMR spectra are recorded on Perkin-Elmer Jeol FX 90 QC 300 MHz instrument in CDC13, chemical shifts are reported in d values using TMS as an internal standard. Organic solutions were dried over anhydrous Na2SO4 and concentrated below 40 °C in vacuum.

2.1. Procedure for the synthesis of Baylis-Hillman adduct (6)

To stirred mixture of benzaldehydes 1.06 g (10 mmol) in 5 mL DMSO, then add methyl acrylate (10 mmol) and catalytic amount of molecular iodine 2 mg (0.015 mmol) was added. The reaction mixture was stirred at room temperature for 2 hrs. Progress of the reaction was monitored on TLC. After completion of reaction, the mixture was poured onto crushed ice and the mixture was further stirred for 30 minutes. The reaction mixture was extracted with ether (3 X 10 mL), washed with aqueous sodium thiosulphate solution to remove iodine and subsequently with water. After the usual aqueous workup and using flash column chromatography (hexane/ethyl acetate, 8:2), we could obtain the desired compound in 81% isolated yield as a thick liquid.

2.2. Spectral Data

**Methyl-3-hydroxy-3-phenyl-2-methylene propanoate (1):** Colourless oil. Yield: 86%. IR (cm⁻¹) 3308, 1708,1628; ¹H-NMR (δ): 3.09 (1H, b), 3.70 (3H, s), 5.54 (1H, s), 5.80 (1H, s), 6.31 (1H, s), 7.28−7.41 (5H, m); ¹³C-NMR (δ): 175.00,150.82, 126.86, 126.09, 123.74, 117.04, 108.22, 58.97, 40.07; MS (m/z): 192, 174, 161, 105, 77,55.

**Methyl-hydroxy-3-(4-methylphenyl)-2-methylene propanoate (2):** Colorless oil. Yield: 80%. IR (cm⁻¹) 3445, 1722, 1630; ¹H-NMR (δ): 2.36 (3H, s), 2.90 (1H, b), 3.74 (3H, s), 5.56 (1H, b), 5.87 (1H, d), 6.35 (1H, s), 7.18 (2H, d), 7.30 (2H, d); ¹³C-NMR (δ): 166.75, 142.28, 138.49, 137.46, 129.09, 126.57, 125.60, 72.93, 51.58.

**Methyl-3-hydroxy-3-(4-methoxyphenyl)-2-methylene propanoate (3):** Colourless oil. Yield: 85%. IR (cm⁻¹) 3433, 1720,1630; ¹H-NMR (δ): 3.14 (1H, b), 3.68 (3H,s), 3.76 (3H, s), 5.59 (1H, s), 5.85 (1H, s), 6.29(1H, s), 6.86 (2H, dd), 7.28 (2H, dd); ¹³C-NMR (δ): 166.73,159.17, 142.26, 133.52, 127.89, 125.32, 113.72, 72.43, 55.06, 51.71; MS (m/z): 222, 143, 115, 105, 91, 83.

**Methyl-3-hydroxy-3-(4-nitrophenyl)-2-methylene propanoate (4):** Colourless oil. Yield: 82%. IR (cm⁻¹) 3433, 1720,1630; ¹H-NMR (δ): 3.12 (1H, b), 3.71 (3H, s), 5.61 (1H, s), 5.88 (1H, s), 6.37 (1H, s), 7.55 (2H,d), 8.16 (2H,d); ¹³C-NMR (δ): 166.43, 148.72, 147.48, 144.09, 127.37, 127.16, 123.58, 72.51, 52.09; MS (m/z): 237, 220, 205, 177, 150, 115, 77,55.

**Methyl-3-hydroxy-3-(4-chlorophenyl)-2-methylene propanoate (5):** Colourless oil. Yield: 80%. ¹H-NMR (δ): 3.14 (1H, b), 3.55 (3H, s), 5.85 (1H, s), 5.90 (1H, s), 6.37 (1H, s), 6.99 (2H, dd), 7.26 (2H, dd); ¹³C-NMR (δ): 173.6, 139.3, 133.2, 128.8, 127.7, 73.4, 51, 38.5.
Ethyl 3-hydroxy-3-phenyl-2-methylenepropionate(6): Colourless oil. Yield: 81%. IR (cm⁻¹): 3216, 1704, 1651; ¹H-NMR (δ): 1.30 (3H, t), 3.10 (1H, b), 4.20 (2H, q), 5.54 (1H, s), 5.80 (1H, s), 6.31 (1H, s), 7.20–7.60 (5H, m); ¹³C-NMR (δ): 175.43, 133.81, 129.55, 128.14, 128.43, 67.60, 65.01, 48.56; MS (m/z): 205, 191, 121, 105, 91, 77.

Lack of iodine, the reaction cannot proceed, even after time period of 24 hr. We have demonstrated an efficient and mild protocol for the synthesis of Baylis-Hillman adduct in DMSO using catalytic amount of molecular iodine in excellent yields at room temperature (Table 2).

3. RESULTS AND DISCUSSION

In recent years, the use of molecular iodine in organic synthesis has received considerable attention as an inexpensive, non-toxic and readily available reagent. In a model reaction benzaldehyde arylaldehyde and methyl acrylate thylacrylate were added in DMSO solvent (Scheme 1). To this mixture catalytic amount of molecular iodine is added and the mixture is stirred at room temperature for appropriate time. The progress of the reaction was monitored on TLC. To evaluate the use of this procedure a various substituted compounds were synthesized using same procedure. The reaction proceeds effectively at room temperature and no undesirable side products were obtained. The substrates, products and yield of Baylis-Hillman adducts are reported in Table 1.

In the absence of iodine, the reaction cannot proceed, even after time period of 24 hr. We have demonstrated an efficient and mild protocol for the synthesis of Baylis-Hillman adduct in DMSO using catalytic amount of molecular iodine in excellent yields at room temperature (Table 2).
Table 1. Effect of solvent on the yield of final products.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Yield (%)</th>
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<tbody>
<tr>
<td>1</td>
<td>Ethanol</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>Methanol</td>
<td>14</td>
</tr>
<tr>
<td>3</td>
<td>Acetonitrile</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>DMF</td>
<td>25</td>
</tr>
<tr>
<td>5</td>
<td>DMSO</td>
<td>80-90</td>
</tr>
</tbody>
</table>

Table 2. Optimization of the reaction condition.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Amount of iodine(mmol)</th>
<th>Temp (°C)</th>
<th>Time (min)</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10</td>
<td>100</td>
<td>30</td>
<td>----</td>
</tr>
<tr>
<td>2</td>
<td>08</td>
<td>100</td>
<td>60</td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td>06</td>
<td>70</td>
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<tr>
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<td>04</td>
<td>40</td>
<td>100</td>
<td>60</td>
</tr>
<tr>
<td>5</td>
<td>02</td>
<td>r.t.</td>
<td>120</td>
<td>80-90</td>
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</table>

4. CONCLUSION
An efficient protocol for the synthesis of Baylis-Hillman adducts has been reported. This method offers several advantages such as simple experimental and workup procedure, cleaner reaction profiles and high yield of products.

5. ACKNOWLEDGMENTS
The authors are thankful to the Principal and Head, Dept. of chemistry, Govt. College of Arts & Science, Aurangabad, for providing laboratory facilities.

6. REFERENCES AND NOTES

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