THE STUDY OF CROSSED ALDOL CONDENSATION AT THE SYNTHESIS OF ASYMMETRIC DIBENZALACETONE

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Abstract: The synthesis of asymmetric dibenzalacetone has been done by crossed aldol condensation. It can be made from 3,4-dimethoxybenzaldehyde, benzaldehyde and acetone as the starting materials. As a nucleophile, acetone, has α-hydrogens in two side. So, it can attack two kinds of aldehydes. The product will be characterized by 1H-NMR, 13C-NMR, HMQC and HMBC spectrometer. Therefore, it was identified as 1(E),4(E)-1-phenyl-5-(3',4'-dimethoxyphenyl)-penta-1,4-diene-3-one.

Introduction

Aldol Condensation is occured by a nucleophilic addition of the enolate ion to a carbonyl. Acetone also undergoes aldol condensation, but the equilibrium concentration of the product is generally small. Cross aldol condensation between p-anisaldehyde from fennel oil with acetophenone produce 2-hydroxy-4-anisaldehyde from 3,4-dimethoxybenzaldehyde (0.01 mol, 1.66 g) were added to a solution of NaOH (0.025 mol, 1g) in aqueous ethanol (1:1) that was prepared at ambient temperature, benzaldehyde (0.01 mol, 1.06 g), acetone (0.01 mol, 0.58 g) and 3,4-dimethoxybenzaldehyde (0.01 mol, 1.66 g) were added drop wise alternately. After additional stirring for 60 minutes, water (20 ml) was added to the reaction mixture which was then filtered. The extract was washed with water (20 ml x 3) and separated by column chromatography (EtOAc-hexane, 1:9) to provide the product 5 (15.53%) as pale yellow oil.

Handayani and Arty have synthesized 1.5-diphenyl-penta-1,4-diene-3-one and its derivatives known as symmetrical dibenzalacetone. It made by crossed aldol condensation between acetone : benzaldehyde by 1.2 mol ratio. It also tested as a radical hydroxyl scavengers [4]. Asymmetric crossed aldol condensation have been done with various catalyst [5,6,7]. Tutik D had synthesized of a symmetrical dibenzalacetone that have a similar structure with the cinnamic acid derivatives[8]. From its structure, it is estimated that benzalacetone and dibenzalacetone will absorb ultraviolet in the same range. Thus, asymmetric dibenzalacetone will act as a radical scavenger and also a sun screen. In this research asymmetric dibenzalacetone, compound 5 namely 1(E),4(E)-1-phenyl-5-(3',4'-dimethoxyphenyl)-penta-1,4-diene-3-one will be synthesized. This compound was made by crossed aldol condensation between acetone with two aldehydes which are the benzaldehyde and 3,4-dimethoxybenzaldehyde.

Materials and Methods

General. All materials were from Merck, among other acetone, benzaldehyde, 3,4-dimethoxybenzaldehyde, ethanol, chloroform, hexane, and ethyl acetate. TLC was carried out using 0.25-mm plate Silica gel Merck 60 F254, column chromatography were performed by Silica gel 60 (230-400 mesh). The 1H-NMR, 13C-NMR, HMQC and HMBC spectra were recorded on 500 MHz Jeol instrument. IR spectra were conducted using a Shimadzu 8300 FTIR spectrometer.

1(E),4(E)-1-phenyl-5-(3',4'-dimethoxyphenyl)-penta-1,4-diene-3-one (5). Into a solution of NaOH (0.025 mol, 1g) in aqueous ethanol (1:1) that was prepared at ambient temperature, benzaldehyde (0.01 mol, 1.06 g), acetone (0.01 mol, 0.58 g) and 3,4-dimethoxybenzaldehyde (0.01 mol, 1.66 g) were added drop wise alternately. After additional stirring for 60 minutes, water (20 ml) was added to the reaction mixture which was then filtered. The extract was washed with water (20 ml x 3) and separated by column chromatography (EtOAc-hexane, 1:9) to provide the product 5 (15.53%) as pale yellow oil.

Results and Discussion

Improved Synthesis of 1(E),4(E)-1-phenyl-5-(3',4'-dimethoxyphenyl)-penta-1,4-diene-3-one (5). The preparation of compound 5 was initiated by the mixing of 1, 2 and 4 to give 5 ((Figure 1). The product of crossed aldol condensation between benzaldehyde, 3,4-dimethoxybenzaldehyde and acetone is a mixture of 4 compounds. There was separated by Column Chromatography (EtOAc-hexane, 1:9) to give the asymmetric dibenzalacetone 5 (%53%) as pale yellow oil.

The multiple bond correlation of HMBC supported the structure (Table 1, Figure 2). In the 1H-NMR spectrum (500 MHz, CDCl3), three protons singlet and three protons doublet were observed. The singlet at δ = 7.37 was assignable to H2', 3.8 to H3' and 3.9 to H4'. The double dublet at δ = 7.2; 7.63; and 6.9 was
assignable to H3”, H4” and H5” respectively. Two
equivalence methoxy signals at δ 3.8 and 3.9 were
assigned to C3’ and C4’ . Support spectra data
provided by the IR (KBr), which indicates the
existence of C=O (1645 cm⁻¹), aromatic C=C (1514-
1417 cm⁻¹) and CO ether (1255-1139 cm⁻¹). Therefore,
the structure of 5 was 1(E),4(E)-1-phenyl-5-(3’,4’-
dimethoxyphenyl)-penta-1,4-diene-3-one.

Figure 1. Synthesis of 1(E),4(E)-1-phenyl-5-(3’,4’-
dimethoxyphenyl)-penta-1,4-diene-3-one.

Table 1. ¹H and ¹³C-NMR data of compound 5
(CDCl₃)

<table>
<thead>
<tr>
<th>C no.</th>
<th>δH (ΣH; m; J Hz) ppm</th>
<th>δC ppm</th>
<th>HMBC (500 MHz)</th>
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<tbody>
<tr>
<td>1</td>
<td>7.7 (1H; d; 16)</td>
<td>143</td>
<td>C6”, C2,C3</td>
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<tr>
<td>2</td>
<td>6.95 (1H; d; 15)</td>
<td>124</td>
<td>C3</td>
</tr>
<tr>
<td>3</td>
<td>-</td>
<td>189</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>7.1 (1H; d; 16.5)</td>
<td>125</td>
<td>C3, C5,C4’</td>
</tr>
<tr>
<td>5</td>
<td>7.4 (1H; d; 12.5)</td>
<td>129</td>
<td>C1’</td>
</tr>
<tr>
<td>1’</td>
<td>-</td>
<td>135</td>
<td>-</td>
</tr>
<tr>
<td>2’</td>
<td>7.37 (1H; s)</td>
<td>145</td>
<td>C5</td>
</tr>
<tr>
<td>3’</td>
<td>-</td>
<td>148</td>
<td>-</td>
</tr>
<tr>
<td>3’-OMe</td>
<td>3.8; (3H, s)</td>
<td>56</td>
<td>C4’</td>
</tr>
<tr>
<td>4’</td>
<td>-</td>
<td>149</td>
<td>-</td>
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<td>4’-OMe</td>
<td>3.9 (3H, s)</td>
<td>56</td>
<td>C3</td>
</tr>
<tr>
<td>5’</td>
<td>6.85 (1H; d; 7)</td>
<td>111</td>
<td>C4’, C1’</td>
</tr>
<tr>
<td>6’</td>
<td>7.33 (1H; d; 3)</td>
<td>129</td>
<td>C1’, C5</td>
</tr>
<tr>
<td>1’’</td>
<td>-</td>
<td>151</td>
<td>-</td>
</tr>
<tr>
<td>2’’</td>
<td>7.14 (1H; d; 2)</td>
<td>110</td>
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<td>7.2 (1H; dd; 7.5)</td>
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<tr>
<td>4’’</td>
<td>7.63 (1H; dd; 7.5)</td>
<td>128</td>
<td>-</td>
</tr>
<tr>
<td>5’’</td>
<td>6.9 (1H; dd; 10)</td>
<td>120</td>
<td>C4’’</td>
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<tr>
<td>6’’</td>
<td>7.06 (1H; d; 3.5)</td>
<td>110</td>
<td>C4’’, C1’’, C1</td>
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</table>

Figure 2. The HMBC of compound 5

Conclusions
1(E),4(E)-1-phenyl-5-(3’,4’-dimethoxyphenyl)-penta-
1,4-diene-3-one can be made from acetone, benzaldehyde and 3,4-dimethoxybenzaldehyde by
crossed aldol condensation.

Acknowledgement
This experiment was sponsored by Hibah Bersaing
Project, Ditjen Dikti RI.

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