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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 ^{1}H-NMR, ^{13}C-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*-annisaldehyde from fennel oil with acetophenone produce 2-hydroxy-4-methoxychalcone [1]. The influence of the base concentration and reaction time on the cross aldol condensation reaction also has been reported [2]. Alnustone or 4(E),6(E)-1,7-diphenyl-4,6-heptadiene-3-one is an asymmetric compound that isolated from Curcuma xanthorrhiza (*Zingiberaceae*). This compound was synthesized by Goksu, et al. using crossed aldol condensation between benzaldehyde and acetone, followed by reaction with cinnamaldehyde [3].

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 ^{1}H-NMR, ^{13}C-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 (d 2.5 cm, h 50 cm), with silica gel 60 (230-400 mesh) as the stationary phase and ethylacetate-hexane by 1:9 as the eluent. Four fractions were obtained from the column chromatography. The target compound was identified using thin layer chromatography with chloroform-hexane 4: 6.

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 provide the asymmetric dibenzalacetone **5** (15.53%) as pale yellow oil.

The multiple bond correlation of HMBC supported the structure (Table 1, Figure 2). In the ^{1}H-NMR spectrum (500 MHz, $CDCl_3$), three protons singlet and three protons double dublet 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 (1645cm^{-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.

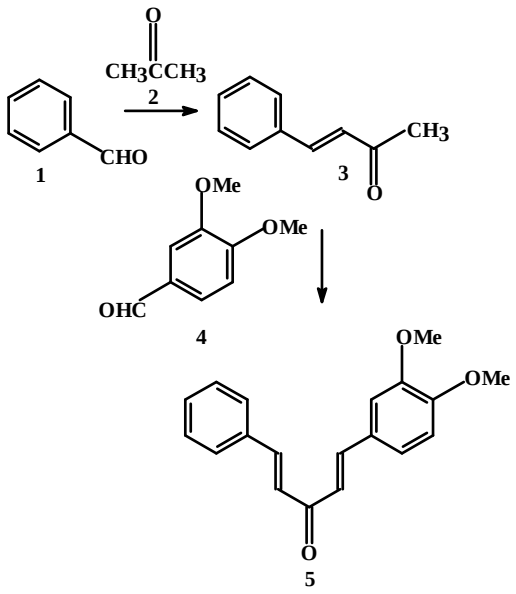

Figure 1. Synthesis of 1(E),4(E)-1-phenyl-5-(3',4'-dimethoxyphenyl)-penta-1,4-diene-3-one.

Table 1. ^{1}H and ^{13}C-NMR data of compound **5** ($CDCl_3$)

C no.	δH (∑H; m; *J* Hz) ppm	δC ppm	HMBC (500 MHz)
1	7.7 (1H; d; 16)	143	C6'', C2,C3
2	6.95 (1H; d; 15)	124	C3
3	-	189	-
4	7.1 (1H; d; 16.5)	125	C3, C5,C4'
5	7.4 (1H; d; 12.5)	129	C1'
1'	-	135	-
2'	7.37 (1H; s)	145	C5
3'	-	148	-
3'-OMe	3.8; (3H, s)	56	C4'
4'	-	149	-
4'-OMe	3.9 (3H; s)	56	C3'
5'	6.85 (1H; d; 7)	111	C4', C1'
6'	7.33 (1H; d; 3)	129	C1', C5
1''	-	151	-
2''	7.14 (1H; d; 2)	110	C1'', C6'', C1
3''	7.2 (1H; dd; 7.5)	123	C2'', C1''
4''	7.63 (1H; dd; 7.5)	128	-
5''	6.9 (1H; dd; 10)	120	C4''
6''	7.06 (1H; d; 3.5)	110	C4'', C1'', C1

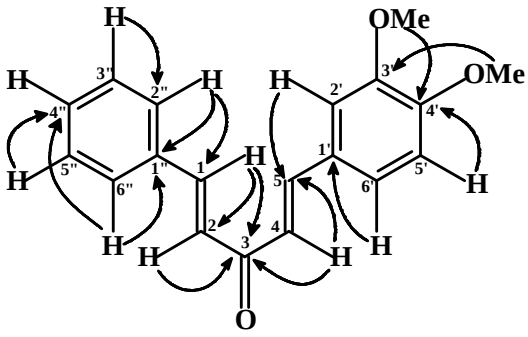

Figure 2. The HMBC of compound **5**

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

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