SYNTHESIS OF CURCUMIN FROM PIPERONAL AND ITS SPECTROMETRIC CHARACTERIZATION USING DFT-B3LYP/6-31G(d) METHOD

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ABSTRACT

Synthesis of curcumin analog of 1,5-bis(1,3-benzodioxol-5-yl)penta-1,4-dien-3-one via condensation reaction between piperonal and acetone in ethanol has been performed. The product was characterized using LC, MS, FT-IR, ¹H and ¹³C-NMR spectrometers. The product was obtained as pale-yellow solid in 94.87% yield and purity of 100%. Then, the spectroscopic characterization of the analog was conducted using Gaussian'09 with the method of DFT-B3LYP/6-31G(d). It was shown that the method gave similar IR vibration, ¹H and ¹³C-NMR spectra as those of experimental results.

Keywords: Curcumin Analog, Piperonal, DFT-B3LYP/6-31G(d).

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INTRODUCTION

The research on the field of curcumin has obtained more attention due to its biological activities, such as anti-oxidant¹⁻³, anti-tumour³, anti-cancer agents³, anti-inflammatory⁴⁻⁵, and anti-microbial. The activity and stability of the parent compound can be improved by modifying the side chain of the aromatic ring pharmacophore with asymmetric or symmetric substituents and the dienone functional group to monacetone.⁶ Research by Robinson et al. showed that the activity of curcumin analogs as anticancer is better in the presence of changes in the structure of α , β unsaturated ketones to β dicetone. This proves that these structural changes provide better activity than curcumin itself.⁷

Computational chemistry could be precisely employed to elucidate the chemical structure. It may predict the infrared, raman⁸⁻⁹, UV-Vis¹⁰, and NMR.⁹ Density Functional Theory (DFT) has been well developed during the last decade as the effective method in the chemical simulation¹¹. This theory has based on the energy of the electronic system which might be defined as the equation of the electron probability density, ρ . For the system with the n electron, $\rho(r)$ described the total electron density in a certain scope, r . Based on the formalism of DFT, electronic energy was considered as the function of electron density $E[\rho]$, at which the function of $\rho(r)$ related to the single energy. For instance, one correspondent between the electron density on the system and its energy. The results obtained from DFT were varied and depended on the choice of basis set. Recently, B3LYP is the commonly used method.¹²

EXPERIMENTAL

Materials

The materials employed in the synthesis were piperonal, acetone, methanol, ethanol, and potassium hydroxide. All the chemicals were purchased from E. Merck with pure analysis grade.

Instrumentation

The tools used for the structure elucidation were HPLC (LC-20AD Prominence, Shimadzu), FTIR (Shimadzu FTIR Prestige 21), MS Direct Inlet (MS, Shimadzu QP2010S), ¹H and ¹³C-NMR spectrometers (NMR JEOL JNM ECA 500 MHz).

The software utilized was Gaussian 09W as well as the set of computers with the specification of the processor of Intel® Core™ i5- 3317U CPU @1,70 GHz, RAM 4 GB, and hard disk of 500 GB.

Synthesis of 1,5-bis(1,3-benzodioxol-5yl)penta-1,4-dien-3-one from Piperonal and Acetone

As much as 3.0 g (0.02 mol) of piperonal was placed in the 125 mL of round-bottomed-flask. Acetone (0.58 g, 0.01 mol) and ethanol (30 mL) were then added. The solution was stirred for 20 min. Then, 0.65 g (0.01 mol) of KOH was added and the mixture was stirred at room temperature for 6 h until the formation of solid. The solid was filtered, washed with aquadest and cold ethanol. The solid was recrystallized from ethanol. The product was elucidated by using LC, IR, MS, ^1H and ^{13}C -NMR spectrometers.

Spectroscopic Characterization of 1,5-bis(1,3-benzodioxol-5yl)penta-1,4-dien-3-one using DFT-B3LYP/6-31G(d) Method

The 3D structure compound was drawn and saved (*.PDB). Geometry optimization was conducted using the program of Gaussian'09 with the method of DFT-B3LYP and the basis set of 6-31G(d). It was aimed to obtain the structure with the minimum surface potential energy and well-defined structure. The computational calculation included geometry optimization, frequency, NMR calculation. The obtained IR, NMR spectra from the calculation were compared with the experimental results.

RESULTS AND DISCUSSION

Synthesis of 1,5-bis(1,3-benzodioxol-5yl)penta-1,4-dien-3-one from Piperonal and Acetone

The compound of 1,5-bis(1,3-benzodioxol-5yl)penta-1,4-dien-3-one was obtained as the pale yellow solid with the m.p. of 199.8 in 94.87% yield. The LC analysis (Fig.-1) that the purity of the product was 100% (retention time of 3.385 min). The mass spectrum (Fig.-2) gave several peaks at m/z of 32, 51, 63, 76, 89 (base peak), 103, 117, 135, 145, 160, 175, 189, 200, 217, 235, 247, 264, 293, 321 and 322 [$\text{C}_{19}\text{H}_{14}\text{O}_5$] $^{+}$. The mass spectrum showed that the molecular mass of the product was 322 g/mol which was in full agreement with the mass of 1,5-bis(1,3-benzodioxol-5yl)penta-1,4-dien-3-one. The IR spectrum (Fig.-3) showed the absorption at 1643 cm^{-1} from the carbonyl ($\text{C}=\text{O}$) group. Additionally, the peaks at 1581 and 1496 cm^{-1} represented the stretching of aromatic $\text{C}=\text{C}$ and aliphatic $\text{C}=\text{C}$ bonds, respectively. It was strengthened by the appearance of the peak at 1257 cm^{-1} from the methylenedioxy (OCH_2O) group.

Fig.-1: Chromatogram of 1,5-bis(1,3-benzodioxol-5yl)penta-1,4-dien-3-one

Fig.-2: Mass spectrum of 1,5-bis(1,3-benzodioxol-5yl)penta-1,4-dien-3-one

Fig.-3: IR spectrum of 1,5-bis(1,3-benzodioxol-5-yl)penta-1,4-dien-3-one

Further analysis using a ^1H -NMR spectrometer (Fig.-4, 500 MHz in DMSO- D_6) gave 6 peaks depicted the 6 protons with different chemical environments. There were signals A ($\delta=6.1$ ppm, s, 4H, OCH_2O -), B ($\delta=7.0$ ppm, d, $J=7.8$ Hz, 2H, $\text{H}^5, \text{H}^{5'}$ Ar), C ($\delta=7.1$ ppm, d, $J=16.2$ Hz, 2H, $=\text{CH}-\text{C}=\text{O}$), D ($\delta=7.2$ ppm, d, $J=7.8$ Hz, 2H, $d, \text{H}^6, \text{H}^{6'}$ Ar), E ($\delta=7.4$ ppm, s, 2H, $\text{H}^2, \text{H}^{2'}$ Ar) and F ($\delta=7.6$ ppm, d, $J=16.2$ Hz, 1H, $\text{Ar}-\text{CH}=\text{CH}$). The ^{13}C -NMR spectrum (Fig.-5) gave several peaks with the chemical shifts of 101.6 (2 x - OCH_2O -), 106.6 ($\text{C}^2, \text{C}^{2'}$ Ar), 108.6 ($\text{C}^5, \text{C}^{5'}$ Ar), 123.9 ($\text{C}^6, \text{C}^{6'}$ Ar), 125.2 ($\text{C}^1, \text{C}^{1'}$ Ar), 129.2 ($=\text{CH}-\text{C}=\text{O}$), 142.3 ($\text{C}^4, \text{C}^{4'}$ Ar), 148.0 ($\text{C}^3, \text{C}^{3'}$ Ar), 149.4 ($\text{Ar}-\text{CH}=\text{CH}$) and 188.2 ($\text{C}=\text{O}$) ppm. The proposed mechanism of the condensation reaction between acetone and piperonal was presented in Fig.-6.

Fig.-4: ^1H -NMR Spectrum of 1,5-bis(1,3-benzodioxol-5-yl)penta-1,4-dien-3-one

Spectroscopic Characterization of 1,5-bis(1,3-benzodioxol-5-yl)penta-1,4-dien-3-one using DFT-B3LYP/6-31G(d) Method

The optimized structure of 1,5-bis(1,3-benzodioxol-5-yl)penta-1,4-dien-3-one had the lower energy level of -1108.50033699 a.u. with the RMS gradient of 0.00000091 a.u. The prediction of the IR spectrum

could be seen in Table-1. It was shown that the differences between the experimental and the computational spectrum were low. The differences might be due to the geometry optimization have not given the same structure of the product as in nature yet. Both calculated ^1H and ^{13}C -NMR spectra could be observed in Table-2 and Table-3. Similarly, the differences between the experimental and calculated results were low. The calculation was conducted without considering the presence of the solvent, thus it gave a few differences.

Fig-6: Mechanism of the Synthesis of 1,5-bis(1,3-benzodioxol-5-yl)penta-1,4-dien-3-one

Table-1: IR Spectrum of 1,5-bis(1,3-benzodioxol-5-yl)penta-1,4-dien-3-one

Functional Group	Experiment (cm^{-1})	DFT-B3LYP/6-31G(d) (cm^{-1})
C=O	1643.35	1636.71
C=C aromatic	1581.63	1542.28
C=C aliphatic	1496.76	1404.36
OCH ₂	1257.59	1291.43

Table-2: ^1H -NMR Spectrum of 1,5-bis(1,3-benzodioxol-5-yl)penta-1,4-dien-3-one

Information	Experiment (ppm)	DFT-B3LYP/6-31G(d) (ppm)
s, OCH ₂ O, 4H	6.1	6.1
d, H ⁵ , H ^{5'} Ar	7.0	6.3
d, =CH-C=O, 2H	7.1	6.4
d, H ⁶ , H ^{6'} Ar	7.2	6.7
s, H ² , H ^{2'} Ar	7.4	7.4
d, Ar-CH=CH	7.6	7.6

Table-3: ¹³C-NMR Spectrum of 1,5-bis(1,3-benzodioxol-5yl)penta-1,4-dien-3-one

Information	Experiment (ppm)	DFT-B3LYP/6-31G(d) (ppm)
2 x -OCH ₂ O	101.6	96.2
C ² ,C ^{2'} Ar	106.6	96.9
C ⁵ ,C ^{5'} Ar	108.6	97.8
C ⁶ ,C ^{6'} Ar	123.9	104.6
C ¹ ,C ^{1'} Ar	125.2	111.7
=CH-C=O	129.2	114.1
C ⁴ ,C ^{4'} Ar	142.3	128.3
C ³ ,C ^{3'} Ar	148.0	128.8
Ar-CH=CH	149.4	131.9
C=O	188.2	160.2

CONCLUSION

The curcumin analog of 1,5-bis(1,3-benzodioxol-5yl)penta-1,4-dien-3-one could be synthesized from piperonal and acetone via condensation reaction with a yield of 94.87% and purity of 100%. Spectroscopic characterization of the analog using Gaussian'09 with DFT-B3LYP/6-31G(d) method gave similar IR vibration, ¹H and ¹³C-NMR spectra as those of experimental results.

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