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Original Research Article

SYNTHESIS, CHARACTERIZATION, AND ANTIMICROBIAL EFFECT OF BISBENZYLIDENE DERIVATIVES OF CYCLOHEXANONE AND CYCLOPENTANONE

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ABSTRACT

Dibenzylidene derivatives of cyclohexanone and cyclopentanone were synthesized by reacting appropriate aromatic aldehyde, such as benzaldehyde, anisaldehyde and piperonal, to obtain dibenzylidene derivatives of cyclohexanone and cyclopentanone using the Claisen-Schmidt condensation reaction. The reaction was catalysed with 30% sodium hydroxide solution at 0-10°C and was kept in the refrigerator for 7 days. The progress of the reaction was monitored using TLC in a solvent system (Ethyl acetate: Methanol 1:1), and thereafter treated with acetic acid and the precipitates collected, dried and recrystallized in methylated spirit, filtered and dried. The yield, melting point and spectral analysis were determined. The antimicrobial assay was carried out using the broth dilution method at 512, 256, 128, 64, 32, 16, 8, 4, 2, and 1µg/mL against *S. aureus, Escherichia spp., Bacillus spp, Klebsiella spp. and Candida albicans.* The yield of the compounds ranges (50.3-99%), the melting point ranges (108-246°C) and the spectral analyses conformed as projected. This was revealed by ^{1}H, ^{13}C-NMR, and HRMS (ESI) data. The compounds had no antibacterial effect at the concentration assessed.

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INTRODUCTION

Synthesis of cyclopentanone and cyclohexanone bis derivatives using milling, microwave, and conventional method of aldol condensation reaction could lead to the formation of carbon-carbon bond and could be utilised in the production of chalcones or employed in the field of organic and medicinal Chemistry. These compounds were created using the conventional method. [1-7]. This class of compounds are reported to have a wide array of biological activities, which include anticancer, antimicrobial, anti-inflammatory, analgesic, and anticonvulsant. These analogues could serve as useful intermediates for the synthesis of heterocycles such as pyrimidine, isoxazole, pyrazoline, benzodiazepine, Oxazines [1, 2, 8, 9]. The study aimed to synthesize, characterize, and evaluate the antimicrobial effect of cyclohexanone and cyclopentanone derivatives using the broth dilution method.

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MATERIALS AND METHODS

Chemical and Reagents

The materials and reagents were purchased from reputable pharmaceutical and chemical companies. These reagents include, piperonal (Aldrich), Acetic acid (Sigma, UK), ethanol (JHD, China), methanol (JHD, China), ethyl acetate (Sigma, UK), benzaldehyde (JHD, China), sodium hydroxide (Loba Chemie, India), anisaldehyde (Loba Chemie, India), Dimethylsulphoxide (JHD, China), Ciprofloxacin 200 mg (Fidson, India) Cyclopentanone (BDH, UK), Cyclohexanone (CDH, India), TLC Silica gel 60 F_{254} (Merck, Germany).

Microorganism

The microorganisms are clinical isolates: *Staphylococcus aureus, Bacillus spp.*, *Escherichia spp, Klebsiella spp* and *Candida spp.*

Instruments and Equipment

NMR Ascend™ Bruker (400 and 600 MHZ, USA), Agilent 6520 Q-TOF (USA).

Methods

Equivalent quantity of cyclohexanone (0.015 M)was condensed with anisaldehyde (0.03 M), benzaldehyde (0.03 M), piperonal(0.03 M) and equivalent amount of cyclopentanone(0.02 M) was condensed with each of anisaldehyde (0.04 M), benzaldehyde (0.04 M), piperonal (0.04 M), the samples were dissolved with 50 mL of ethanol and immersed in an ice bath and stirred until 0-10°C ascertained by the thermometer. Thereafter, 30 mL of 30% potassium hydroxide was added in a dropwise manner. After the addition, it was stirred for 30 minutes and kept in a refrigerator for 7 days. The progress of the reaction was monitored using thin layer chromatography (TLC) in a solvent system (Ethyl acetate; Methanol (1:1) and thereafter it was acidified using 30% acetic acid and precipitates collected via filtration, dried and recrystallized using methylated spirit and subjected to spectroscopic analysis [2-8].

Antimicrobial Assay

The antimicrobial assay was determined using the broth dilution method at a concentration of 512, 256, 128, 64, 32, 16, 8, 4, 2, and 1 µg/mL, and it was incubated for 18-24 h and observed for growth or turbidity and compared to the standard drugs [10].

RESULTS

2,6-bis[(4-methoxyphenyl)methylidene]cyclohexan-1-one (A2)

A2 ^{1}H –NMR displayed the presence of aromatic and methylidene protons which appeared at δ 7.76 ppm with a doublet peak (J = 2.1 Hz) integrated for two protons (2H), and multiplet peaks 7.52 – 7.39 ppm integrated for four protons (4H), 7.00 – 6.86 integrated four (4H) protons and the presence of methoxyl protons at δ 3.85 ppm integrated for six protons, this indicates the formation of a bisbenzylidene derivative. The doublet of triplets' peaks at δ 2.92 ppm, with a coupling constant (J = 6.4, 3.2 Hz) due to H_3 and H_5 methylene protons of cyclohexanone, integrated four protons (4H) as shown in Figure 1. When compared to sample A4 (Figure 5) without the methoxyl group, it was observed the absence of methoxyl protons was observed, while A7 (Figure 13), a cyclopentanone analogue of A2, showed the presence of a methoxyl peak at δ 3.86 ppm [11-12].

The ^{13}C-NMR spectrum of A2 displayed nine peaks (Figure 2) with a downfield peak at δ 190.27 ppm (C-1), 159.92 (C-11), due to a tertiary aromatic carbon attached to a methoxyl group, 136.54 (C-2 and C-6) due to the formation of a carbon-carbon double bond, as shown in Figure 2. The ^{13}C-NMR of sample A4 (Figure 6), also showed the absence of δ 159.9 and 55.34 ppm peaks due to the absence of the methoxyl (-OCH_3) group from the chemical structure when compared to A2. which is a methoxyl derivative [11-12].

Based on the result of High-Resolution Mass Spectrometry [HRMS (ESI)]: Compound A2 has a molecular formular ($C_{22}H_{23}O_3$), m/z $[M+H]^+$ calculated for: 335.1642, and found: 335.1639, further confirming the synthesis of this compound as shown in Figure 3.

The chemical structure of sample (A2) [2,6-bis[(4-methoxyphenyl)methylidene]cyclohexan-1-one] synthesized using Anisaldehyde and cyclohexanone, as revealed by ^{1}H-NMR, ^{13}C-NMR and Mass Spectrometry analyses, as shown in Figure 4.

2,6-dibenzylidenecyclohexan-1-one (A4)

The proton NMR of A4 displayed a downfield peak due to aromatic protons. The aromatic and methylidene protons appeared downfield at δ 7.81-7.32 ppm, and the methylene protons appeared upfield at δ 2.96-2.93 ppm due to H_3 and H_5 protons and multiplet peak δ1.80 ppm due to H_4, as illustrated in Figure 5.

The ^{13}C-NMR spectrum of sample A4 displayed nine peaks. The spectrum showed a carbonyl group appearing at δ 190.43 ppm, the most downfield signal due to C-1 and at δ 136.96 clearly showed the formation of the carbon- carbon double bond which implies transformation of C-2 and C-6 position of cyclohexanone [methylene (CH_2)] Sp3 carbon to Sp^2 (C-2 and C-6) as shown in Figure 6 and the methylidene bridge that linked cyclohexanone and phenyl ring at δ 136.00 (C-7) as shown in Figure 8.

The high resolution mass spectrum showed that the sample m/z $(M+H)^+$ was found to be 275.1432 which is equivalent to a molecular formular ($C_{20}H_{19}O$) as shown in Figure 7.

Based on the spectroscopic data, ^{1}H-NMR, ^{13}C-NMR and high-resolution mass spectrometry data, we concluded that the reaction of Cyclohexanone and benzaldehyde was successful.

2,6-dibenzylidenecyclohexan-1-one (A4) was synthesized as illustrated in Figure 8.

2,6-dibenzodioxylmethylidenecyclohexan-1-one (A5)

The ^{1}H-NMR of A5 (Figure 9) revealed the presence of a doublet peak at δ 7.70 ppm downfield due to two equivalent aromatic protons in a ring with a coupling constant (J = 2.1 Hz), integrated for two protons. The aromatic signal at δ 7.0 ppm is multiplet-integrated for four protons due to the methine proton (=CH-R) and aromatic protons, because these protons are intertwined. Also, the protons at δ 6.85 ppm with a doublet peak is due to aromatic protons, with a coupling constant (J = 7.9 Hz). Also signal at 6.00 ppm, integrated for four protons due to the methylene bridge. Multiplet signal at δ 2.96-2.85 ppm, due to H_3 and H_5 equivalents of methylene Sp3 protons in cyclohexanone. The upfield signal at δ 1.81 ppm multiplet due to H_4 methylene Sp^3 protons.

The proton NMR showed six diagnostic peaks with assignment with downfield signals due to aromatic protons at δ 7.70 [(2H) H-7], 7.00 (m, 4H)-H4 and H6'], 6.85 [(2H), methylidene], 6.00 [(s, 4H)-H-2'] due to the methylene signal. The protons of cyclohexanone ring appeared multiplet 2.96 – 2.85 [(m, 4H)-H-3 & H-5], 1.81 (m, 2H)-H-4 as shown in Figure 9.

The ^{13}C-NMR revealed a diagnostic downfield signal at δ 190.10 ppm due to C-1 carbonyl carbon and 148.02 (C-7a'), 147.72 (C-3a') ppm due to tertiary aromatic carbon linked to oxygen atoms, at δ 136.72 ppm (C-2 and C-6) positions of cyclohexanone ring, 134.68 due to methylidene bridge, 130.22 due to C-5' and 125.85 (C-6'), 110 ppm due to quarternary carbon at C-7' and at 108.45 ppm due to Sp^2 hybridized carbon at C-4' position and 101.38 ppm due to Sp3 methylene carbon in dioxyl ring. The peaks at 28.5 ppm are due to C-3 and C-5 methylene carbon, δ 22.96 ppm due to C-4 methylene carbon of the cyclohexanone ring, as shown in Figure 10.

The result of the mass spectrometry revealed a molecular formular $C_{22}H_{19}O$ $[M+H]^+$ calculated for: 363.1227, found: 363.1227 as shown in Figure 11.

The chemical structures of 2,6-dibenzodioxylmethylidenecyclohexan-1-one (A5) as revealed by spectroscopic data, as shown in Figure 12.

2,5-bis[(4-methoxyphenyl)methylidene]cyclopentan-1-one (A7)

The ^{1}H-NMR spectrum of A7 displayed four peaks with a downfield signal at δ 7.57 (6H), due to H_6, H_8 and H_{12} aromatic and methylidene proton, and at δ7.03 – 6.87 (4H) doublet peak due H_9 and H_{11} protons and singlet peak at δ3.86 ppm (6H) due to methoxyl group and triplet peak at δ 3.09 ppm with a coupling constant(J = 1.2 Hz) integrated for four methylene protons (4H) H_3 and H_4 protons of cyclopentanone ring as shown in Figure 13.

The ^{13}C-NMR of A7 displayed nine peaks the downfield peak at δ 196.30 (C-1) due to carbonyl carbon, 160.53 (C-10) aromatic carbon directly linked to methoxyl group, and at 135.31 (C-2 and C-5) which is diagnostically for the formation of new compound due to carbon-carbon (C=C) double bond and peak at δ 26.48 ppm is due to equivalent methylene carbon at C-3 and C-4 of cyclopentanone ring, while at δ 114.31 ppm due to methylidene bridge is an Sp2 hybridized carbon linked to C-2 and C-5 positions of cyclopentanone ring [13] as shown in Figure 14.

The high-resolution mass spectrum showed m/z $[M+H]^+$, which points to a molecular formula $C_{21}H_{21}O_3$ calculated for: 321.1485 and found 321.1486 as shown in Figure 15.

The chemical structure of 2,5-bis[(4-methoxyphenyl)methylidene]cyclopentan-1-one (A7), as revealed by ^{1}H-NMR, ^{13}C-NMR and high-resolution mass spectrometry as shown in Figure 16.

2,5-diphenylmethylidenecyclopentan-1-one (A9)

Sample A9 displayed downfield peak at δ 7.61 ppm multiplet due to methylidene protons and aromatic protons intertwined, integrated for six protons respectively. 7.50-7.34 ppm integrated for six protons. The signal at δ 3.13 ppm appeared triplet with a coupling constant of 1.2 Hz integrated for four protons due methylene (CH_2) protons at H_3 and H_4 position of cyclopentanone ring as shown in Figure 17.

The ^{13}C-NMR spectrum of sample A9 carbonyl peak resonated at δ 196.42 ppm due to C-1, 137.32 due to C-2 and C-5, while 26.57 ppm due to C-3 and C-4 of the cyclopentanone ring. These peaks at δ 137.32, 135.84, 133.88, 130.76, 129.40 ppm are due to aromatic carbons, while the peak at δ 128.79 ppm is due to methylidene Sp2 carbon. The signal at δ 137.32 (C-2 and C-5) clearly proved the formation of a new derivative, as shown in Figure 18.

The high-resolution mass spectrometry using **the** electron spray ionisation technique confirmed that the projected structure of A9 is in line with m/z $[M+H]^+$ 261.1271, which corresponds to a molecular formular ($C_{19}H_{17}O$) as shown in Figure 19 [8, 14-15].

The chemical structure of 2,5-diphenylmethylidenecyclopentan-1-one (A9) is revealed by spectroscopic data and clearly illustrated in Figure 20.

2,5-dibenzodioxoylmethyledenecyclopentan-1-one (A10)

The sample A10 ^{1}H-NMR spectrum showed various aromatic peaks at the aromatic signals. δ 7.50 singlet peak integrated for two aromatic protons (2H), and multiplet peak at 7.19 – 7.05 ppm integrated for four protons (4H), and doublet peaks at 6.88 ppm with a coupling constant (*J* = 8.0 Hz) integrated for four protons (2H), and methylene singlet peak at δ 6.03 ppm due four protons (4H), and upfield triplet peaks at δ 3.07

ppm with a coupling constant (J = 1.2 Hz) integrated for four protons (4H) due to H_3 and H_4 protons of cyclopentanone ring as shown in Figure 21.

The presence of the signal at δ 135.54 ppm due to (C-2 & C-5) at 133.57 ppm due methylidene (=C-H) further validate new entity was formed as shown in Figure 22.

High resolution mass spectrum showed m/z $[M+H]^+$ of 349.1073 correspond to molecular formular ($C_{21}H_{17}O_5$) as shown in Figure 23.

The structure of 2,5-bis[(2*H*-1,3-benzodioxol-5-yl)methylidene]cyclopentan-1-one (A10), as revealed by spectroscopic data, is shown in Figure 24.

Results of antimicrobial effect

Antibacterial activity of the samples against *Escherichia spp*

The sample had no antibacterial effect against ***Escherichia spp*** when compared to the standard drug ciprofloxacin, as shown in Table 1.

Antibacterial activity of samples against *Staphylococcus spp*

The sample had no antibacterial effect against *Staphylococcus spp* when compared to the standard drug ciprofloxacin, as shown in Table 2.

Antibacterial effect of the sample against *Klebsiella spp*

The samples were inactive against *Klebsiella spp* when compared to the standard drug ciprofloxacin; this could be due to innate resistance or samples are devoid of antibacterial effect, as shown in Table 3.

Antibacterial effect of samples against *Bacillus spp.*

The assessment of the samples using the broth dilution method against *Bacillus spp* clearly proved that the samples were inactive against the organism, as illustrated in Table 4.

The antifungal assay of the samples clearly showed that the samples had no activity against *Candida spp* when compared to the standard drug Fluconazole, as shown in Table 5.

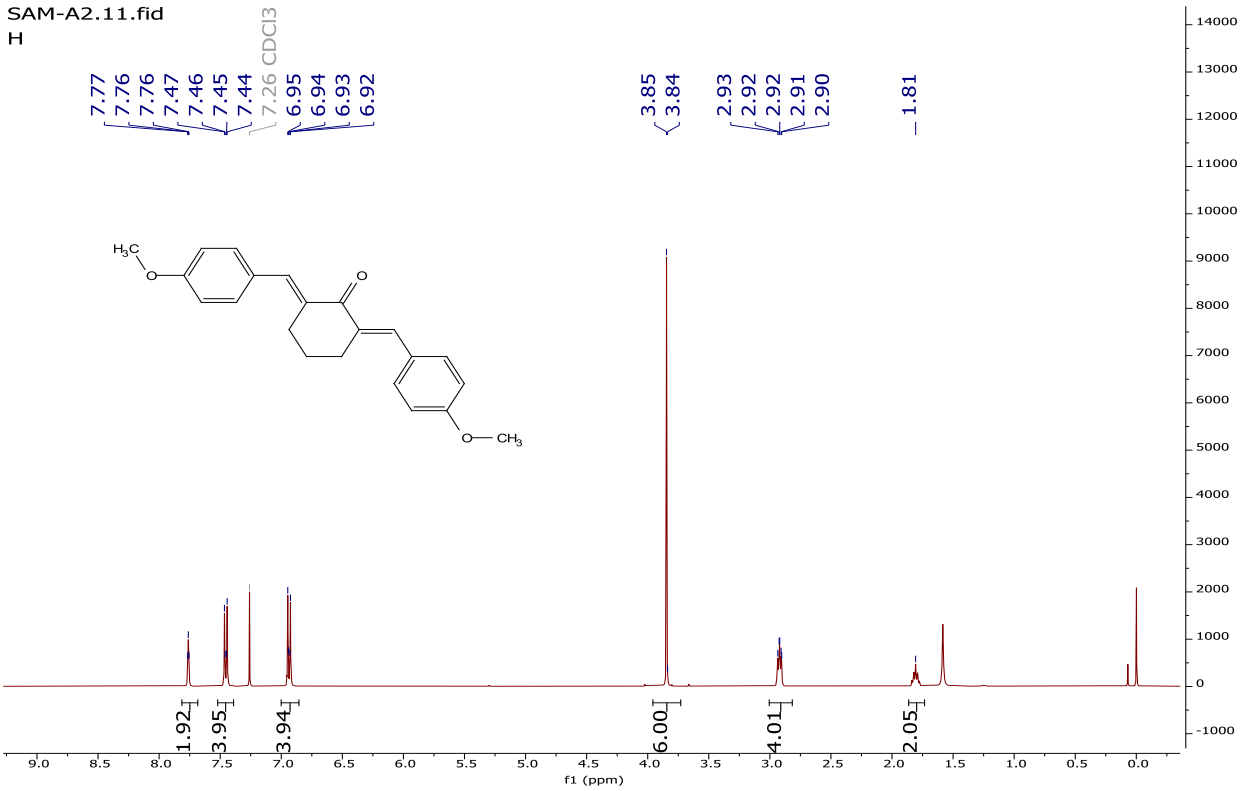


Figure 1. ^{1}H-NMR spectrum of sample A2

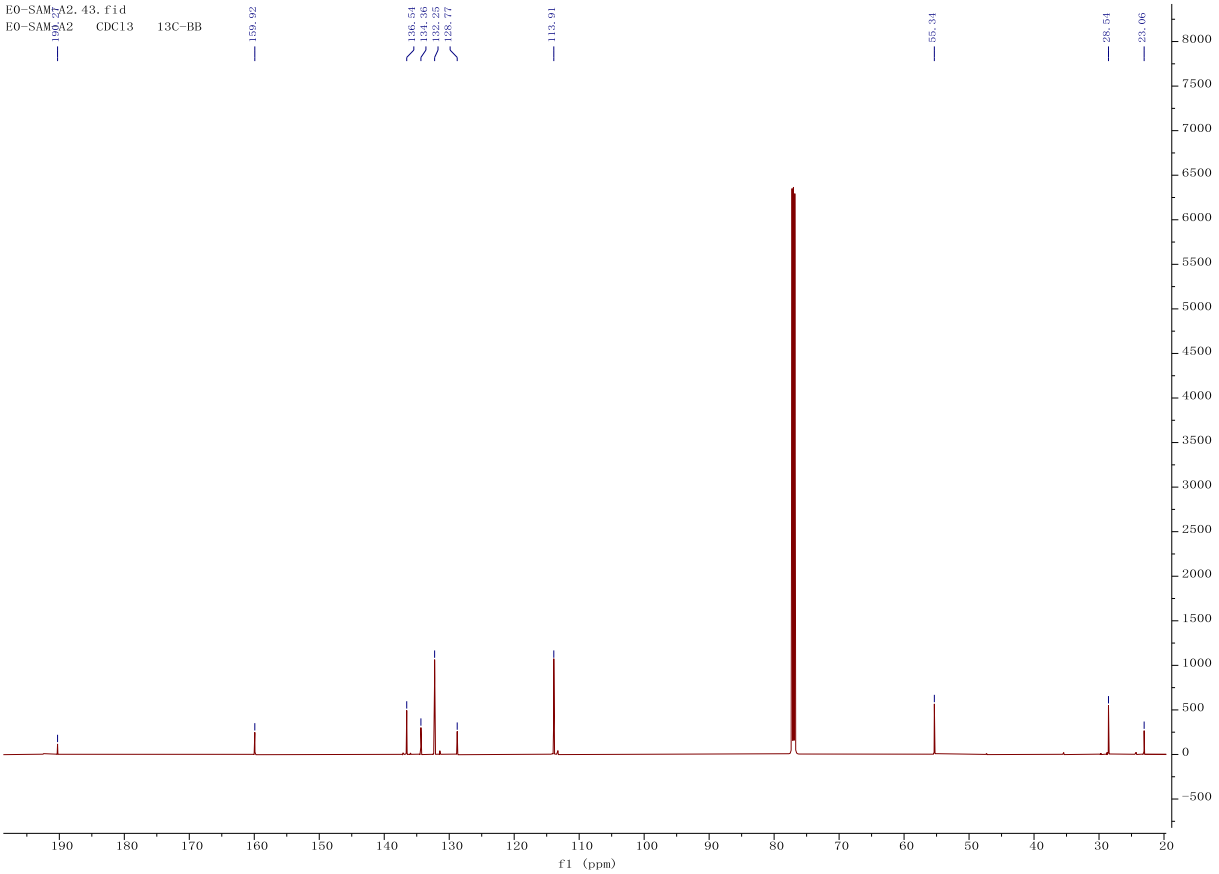


Figure 2: ^{13}C-NMR spectrum of A2

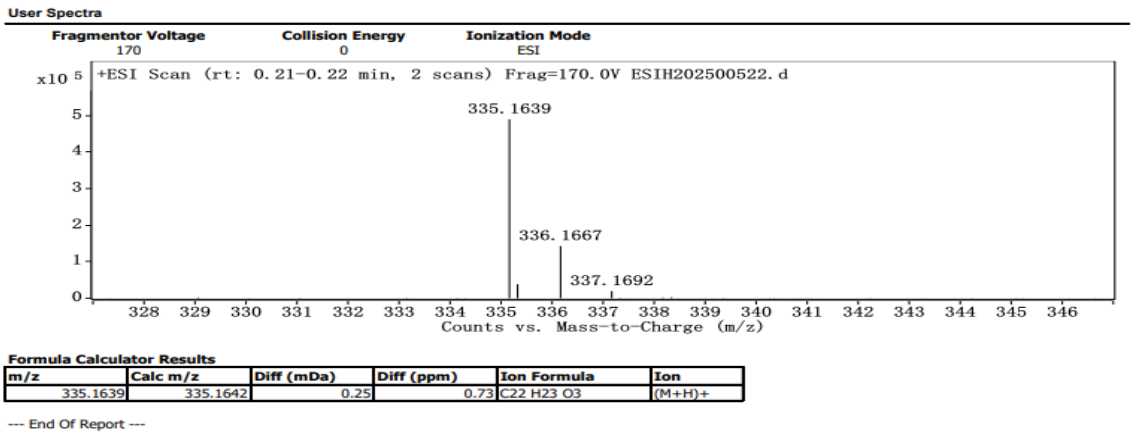


Figure 3: High Resolution Mass spectrum of A2

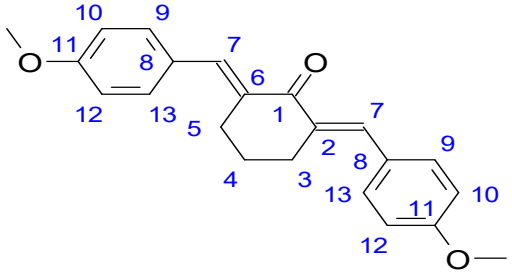


Figure 4 : Chemical structure of 2,6-bis[(4-methoxyphenyl)methylidene]cyclohexan-1-one (A2)

Yield (80%), mp (110-111°C) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 2.1 Hz, 2H), 7.52 – 7.39 (m, 4H), 7.00 – 6.86 (m, 4H), 3.85 (s, 6H), 2.92 (dt, *J* = 6.4, 3.2 Hz, 4H), 1.81 (s, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 190.27 (C-1), 159.92 (C-11), 136.54 (C-2 & C-6),

134.36 (C-7), 132.25 (C-9 & C-13), 128.77 (C-8), 113.91 (C-10 & C-12), 55.34(-OCH_3), 28.54 (C-3 & C-5), 23.06 (C-4). **HRMS (ESI)**: $C_{22}H_{23}O_3$ $[M+H]^+$ calculated for: 335.1642, found: 335.1639.

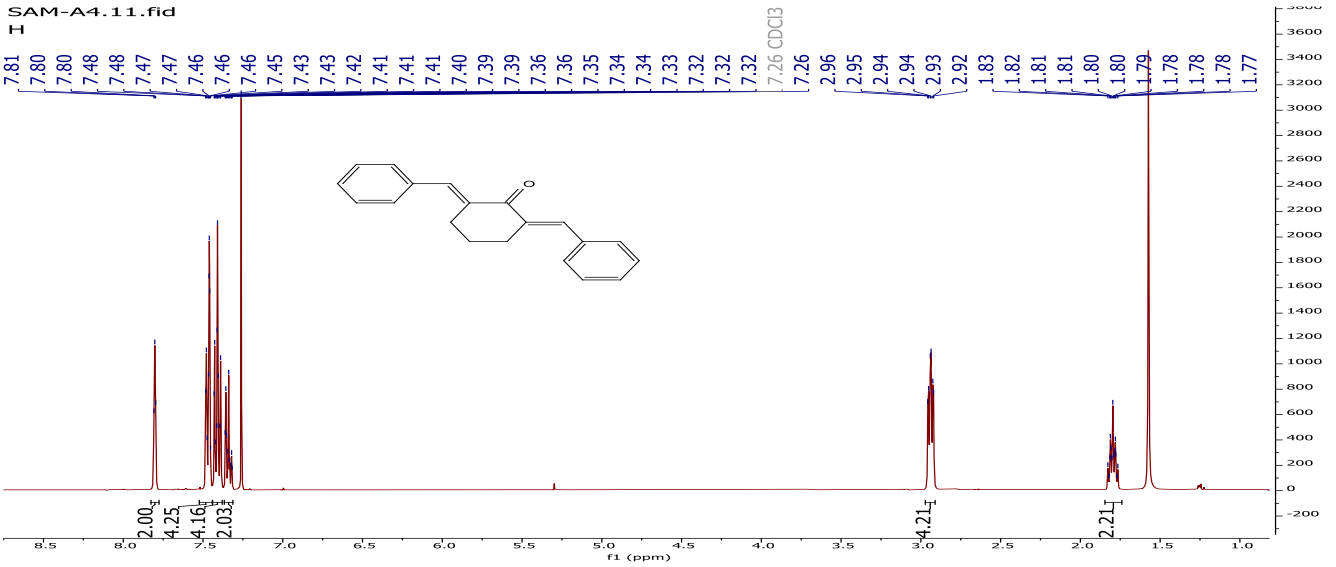


Figure 5: 1H-NMR spectrum of A4

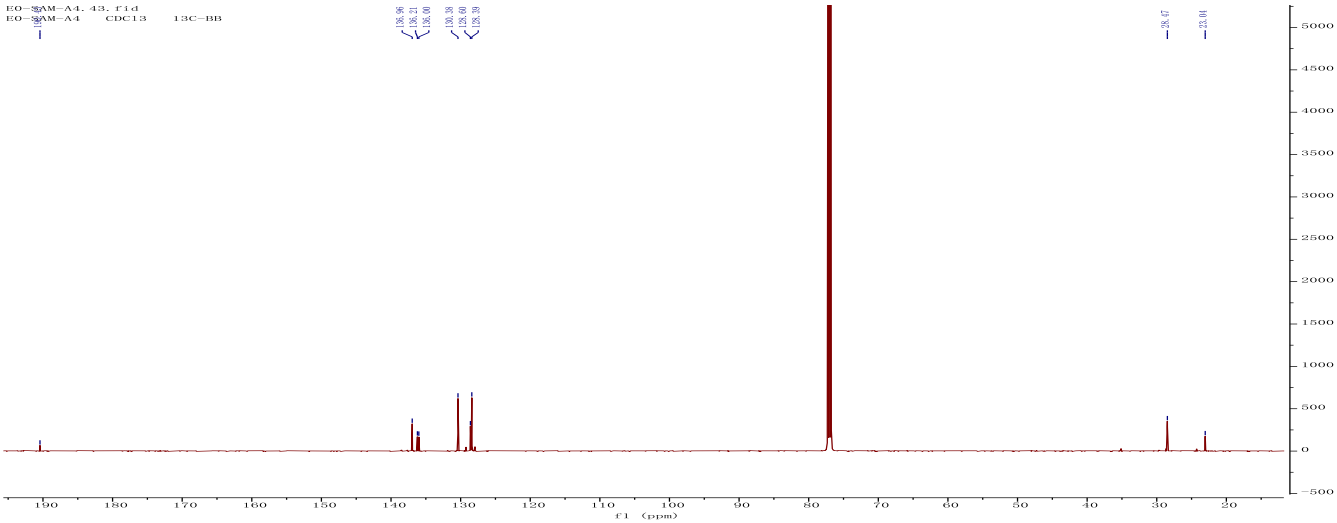


Figure 6: ^{13}C-NMR spectrum of A4

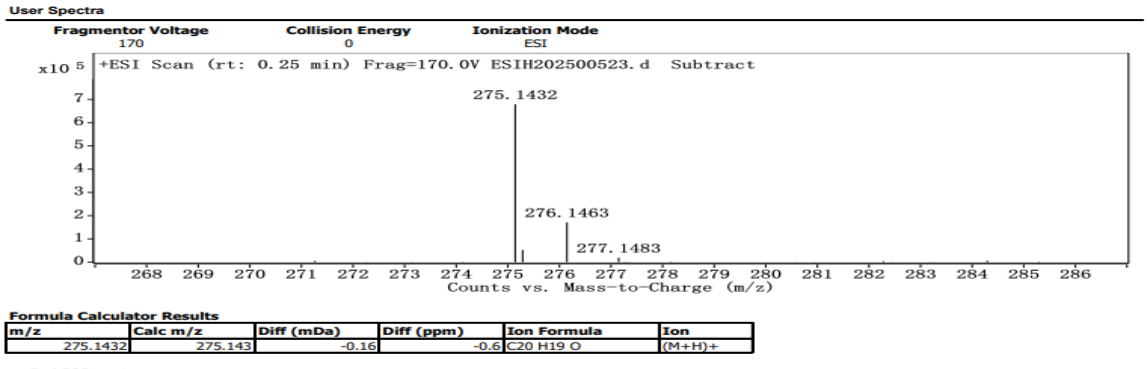


Figure 7: High Resolution Mass Spectrum of A4

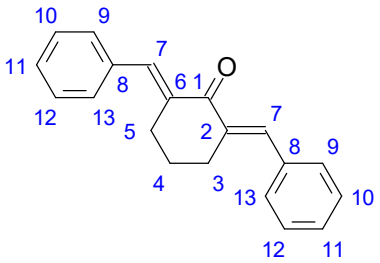


Figure 8: Chemical structure of 2,6-dibenzylidenecyclohexan-1-one (A4)

Yield (53%) mp (108-110°C) **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.80 (d, *J* = 2.1 Hz, 2H)-H_2] and H_6], 7.52 – 7.44 [(m, 4H) =C-H, and H_2 & H_6], 7.41 (m, 4H)-H_3 and H_5], 7.37 – 7.31 (m, 2H)-H4, 2.94 (m, 4H)-H_3 & H_5, 1.80 [(m, 2H)-H_4] **^{13}C NMR** (150 MHz, $CDCl_3$) δ 190.43 (C-1) 136.96 (C-2 and C-6), 136.21 (C-8), 136.00 (C-7), 130.38 (C-10 and C-12), 128.60 (C-9 and C-13), 128.39 (C-11), 28.47 (C-3 and C-5), 23.04 (C-4). **HRMS (ESI)**: $C_{20}H_{19}O$ $[M+H]^+$ calculated for: 275.1430, found: 275.1432.

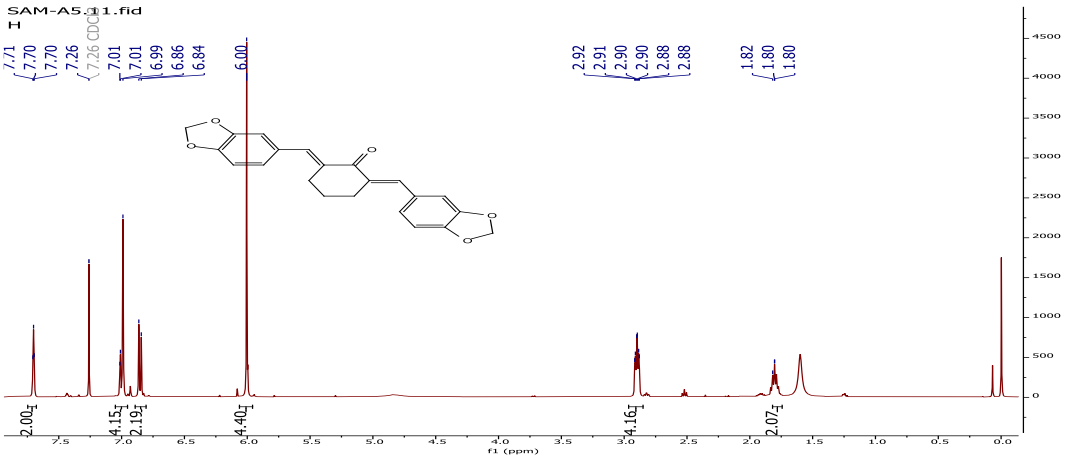


Figure 9: ^{1}H-NMR spectrum of A5

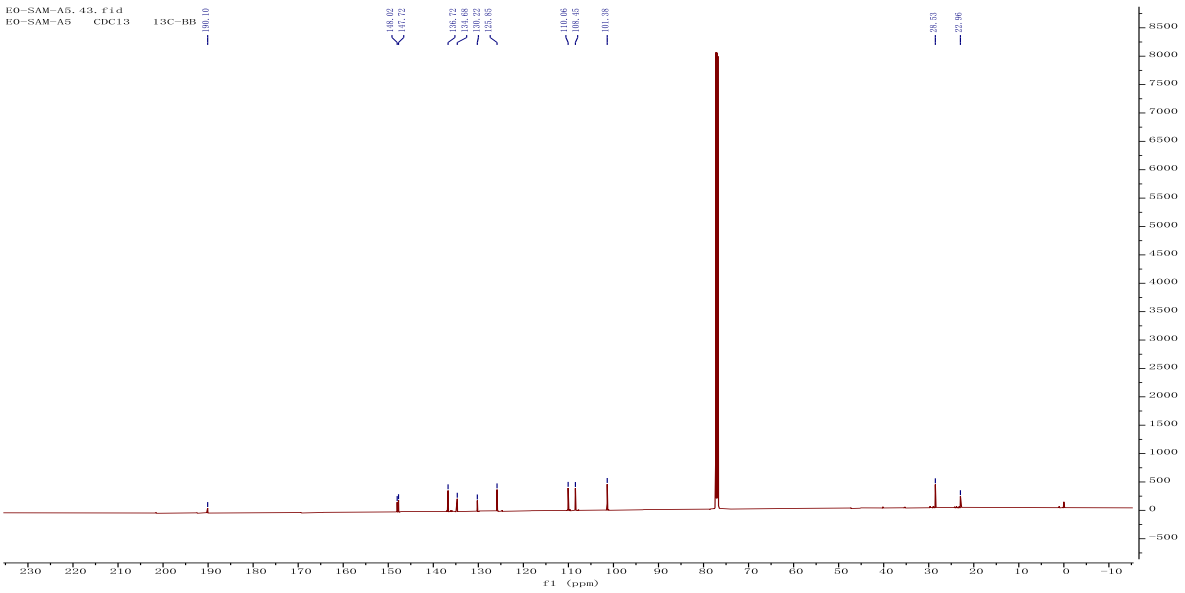


Figure 10: ^{13}C-NMR spectrum of A5

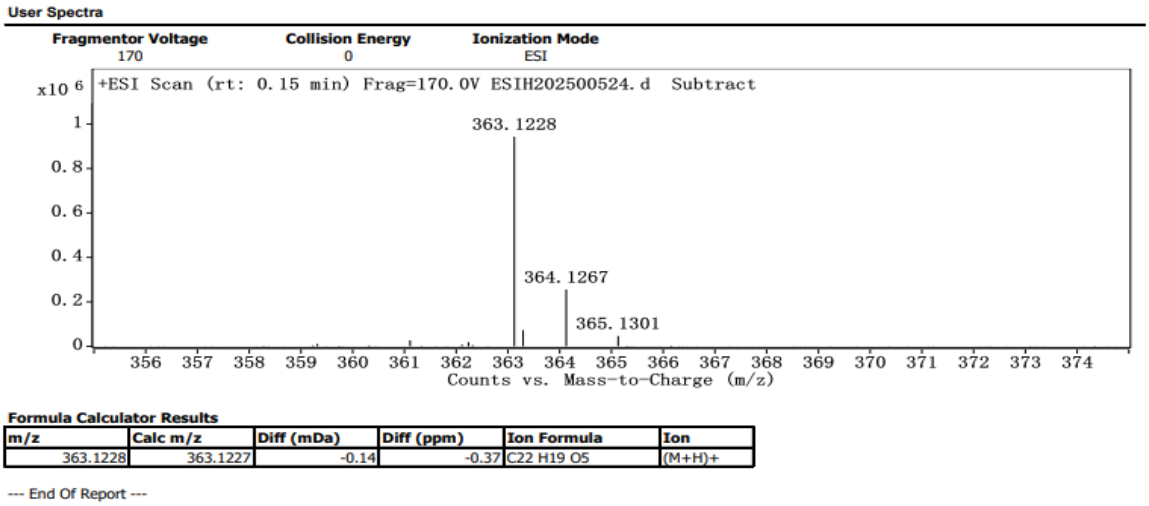


Figure 11: High Resolution Mass Spectrum of A5.

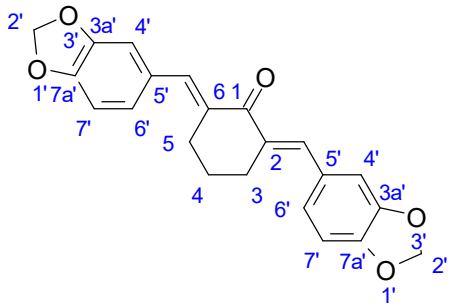


Figure 12: Chemical structure of sample A5

Yield (89.1%), mp (112-114°C), **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.70 (d, *J* = 2.1 Hz, 2H) H-7], 7.00 (m, 4H)-H4 &H6'], 6.85 [(d, *J* = 7.9 Hz, 2H) =C-H, methylidene], 6.00 [(s, 4H)-H-2'] 2.96 – 2.85 [(m, 4H)-H-3 & H-5], 1.81 (m, 2H)-H-4. **^{13}C-NMR** (150 MHz, Chloroform-*d*) δ 190.10 (C-1), 148.02 (C-7a), 147.72(C-3a), 136.72 (C-2 & C-6), 134.68 (methylidene), 130.22 (C-5'), 125.85 (C-6'), 110.06 (C-7'), 108.45 (C-4'), 101.38,(C-2') 28.53 C-3 and C-5), 22.96 (C-4). **HRMS (ESI)**: $C_{22}H_{19}O$ $[M+H]^+$ calculated for: 363.1227, found: 363.1227.

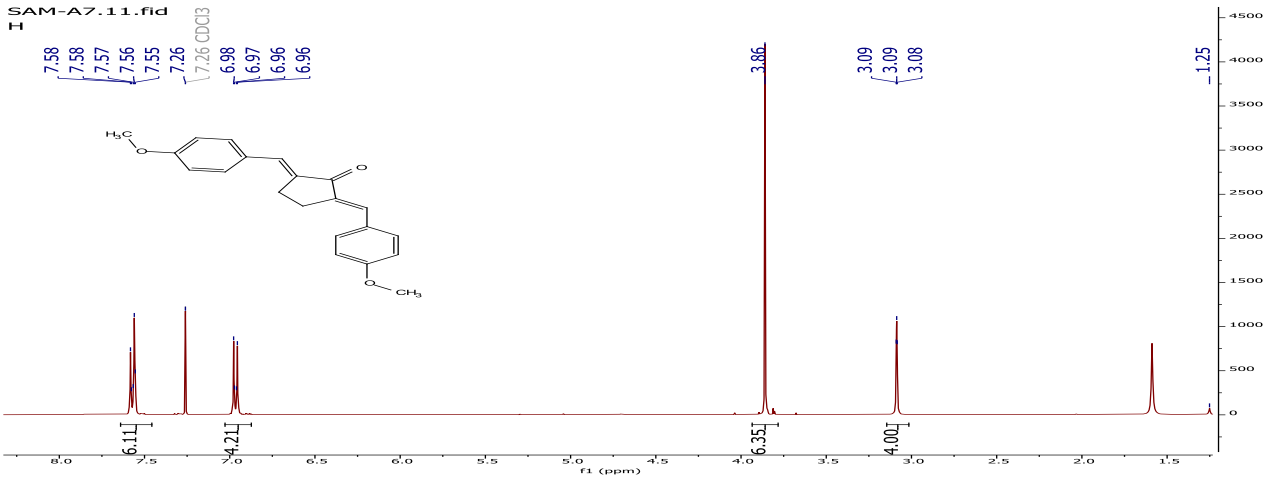


Figure 13: ^{1}H-NMR spectrum of A7

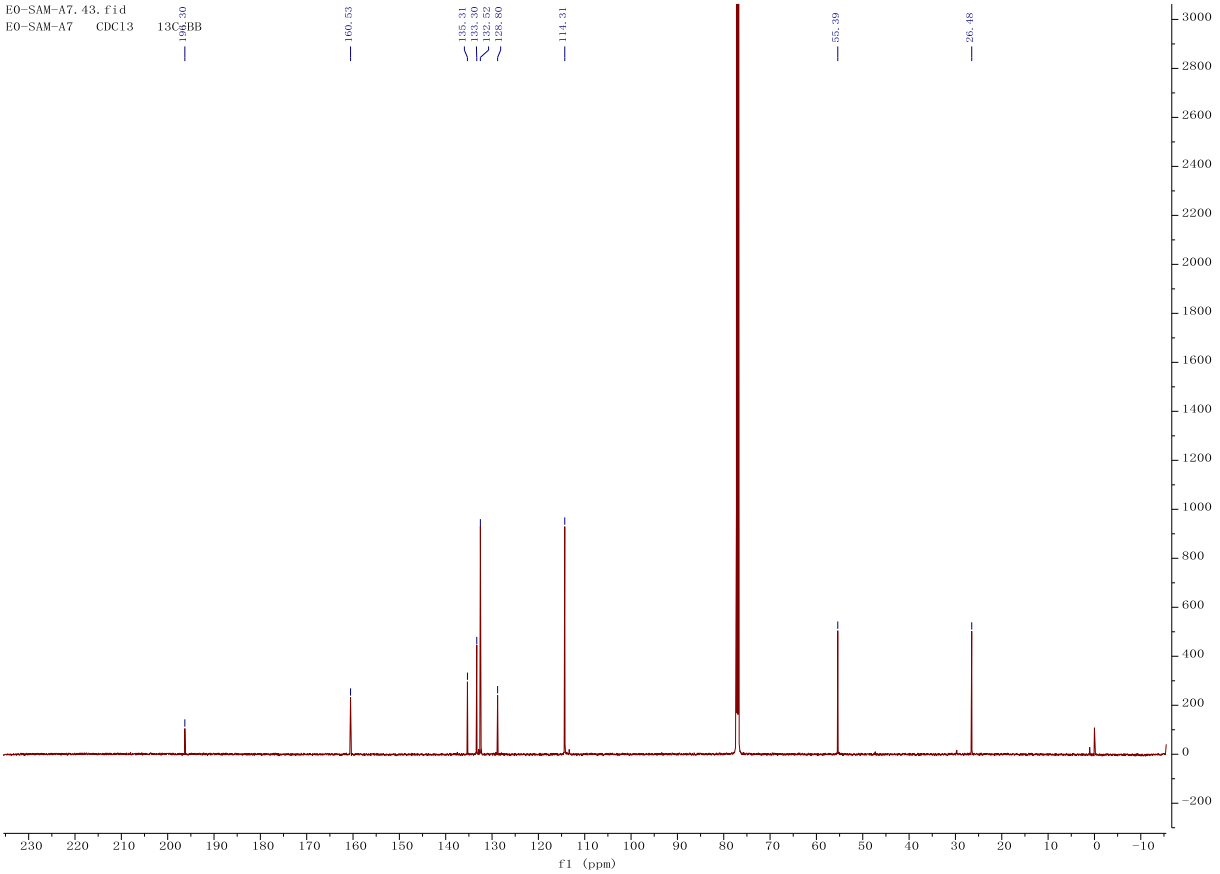
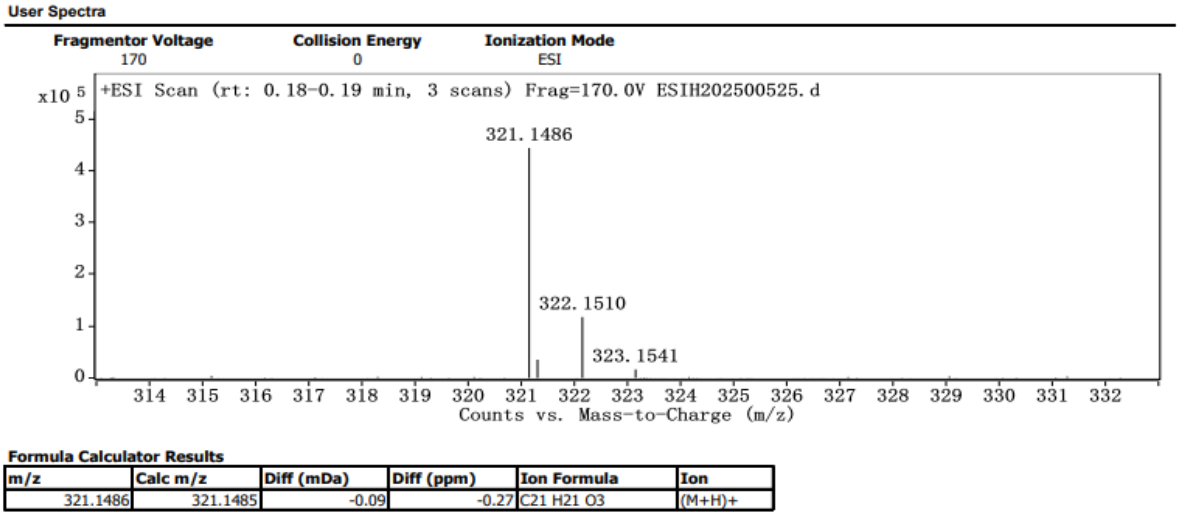


Figure 14: ^{13}C- NMR spectrum of A7



Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
321.1486	321.1485	-0.09	-0.27	C21 H21 O3	(M+H)+

Figure 15: NMR spectrum of A7

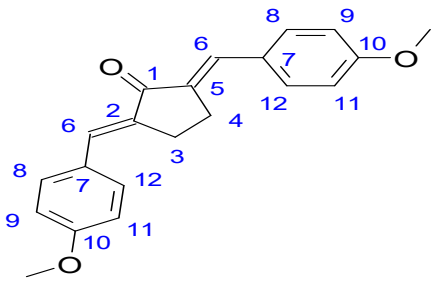


Figure16: 2,5-bis[(4-methoxyphenyl)methylidene]cyclopentan-1-one (A7)

Yield 50.5%, 180-183°C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 9.1, 2.2 Hz, 6H), 7.03 – 6.87 (m, 4H), 3.86 [(s, 6H)-OCH_3] 3.09 [(t, *J* = 1.2 Hz, 4H) H_3 and H_4] **^{13}C-NMR** (150 MHz, $CDCl_3$) δ 196.30 (C-1), 160.53 (C-10), 135.31 (C-2 and C-5), 133.30 (C-6), 132.52 (C-8 and C-12), 128.80 (C-7), 114.31 (C-9 & C-11), 55.39-(OCH_3), 26.48 (C-3 and C-4). **HRMS (ESI)**: $C_{21}H_{21}O_3$ $[M+H]^+$ calculated for: 321.1485, found: 321.1486

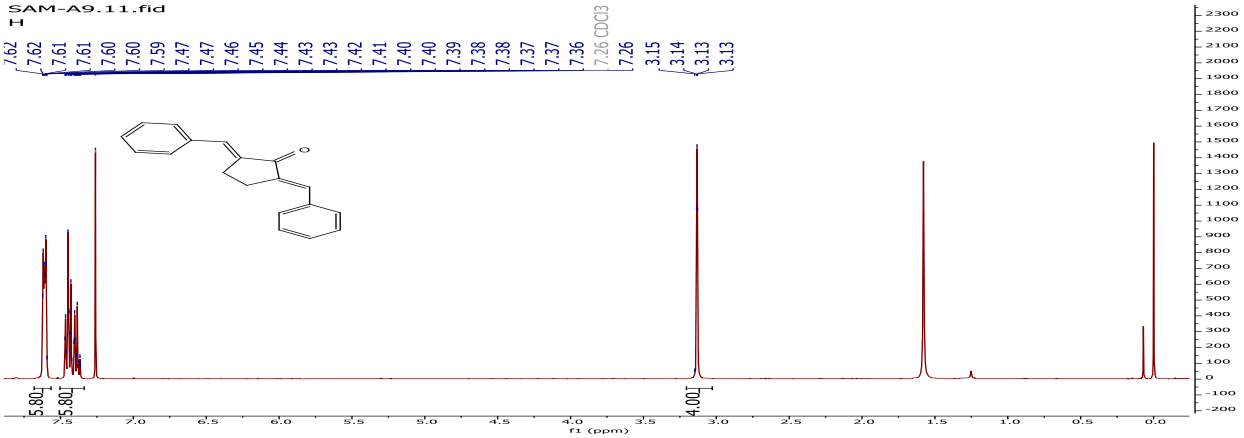


Figure 17: 1H-NMR spectrum of A9

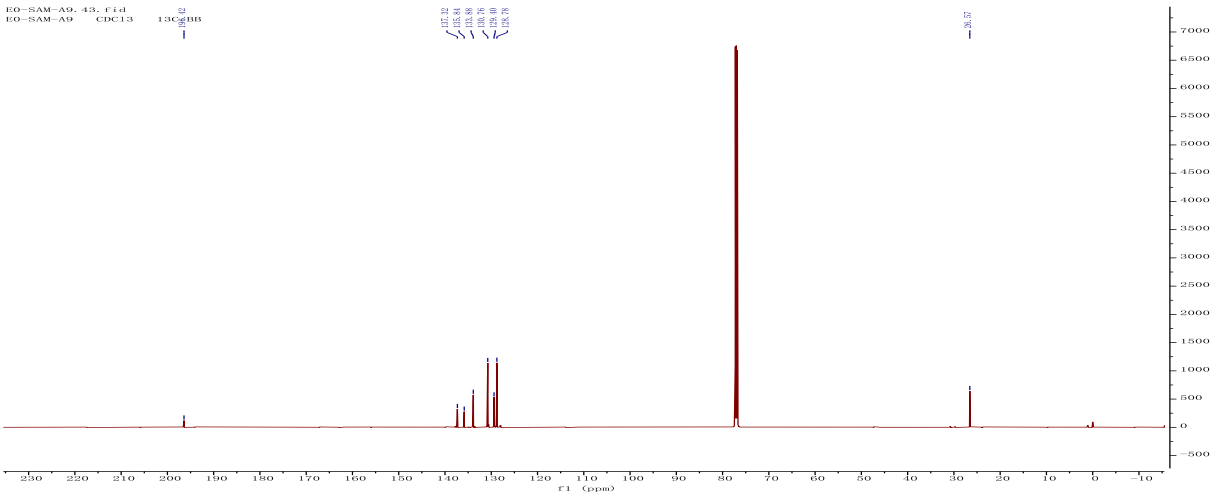


Figure 18: ^{13}C-NMR spectrum of A9

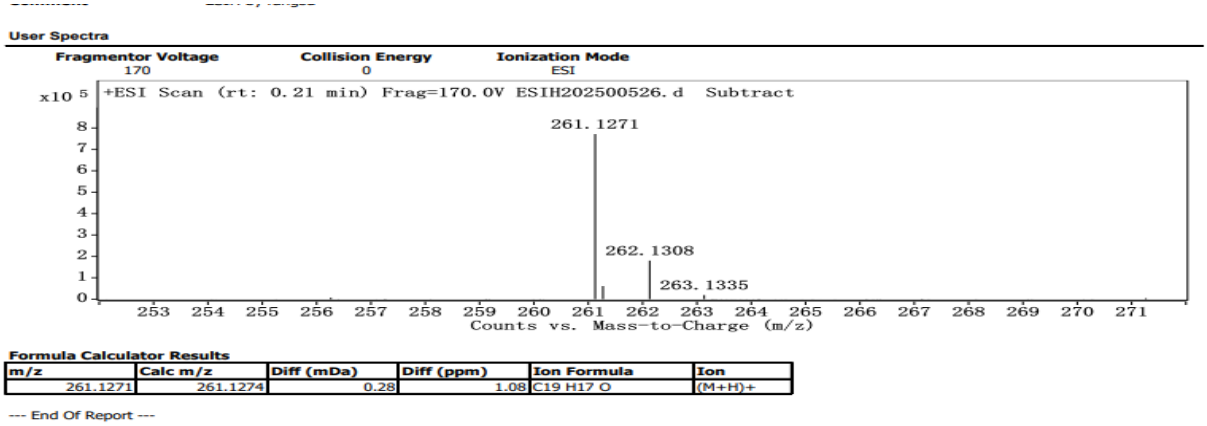


Figure 19: High-resolution mass spectrum of A9

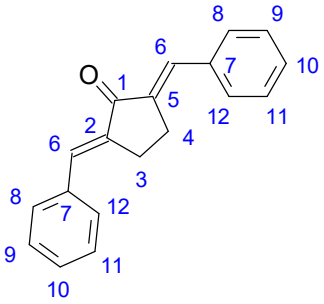


Figure 20: Chemical structure of A9

Yield, (97.8%,), mp (190-192°C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 (m, 6H), 7.50 – 7.34 (m, 6H), 3.13 (t, *J* = 1.2 Hz, 4H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 196.42 C-1), 137.32 (C-2 and C-5), 135.84 (C-7), 133.88 (C-6), 130.76 (C-8 and C-12), 129.40 (C-9 and C-11), 128.78 (C-10), 26.57 (C-3 & C-4). **HRMS (ESI)**: $C_{19}H_{17}O$ $[M+H]^+$ calculated for: 261.1274, found: 261.1271

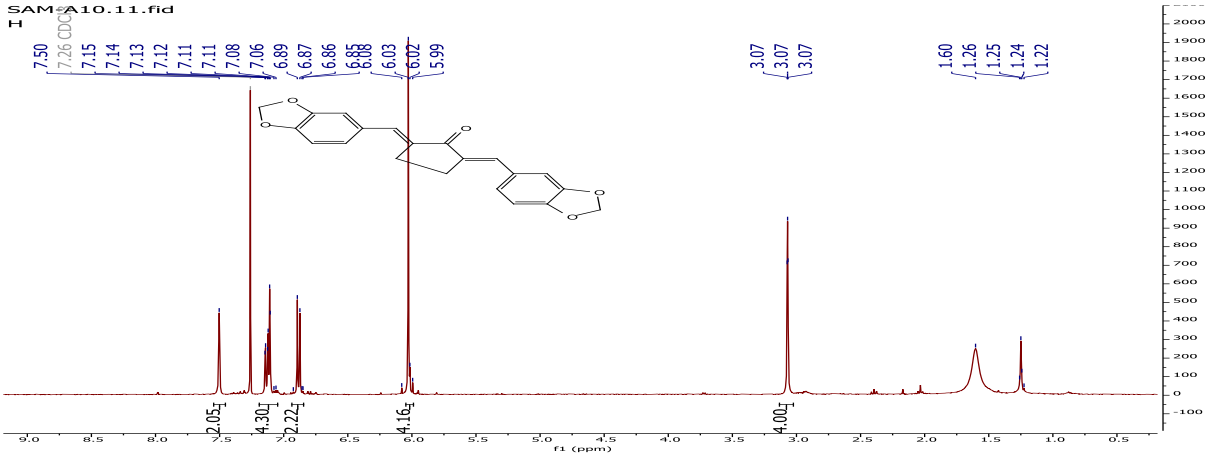


Figure 21: ^{1}H-NMR spectrum of A10

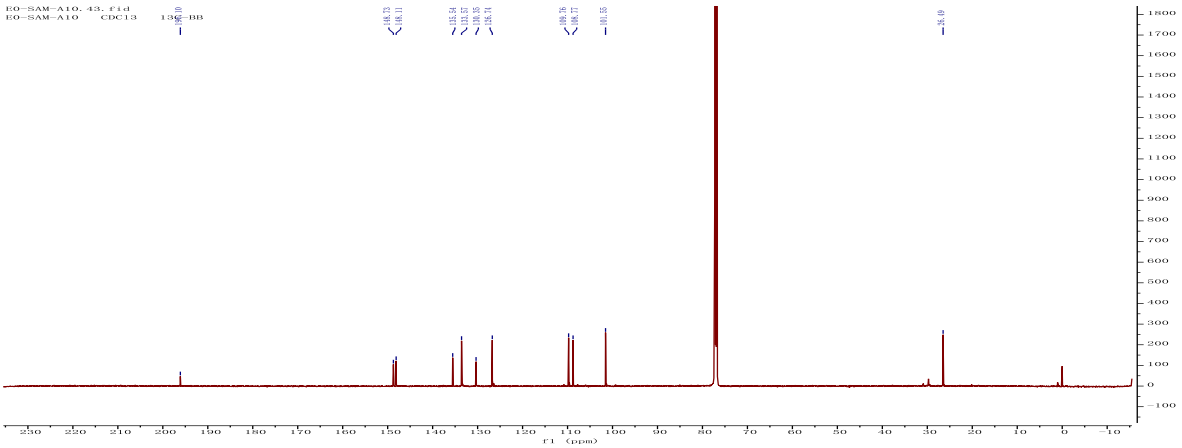


Figure 22: ^{13}C-NMR- spectrum of A10

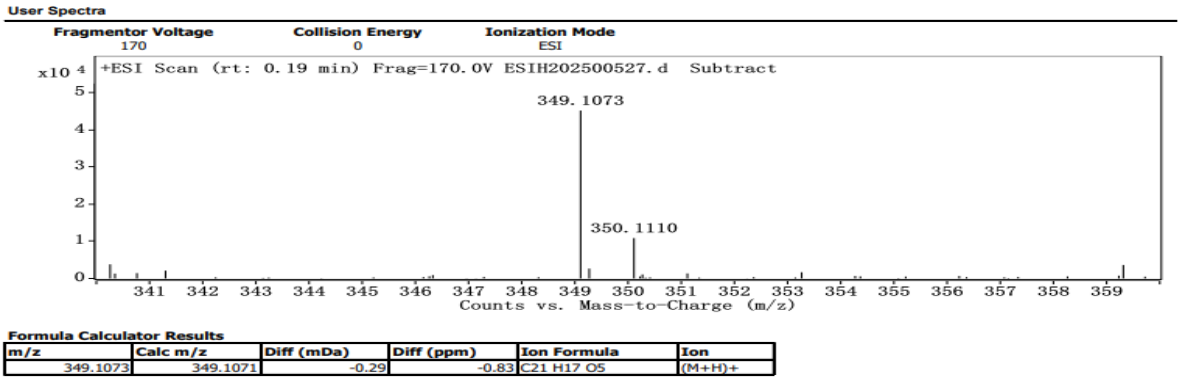


Figure 23: High-resolution mass spectrum of A10

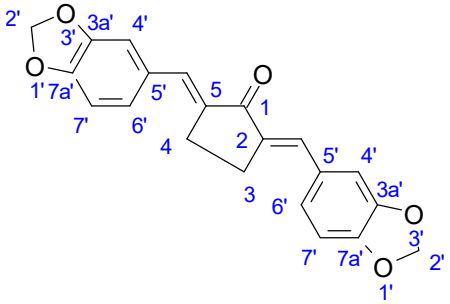


Figure 24: Chemical Structure of 2,5-bis[(2*H*-1,3-benzodioxol-5-yl)methylidene]cyclopentan-1-one (A10).
Yield, (99%), m.p (244-246°C), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50 (s, 2H), 7.19 – 7.05 (m, 4H), 6.88 (d, *J* = 8.0 Hz, 2H), 6.03 (s, 4H), 3.07 (t, *J* = 1.2 Hz, 4H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 196.10 C-1), 148.73 (7a), 148.11 (3a), 135.54 (C-2 & C-5), 133.57 (=C-H, methylidene) 130.35 (C-5'), 126.74 C-6'), 109.76 (C-7), 108.77 (C-4), 101.55 (C-2'), 26.49 (C-4 & C-5). **HRMS (ESI)**: $C_{21}H_{17}O_5$ $[M+H]^+$ calculated for: 349.1071, found: 349.1073.

Table 1: Antibacterial activity of the samples against *Escherichia spp*

Sample	Concentrations (µg/ml)									
	512	256	128	64	32	16	8	4	2	1
Ciprofloxacin	+	+	+	+	+	+	+	+	—	—
A2	—	—	—	—	—	—	—	—	—	—
A4	—	—	—	—	—	—	—	—	—	—
A5	—	—	—	—	—	—	—	—	—	—
A7	—	—	—	—	—	—	—	—	—	—
A9	—	—	—	—	—	—	—	—	—	—
A10	—	—	—	—	—	—	—	—	—	—

Table 2: Antibacterial activity of samples against *Staphylococcus aureus*

Sample	Concentrations (µg/ml)									
	512	256	128	64	32	16	8	4	2	1
Ciprofloxacin	+	+	+	+	+	+	+	+	+	+
A2	—	—	—	—	—	—	—	—	—	—
A4	—	—	—	—	—	—	—	—	—	—
A5	—	—	—	—	—	—	—	—	—	—
A7	—	—	—	—	—	—	—	—	—	—
A9	—	—	—	—	—	—	—	—	—	—
A10	—	—	—	—	—	—	—	—	—	—

Table 3: Antibacterial effect of the sample against *Klebsiella spp*

Sample	Concentrations (µg/ml)									
	512	256	128	64	32	16	8	4	2	1
Ciprofloxacin	+	+	+	+	+	+	+	−	−	−
A2	−	−	−	−	−	−	−	−	−	−
A4	−	−	−	−	−	−	−	−	−	−
A5	−	−	−	−	−	−	−	−	−	−
A7	−	−	−	−	−	−	−	−	−	−
A9	−	−	−	−	−	−	−	−	−	−
A10	−	−	−	−	−	−	−	−	−	−

Table 4: Antibacterial effect of samples against *Bacillus spp.*

Sample	Concentrations (µg/ml)									
	512	256	128	64	32	16	8	4	2	1
Ciprofloxacin	+	+	+	+	+	+	+	+	+	+
A2	−	−	−	−	−	−	−	−	−	−
A4	−	−	−	−	−	−	−	−	−	−
A5	−	−	−	−	−	−	−	−	−	−
A7	−	−	−	−	−	−	−	−	−	−
A9	−	−	−	−	−	−	−	−	−	−
A10	−	−	−	−	−	−	−	−	−	−

Table 5: Antifungal effect of samples against *Candida spp.*

Sample	Concentrations (µg/ml)									
	512	256	128	64	32	16	8	4	2	1
Fluconazole	+	+	+	+	+	+	+	+	+	+
A2	−	−	−	−	−	−	−	−	−	−
A4	−	−	−	−	−	−	−	−	−	−
A5	−	−	−	−	−	−	−	−	−	−
A7	−	−	−	−	−	−	−	−	−	−
A9	−	−	−	−	−	−	−	−	−	−
A10	−	−	−	−	−	−	−	−	−	−

Keys: '+': Antimicrobial activity; '−': No antimicrobial activity.

DISCUSSION

The yield of the compounds ranges between (50.3-99%), and samples melted at a specific temperature range (108-246°C), which suggests the purity of the samples. The cyclopentanone derivatives melted at higher temperatures (180-246°C) compared to cyclohexanone analogues (108-114°C). The spectroscopic data clearly showed that the projected structures conform with ^{1}H-NMR, ^{13}C-NMR and mass spectrometry, colour of the samples ranges from light yellow to yellow. These compounds were pure, and there were no interference peaks in ^{1}H-NMR, ^{13}C-NMR and High-Resolution Mass Spectrometry spectra, which could be due to incomplete reactions or contaminants. This confirmed the successful synthesis of these derivatives of cyclohexanone and cyclopentanone, respectively and spectroscopic data were compared to literature [8, 11-12,14,15].

Microbiological assessment of the compounds showed insignificant antimicrobial activity in all the compounds. The antimicrobial properties of these compounds can be owed to their chemical characteristics, such as their functional group, side chains, bulkiness or even small size. According to the Clinical and Laboratory Standards Institute (CLSI) [16]. Ring expansion and contraction do not have a significant antibacterial effect on the organisms assessed. These compounds are devoid of antibacterial effect (Table 1-5) and corroborate as reported by Ritmaleni et al., which stated that dibenzylidene derivatives of cyclohexanone had no antibacterial effect against organisms [17]. These findings, when compared to dibenzalacetone has been reported to possess antibacterial effect against *E. coli* and antifungal effect

against *candida albican* [10]. However, Chitosan–dibenzylidene acetone based on Schiff base exhibited remarkable antibacterial properties against *S. aureus, E. coli*, *P. aeruginosa* and potent antifungal properties against *candida albican* [18, 19].

CONCLUSION

The compounds synthesized were in line with the predicted structures, as revealed by spectral analysis. The samples had no antimicrobial effect.

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AUTHORS' CONTRIBUTION

ADCO, ASE, WSD, and PUU designed and synthesized the compounds, while DDE and TC carried out the antimicrobial assessment. SJB carried out the Spectroscopic analyses and interpretation of results, and the manuscript was written by ADCO. All authors proofread and approved the manuscript for publication.

CONFLICT OF INTEREST

Authors declare no conflict of interest

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