Original Article

Synthesis, Spectral Studies of Some New Chalcone and Schiff Base Derivatives Derived from Cyclohexanone and Molecular Docking and Biological Activity Studies

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Abstract

Through this study, a new series of novel cyclohexanone derivatives were synthesized as a Schiff Bases or chalcones were prepared by depending on the intermediate compound (Cyclohexanone) all new derivatives were characterized that was prepared by Fourier Transform Infrared Spectroscopy (FT-IR) Analysis, 1HNMR spectroscopic data, and the13C NMR spectrum, some the newly prepared derivatives which are important in the field of medical chemistry which were studied as anti-bacterial and anti fungal.

Keywords: Cyclohexanone, Schiff Bases, Chalcone, Anti-inflammatory Agent, Molecular Docking.

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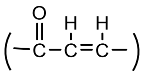
INTRODUCTION

Cyclohexanone a cyclic compound containing six carbon atoms and one oxygen atom with the chemical formula $CO(CH_2)_5$

It is an important industrial compound useful as a raw material in organic synthesis(1), known as(Pimelic ketone, Ketohexa methylene, Oxocyclohexane),(2) it appears as a colorless to pale yellow liquid with a slight smell, less dense than water(3). Cyclohexanone is an important intermediate in the production of ε-caprolactam which is used in the manufacture of Nylon-6 and polyamide resins,(4)additional uses include paint and varnish removers, degreasing of metals and spot remover(5).

Schiff Bases this name is given to organic compounds that contain in their composition azomethine as an active group(6), here the carbonyl group has been replaced by an imine or azomethine group(7).

It has been called Schiff Bases ttributed to its explorer the scientist chemical Nobel Prize Winner German Hugo Schiff in 1864(8). The compounds produced by the condensation of aldehydes with amines are called Aldimines but the compounds that are produced by condensing ketones with primary amines are called Ketimines(9). Schiff bases are promising biologically interesting compounds having a wide range of pharmaceutical properties including antipyretic, anti-inflammatory, and antimicrobial activities(10).

Chalcone named (α,β-unsaturated carbonyl compounds) because it contains effective group  $\left(-\overset{\overset{O}{\parallel}}{C}-\overset{H}{C}=\overset{H}{C}-\right)$,(11) the presence of this group in the composition of chalcones makes it possess a wide range of biological activities, and therefore it has an important place in biochemistry and medicine, due to its therapeutic properties that fight cancer, viruses, infections and combat(12) HIV. the name chalcones was given by the two scholars Tombor, Kostanecki)(13), the compounds in which the main part of its plant structure is chalcone possesses biological and pharmacological activity, including anti-inflammatory, analgesic, antitumor, antimalarial, antihistamine, anti-oxidant, and antiprotozoal)(14).

EXPERIMENTAL

2-1-Materials and methods

All the used chemicals were obtained from commercial sources, with a purity range of 95-98%, that were used as received (without further purification). Melting points of all synthesized compounds were measured in open capillary tubes in a Gallen-Kamp MFB-600 melting point apparatus. FT-IR spectra measurements were recorded using FT-IR-8400S-Shimadizu spectrophotometer.^{1}H-NMR and ^{13}C-NMR spectra were recorded on VARIAN-INOVA 500MHZ spectrophotometer (Germany), $CDCl_3$ and DMSO-d6 were used as solvents, and tetramethylsilane TMS as internal standard.

2-2-General Procedure for Schiff bases derivatives synthesis (3,5,7,9) (15)

In round bottle flask 250 ml, with a condenser and magnetic stirrer, (10mmol) of the compound (cyclohexanone) was added to (10mmol)of the compound (ethanol amine, 4-amino phenol, 3-amino phenol, thiosemicarbazide) respectively in

(30-40ml)of ethanol absolute as a solvent, and added three to four drops of glacial acetic acid as a catalytic, then mixture was raised by reflux condensation for a period of (10-12)hours and at a temperature of (78-80) °C the reaction was followed up using a thin layer chromatography (TLC) technique in a mixture of (Benzene, Methanol) at a ration (4:1) as a mobile phase The solvent is removed by distillation under vacuum pressure to obtain the product.

2-3-Synthesis drivatives of chalcones (11,13) [16]

In round bottle flask 250 ml, with a condenser and magnetic stirrer, (10mmol, 0.98gn) of the compound (cyclohexanone) was added to (20mmol,2.44gm)(20mmol,1.92gm) from the compound (4-hydroxy benzaldehyde, furfural) respectively in 4ml of THF as a solvent, and added 0.5ml of concentrated Hydrochloric acid as a catalytic, were mixed and stirred at room temperature up to 2hours.

Then the temperature was raised to (50-60)°C and stirring was continued for 10 hours until the reaction was completed. The reaction is monitored using mobile phase TLC (Benzene-Methanol) in a ratio (4:1). The crude product was washed out with cold water and ethanol absolute (1:1), then filtered. The second washed out with cold water and ethanol absolute (2:3) up to pH (7-8) reached out, then filtered and dried, a solid Compounds were purified by recrystallization.

4-2. Synthesis derivatives of chalcones (15,17) [17]

In round bottle flask 250 ml,with tow neck, cyclohexanone (10mmol, 0.98gm) and mixture of the aromatic aldehyde such as (4-bromo benzaldehyde (20mmol,3.7 gm) or vanillin (20mmol, 3.034gm), were dissolved in (15ml) of ethanol absolute, stirred mixture for several minutes at ice bath.

Then slowly add 10mL of a 40% sodium hydroxide solution in water to the mixture at room temperature for (6-8) hours, the reaction was followed up using a thin layer chromatography (TLC) technique in a mixture of (Benzene, Methanol) at a ration (4:1) as a mobile phase, the product was filtered and washed with cold water and dried, the product was purified by recrystallized by ethanol absolute.

Table 1.Physical properties of compound (C3-C17)

Comp.	Chemical formula	Color	Solubility	M.P(°C)	Yield %	R*f*
C3	$C_8H_{15}NO$	Black	EtOH	Syrup	82.15	0.53
C5	$C_{12}H_{15}NO$	Black	EtOH	155-158	85	0.42
C7	$C_{12}H_{15}NO$	Black	EtOH	Syrup	76.6	0.49
C9	$C_7H_{13}N_3S$	Pale yellow	EtOH	155-157	83	0.54
C11	$C_{20}H_{18}O_3$	Dark green	THF	260-262	88.46	0.49
C13	$C_{16}H_{14}O_3$	brown	THF	130-132	84.6	0.81
C15	$C_{20}H_{16}Br_2O$	Pale yellow	EtOH	250 d	78	0.48
C17	$C_{22}H_{22}O_5$	yellow	EtOH	166-168	72.18	0.67

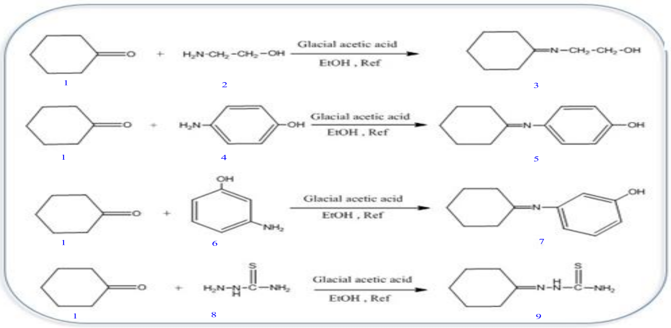


Figure 1. preparation of compound (3,5,7,8)

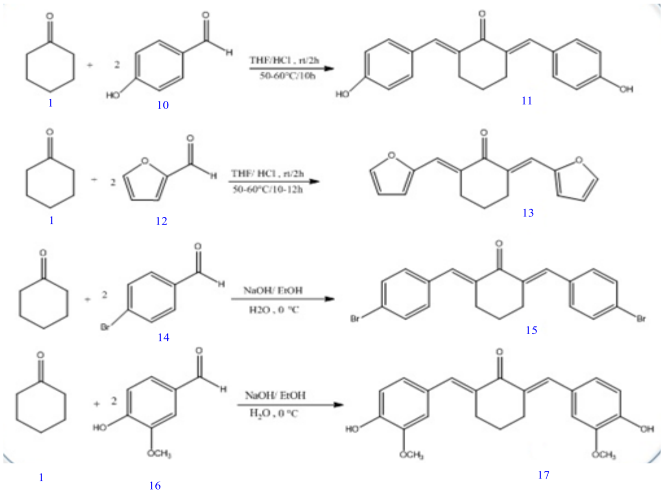


Figure (2) Synthesis compound (11,13,15,17)

RESULT AND DISCUSSION

Chemistry

All new compound have been identification by using FT-IR and ^{1}H-NMR, ^{13}CNMR spectrum and used DMSO as a solvent.

Biological activity

Two different species of Gram-negative bacteria (Escherichia coli) and Gram-positive bacteria (Staphylococcus aureus) were investigated for biological activity in this work at a concentration of (100ppm) in media prepared for bacteria culture. Used a DMSO solvent with a volume of 5 mL with 0.0025 g from prepared derivatives.

Moleculer docking

The molecular docking of the prepared compounds with the protein responsible for breast cancer was studied using AutoDock 4.2.6 program. This study predicted the presence of effective compounds towards the protein responsible for breast cancer.

3-1 The compound (**3**) 2-(cyclohexylidene amino)ethan-1-ol is black syrup,yield 82.15% The infrared spectrum of compound (**3**) showed band at (3263cm^{-1}) for (OH) alcohol, (2927cm^{-1}) for (C-H) aliphatic, (1566cm^{-1})for(C=N) The ^{1}H-NMR compound (**3**) through the use (of DMSO-d6) as a solvent. The proton signal (d,H1) appeared δ (1.77ppm), (s,CH$_2$) appeared δ (3.67ppm), (s,OH) appeared δ (6.95ppm), (s,H2) appeared δ(.79ppm).

3-2 The compound (**5**) *N*-methyl cyclohexanimine phenol is black solid, M.P (155-159 yield 85.28%. The infrared spectrum of compound (**5**) showed band at (1558cm^{-1}) from (C=C) Aromatic, (2931cm^{-1}) for (C-H), (3332cm^{-1}) for (OH) phenol, (1667cm-1) for (C=N). The ^{1}H-NMR (DMSO-d6) compound(**5**) through the use (of DMSO-d6) as a solvent. The proton signal (s,H1) appeared δ (1.63ppm), (d,H2) appeared δ (1.77ppm), (m,H3) appeared δ (2.35ppm) (m, Ar-H) appeared δ(4.8ppm), (s,OH) appeared δ (4.8ppm).). The ^{13}CNMR spectrum was used by (DMSO-d6), showing the signal (C-Ar) appeared δ (115.67-121.1ppm), (C-N) appeared δ (148.67ppm), (C-OH) appeared δ (173.8ppm), (C=N) appeared δ (211.29ppm), (C1) appeared δ (25.73ppm), (C2) appeared δ (27.5ppm), (C3) appeared δ (30.83ppm).

3-3 The compound (**7**) 3-(cyclohexylidene amino) phenol is black syrup, yield 76.6% The infrared spectrum of compound (**7**) showed band at (1402-1433cm^{-1}) for (C=C) Aromatic, (2991cm-1) for (C-H) aliphatic, (1606cm^{-1}) for (C=N), (1039cm^{-1}) for (C-O). The ^{1}H-NMR compound (**7**) through the use (of DMSO-d6) as a solvent. The proton signal (t,H1) appeared δ (1.05ppm), (d,H2) appeared δ (1.51ppm), (s,H3) appeared δ (1.91ppm), (t,OH) appeared δ (5.3ppm), (m,H4) appeared δ (6.79ppm), (s,H5) appeared δ(7.75ppm) (t,H6) appeared δ(6.79ppm). The ^{13}CNMR spectrum was used by (DMSO-d6), showing the signal (C1) appeared δ(20.46ppm), (C2) appeared δ (25.56ppm), (C3)appeared δ (33ppm), (C-Ar) appeared δ (100.85-131.69ppm), (C-N) appeared δ (144.74ppm), (C-OH) appeared δ (149.87ppm), (C=N) appeared δ (158.52ppm).

3-4 The compound (9) 2-cyclohexylidene hydrazine-1-carbothioamide is solid light yellow, M.P (155-157), yield 83.5%. The infrared spectrum of compound (**9**) showed band at (2939cm^{-1}) for (C-H) aliphatic (1072cm^{-1}) for (C=S), (1581cm^{-1}) for (C=N), (3379cm^{-1}) for (N-H) primary, (1300cm^{-1}) for(N-H)bond.

The ^{1}H-NMR compound (**9**) through the use (of DMSO-d6) as a solvent. The proton signal (s,NH) appeared δ (10.156ppm), (s,H1) appeared δ (1.051ppm), (s,NH2) appeared δ(7.96ppm), (t,H2) appeared δ(2.21ppm).). The ^{13}CNMR spectrum was used by (DMSO-d6), showing the signal (C=S) appeared δ (179ppm), (C=N) appeared δ (157.45ppm), (C3) appeared δ (35.02ppm), (C2) appeared δ (27.66ppm), (C1)appeared δ (25.5ppm).

3-5 The compound (**11**) 2,6-bis(E)-4-hydroxybenzylidene)cyclohexan-1-one is is dark green powder yield 88.46% M.P (260-263). The infrared spectrum of compound (**11**) showed band at (1435-1589cm^{-1}) for (C=C) aromatic, (1647cm^{-1}) for (C=O) ketone, (2931cm^{-1}) for (C-H), (3224cm^{-1})f or (OH) phenol.

The ^{1}H-NMR compound (**11**) through the use (of DMSO-d6) as a solvent. The proton signal H1 appeared δ (1.5ppm), t, H2 appeared δ (1.72ppm), (d,CH=CH) appeared δ (6.83ppm),(mH-Ar) appeared δ(7.22-7.96ppm),(d,OH) appeared δ(5ppm). The ^{13}CNMR spectrum was used by (DMSO-d6), showing the signal (C-Ar) appeared δ(116-136.27ppm), (C-OH) appeared δ(158.8ppm), (C=O)appeared δ (188.98ppm), (C1)appeared δ (28.44ppm), (C2)appeared δ(19.03ppm).

3-6 The compound (**13**) (2E, 6E)-2,6-bis(furan-2-ylmethylene)cyclohexan-1-one is solid brown, M.P(130-132), yield 84.38%.

The infrared spectrum of compound (**13**) showed band at (2939cm^{-1}) for (C-H) Aliphatic, (1643cm^{-1}) for (C=O), (1546cm^{-1}) for (C=C), (1284cm^{-1}) for (C-O), (1249cm^{-1}) for (C-O-C). The ^{1}H-NMR compound (**11**) through the use (of DMSO-d6) as a solvent. The proton signal (m, A-rH) appeared δ (6.693-7.401ppm), (s,H1) appeared δ (1.057ppm), (H2) appeared δ (1.84ppm) (d,H3) appeared δ (7.929ppm).). The ^{13}CNMR spectrum was used by (DMSO-d6), showing the signal (C1) appeared δ(27.92ppm), (C2) appeared δ (21.57ppm), (C=O) appeared δ (187.86ppm), (C3) appeared δ (146.23ppm), (C4) in(-CH=) appeared δ (122.92ppm), (C-O) appeared δ (152.18ppm), (C6) appeared δ (113.36ppm), (C7) appeared δ (111.32ppm).

3-7 The compound (**15**) 2,6-bis ((E)-4-bromobenzylidene)cyclohexan-1-one is solid light yellow, yield 80.48%. The infrared spectrum of compound (**15**) showed band at (1666cm^{-1}) for (C=C) aromatic, (2927cm^{-1}) for (C-H) aliphatic, (1006cm^{-1}) for (C-Br), (1770cm^{-1}) for (C=O) Ketone, (1481cm-1) bend for (-CH$_2$-). The ^{1}H-NMR compound (**15**) through the use (of DMSO-d6) as a solvent. The proton signal (m, Ar-H) appeared δ (6.91ppm), (t,H1) appeared δ (2.78ppm), (s,H2) appeared δ(1.05ppm). The ^{13}CNMR spectrum was used by (DMSO-d6), showing the signal(C-Ar) appeared δ(130.2-137.41ppm), (C-Br) appeared δ(122.14ppm), (C=O) appeared δ(189.27ppm).

3-8 The compound (**17**) 2,6-bis((E)-4-hydroxy-3-methoxybenzylidene)cyclohexan-1-one is yellow solid, M.P (166-168), yield 72.18%. The infrared spectrum of compound (**17**) showed band at (3475cm^{-1}) for (OH) phenol, (2970cm^{-1}) for (C-H)aliphatic, (1517cm^{-1}) for (C=C), (1226cm^{-1}) for (C-O), (1662cm^{-1}) for (C=O). The 1H-NMR compound (17) through the use (of DMSO-d6) as a solvent. The proton signal (s,Ar-H) appeared δ (6.092-7.052ppm), (s,OH)appeared δ (5.3ppm), (m,CH_3) appeared δ(3.36-3.38ppm), (s,H1) appeared δ(1.5ppm), (d,H2) appeared δ (1.8ppm). The ^{13}CNMR spectrum was used by (DMSO-d6), showing the signal (CH_3) appeared δ(54.94ppm), (C-OH) appeared δ(117.44ppm), (C-O)appeared δ(171.33ppm), (C=O)appeared δ(85.98ppm).

BIOLOGICAL ACTIVITY

The biological activity in this research was conducted against Staphylococcus aureus, Escherichia Coli of compound (15,13), compound 13 showed the highest antibacterial potential with inhibition zone diameter of 17 mm against Escherichia Coli bacteria, while compound 15 showed antibacterial potential with inhibition zone diameter of 9 mm against Escherichia Coli bacteria. Antibacterial with a diameter of 13 mm against Staphylococcus aureus, while the other compounds showed weak inhibition against Staphylococcus aureus, Escherichia Coli.

Table.2 Biological activity of compound(C11-C17)

Antibacterial Activity				
NO. Sample	**Escherichia Coli**	**Diameter mm**	**Staphylococcus aureus**	**Diameter mm**
11	_	_	_	_
13	++	17	_	_
15	+	9	++	13
17	_	_	_	_

"- =Inactive, + = (5-10) mm =slightly active, + + = (11-20) mm middling.

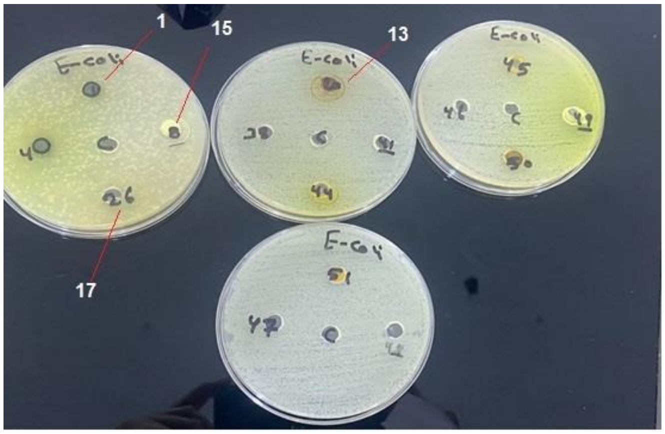


Figure. 26. Shows the effect of the compounds on the (Staphylococcus aureus, Escherichia coli

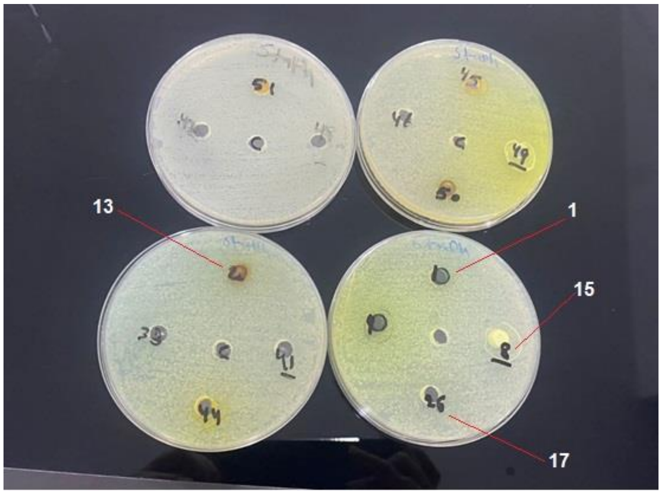


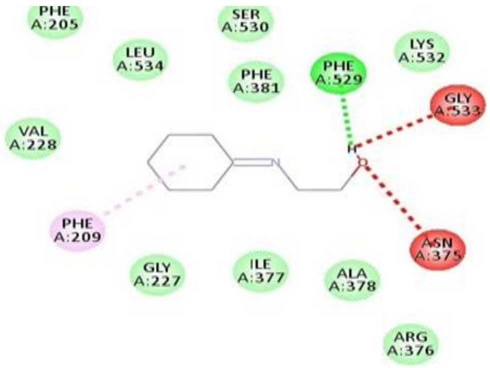
Figure. 26. Shows the effect of the compounds on the (Staphylococcus aureus, Escherichia coli

MOLECULAR DOCKING STUDY

The molecular docking of the prepared compounds with the protein responsible for breast cancer was studied using AutoDock 4.2.6 program, and the following results were obtained, shown in the table 3.

Table 3. Shows the molecular docking values of the breast cancer protein (6COX)

Compound	Lowest Binding Energy	Run
3	-5.59	50
5	-6.37	37
7	-6.90	31
9	-6.13	46
11	-8.88	18
13	-8.05	46
15	-10.13	5
17	-9.15	30



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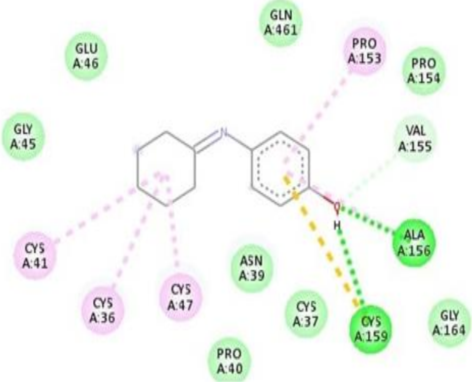

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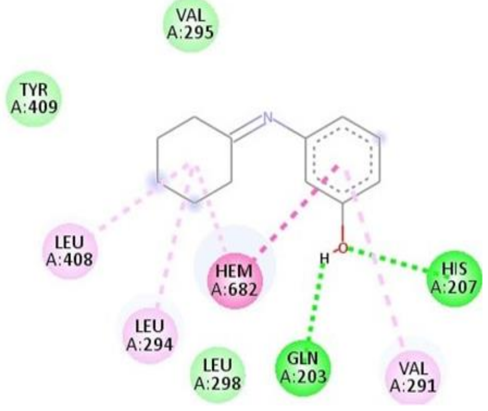

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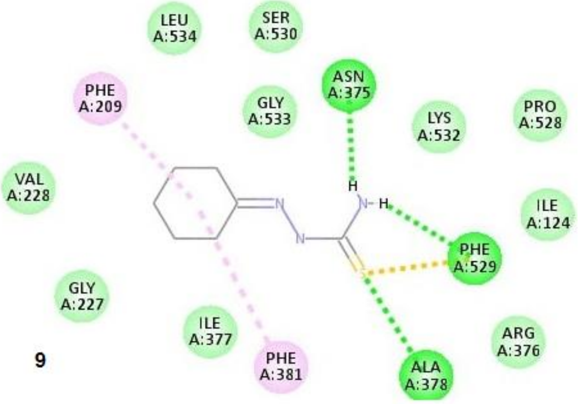

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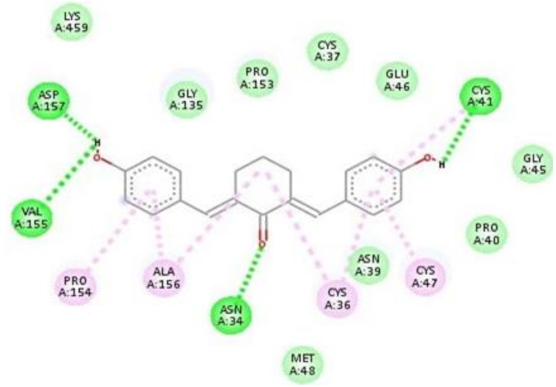

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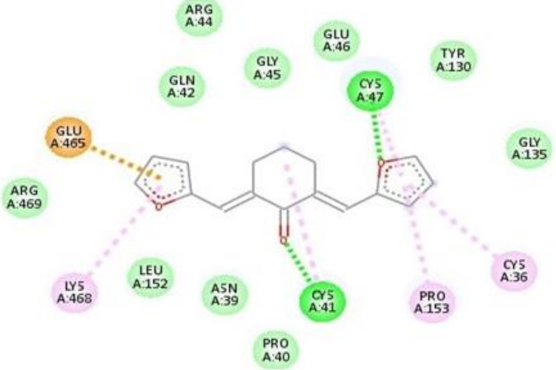

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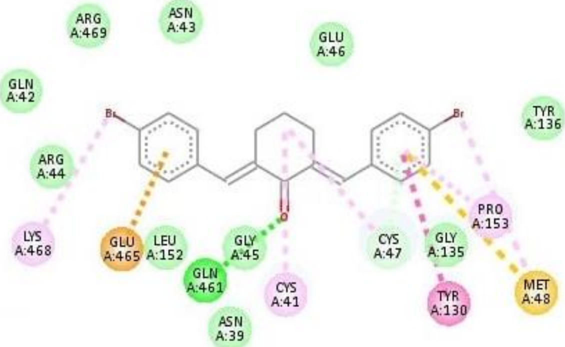

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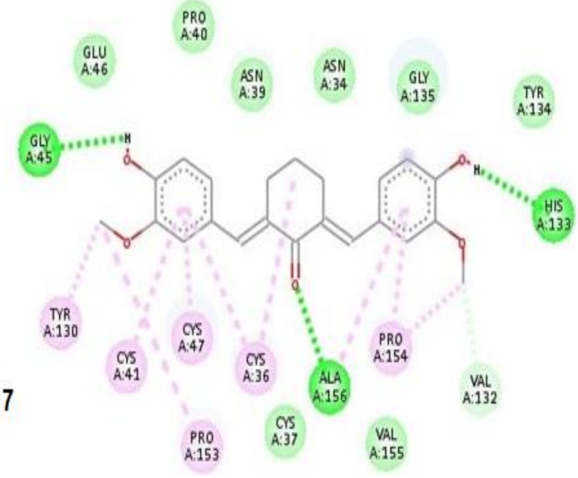

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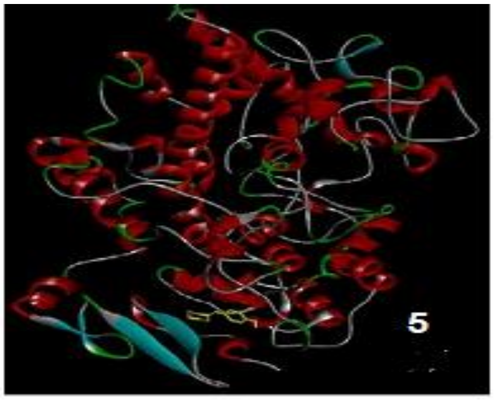
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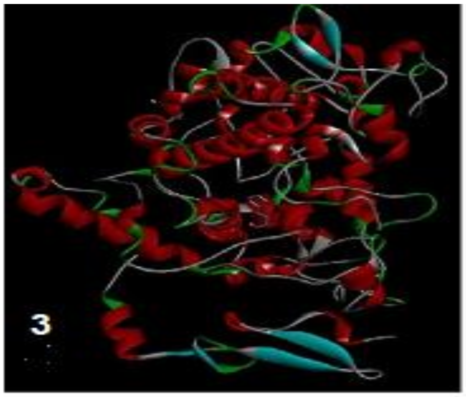
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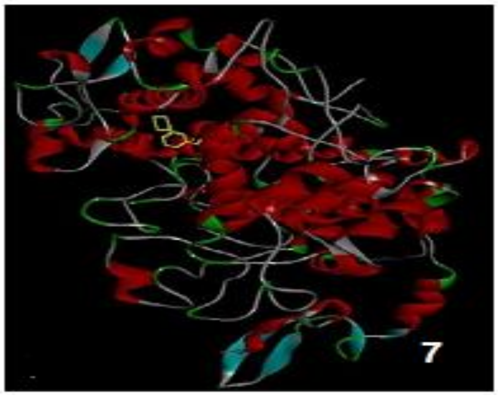
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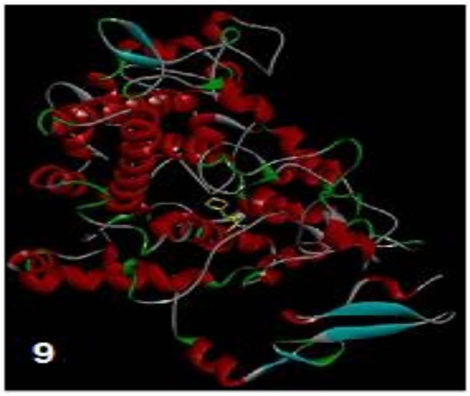
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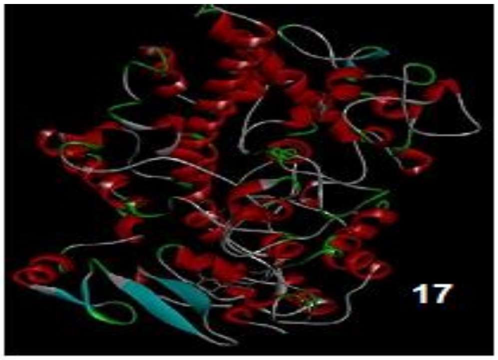
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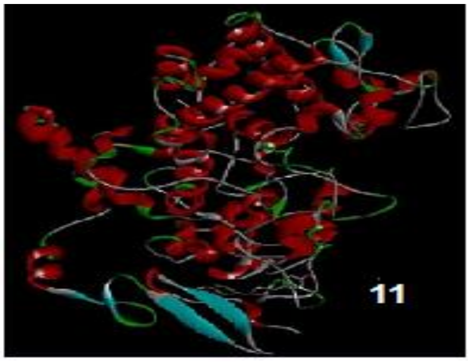
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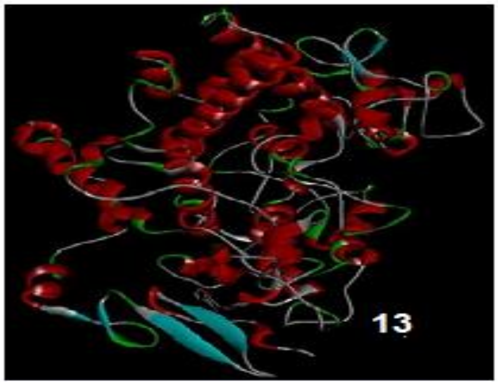
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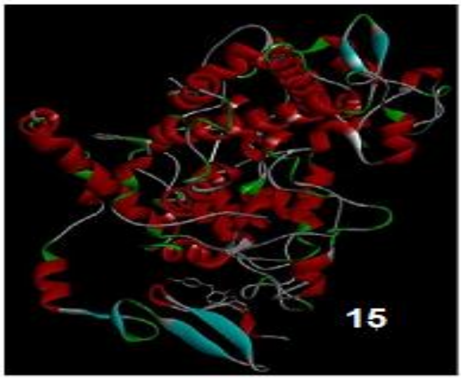
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CONCLUSIONS

To summarize, I prepared a new set of Schiff bases and chalcones derived from cyclohexanone. the compounds were validated by infrared spectroscopy, 1H-NMR and 13C - NMR, then the biological activity, finally, by Moleculer Docking. some compounds showed moderate biological activity against bacteria Staphylococcus aureus, Escherichia Coli, while others showed weak to no activity.

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ANALYSIS OF FT-IR SPECTRA

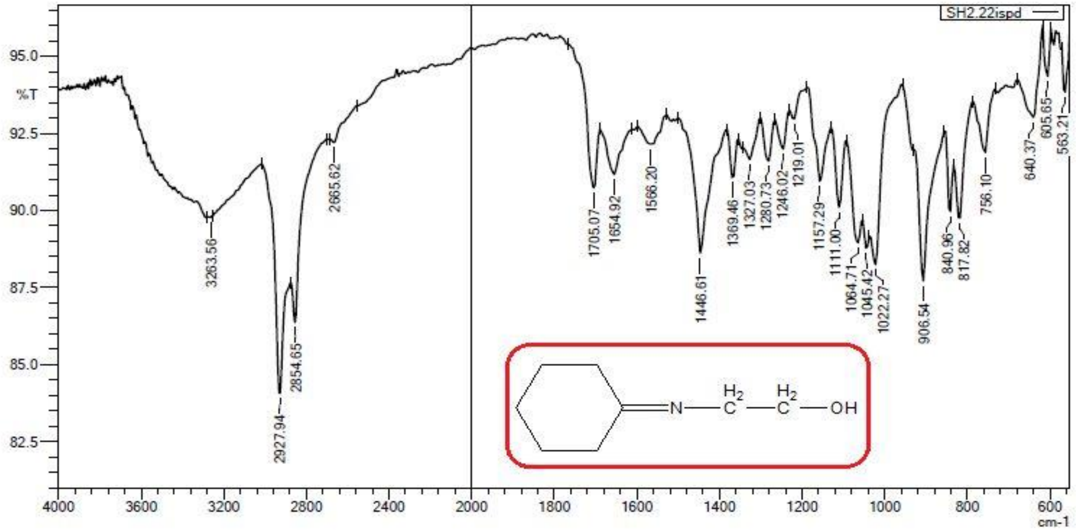


Figure 3. FT-IR spectrum of the compound (3)

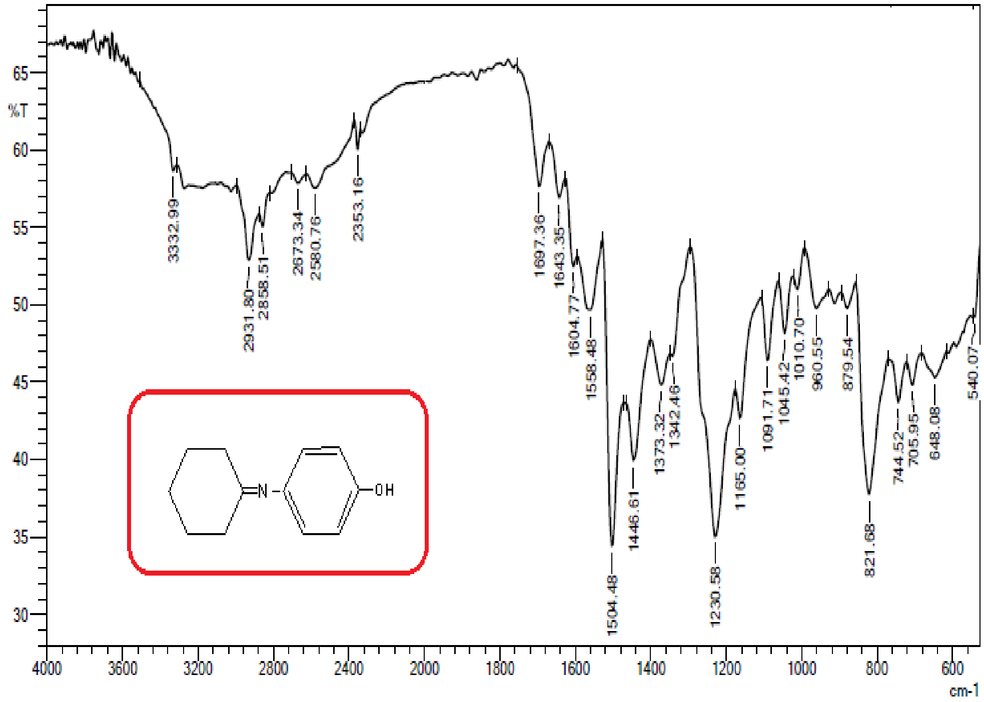


Figure 4. FT-IR spectrum of the compound (5)

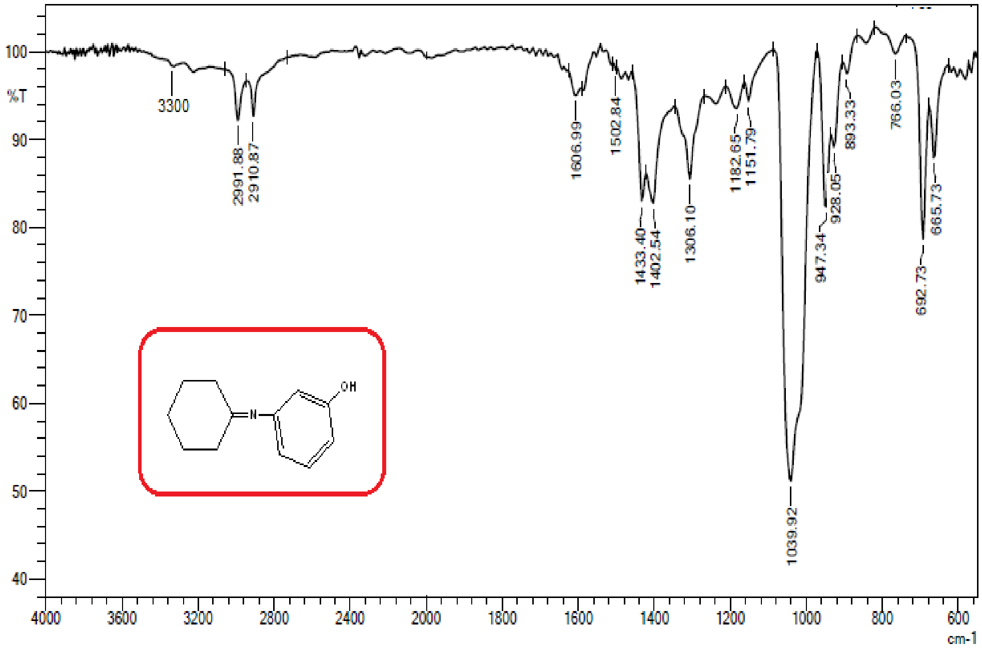


Figure 5. FT-IR spectrum of the compound (7)

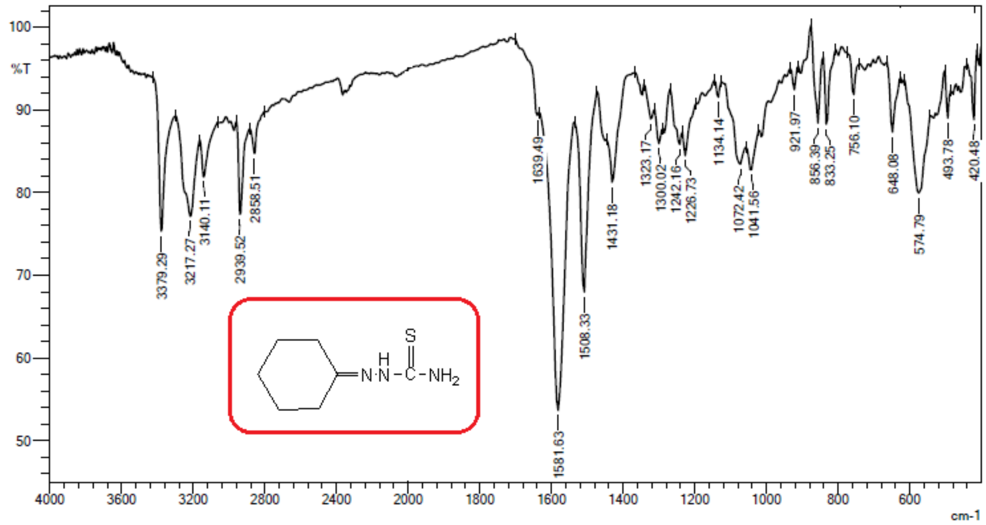


Figure 6. FT-IR spectrum of the compound (9)

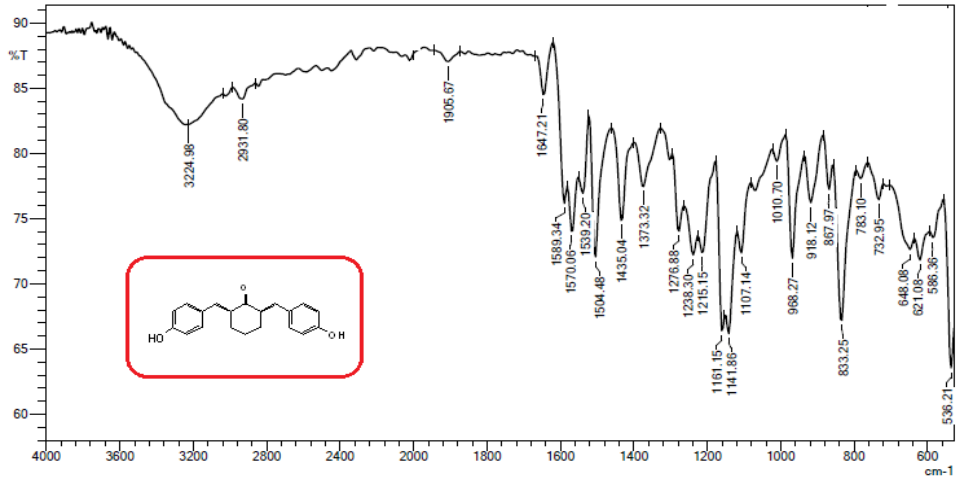


Figure 7. FT-IR spectrum of the compound (11)

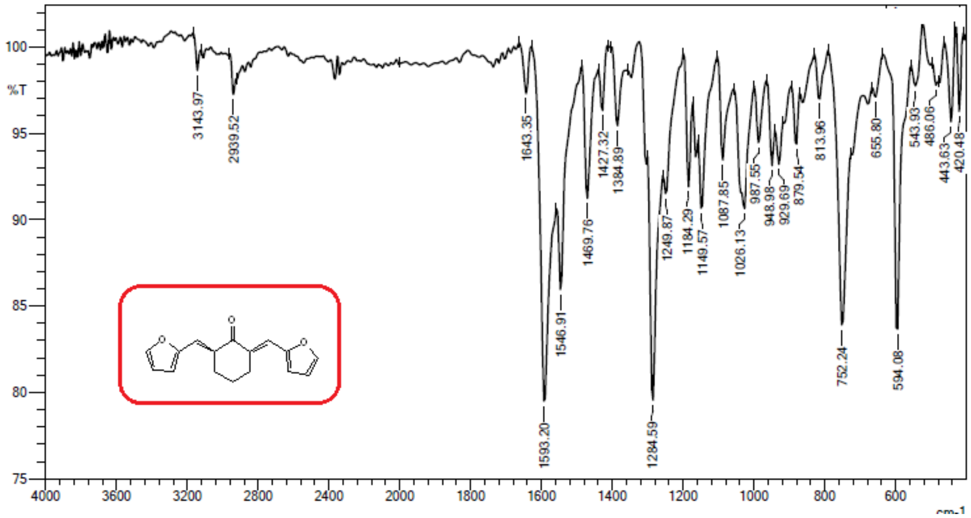


Figure 8. FT-IR spectrum of the compound (13)

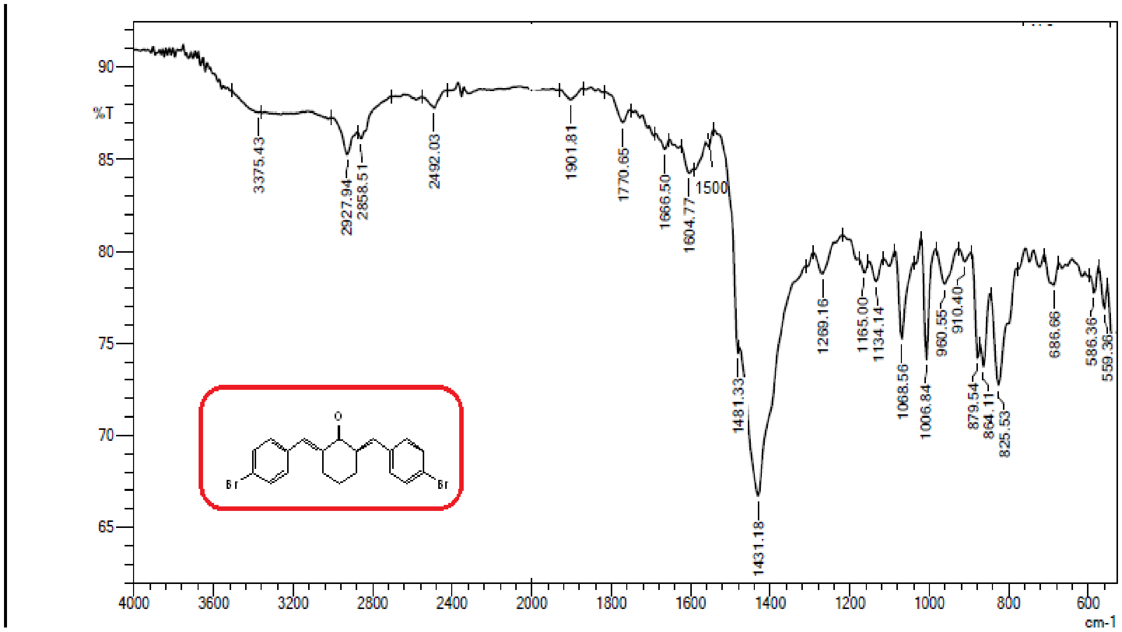


Figure 9. FT-IR spectrum of the compound (15)

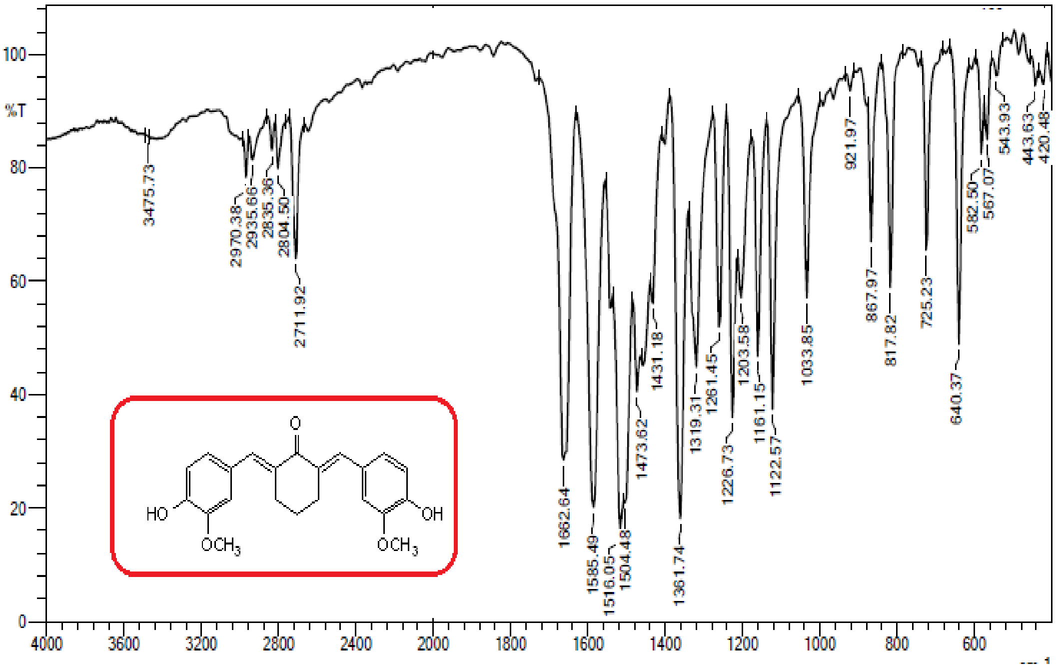


Figure 10. FT-IR spectrum of the compound (17)

^{1}HNMR and ^{13}C NMR spectrum

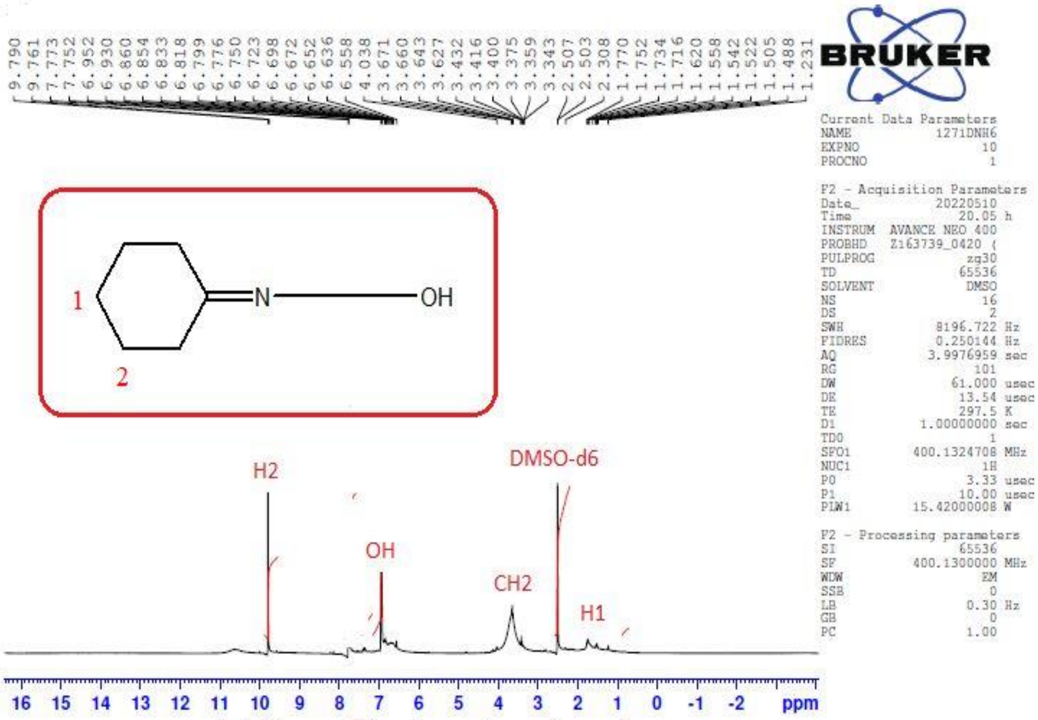


Figure 11. ^{1}HNMR spectrum of the compound (3)

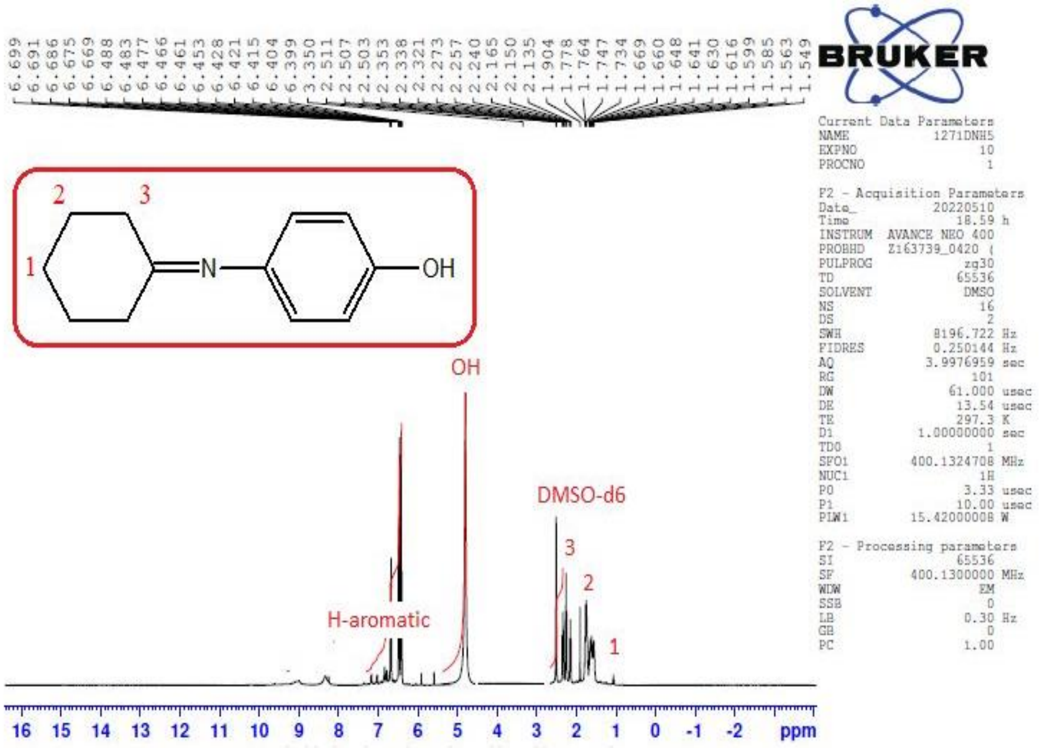


Figure 12. ^{1}HNMR spectrum of the compound (5)

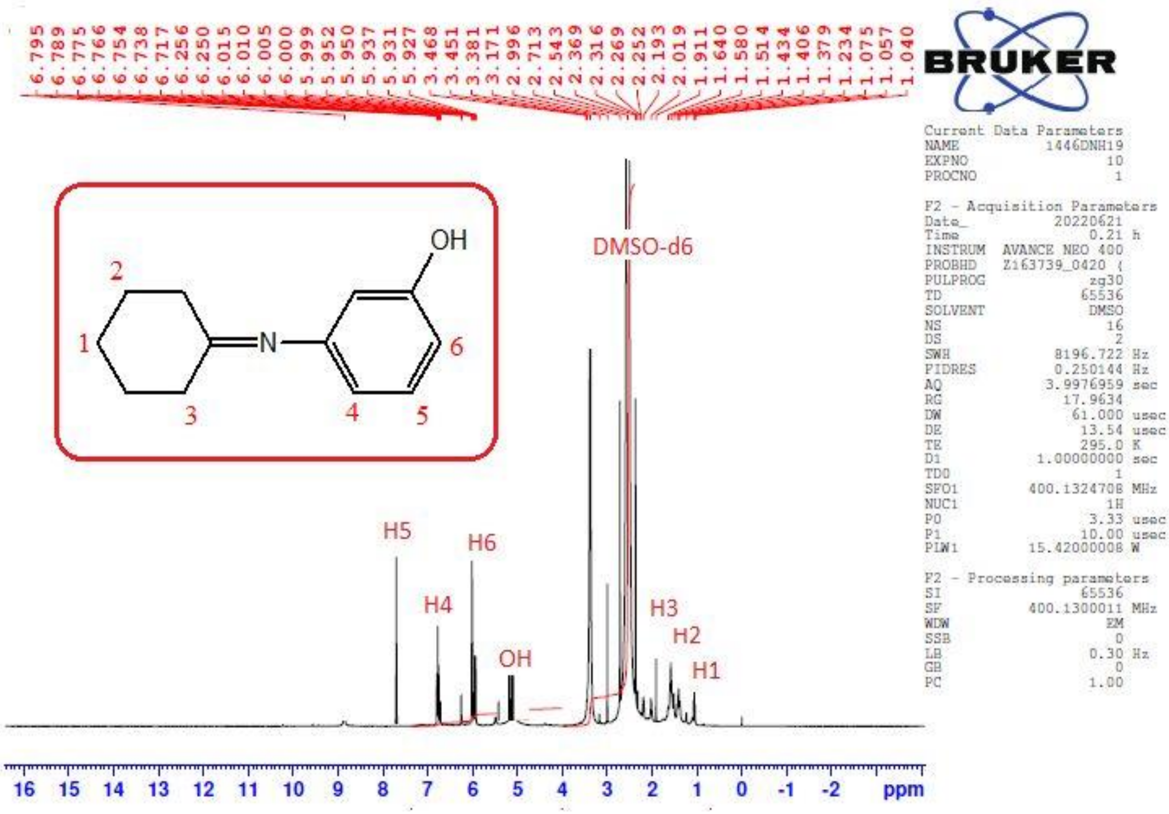


Figure 13. ^{1}HNMR spectrum of the compound (7)

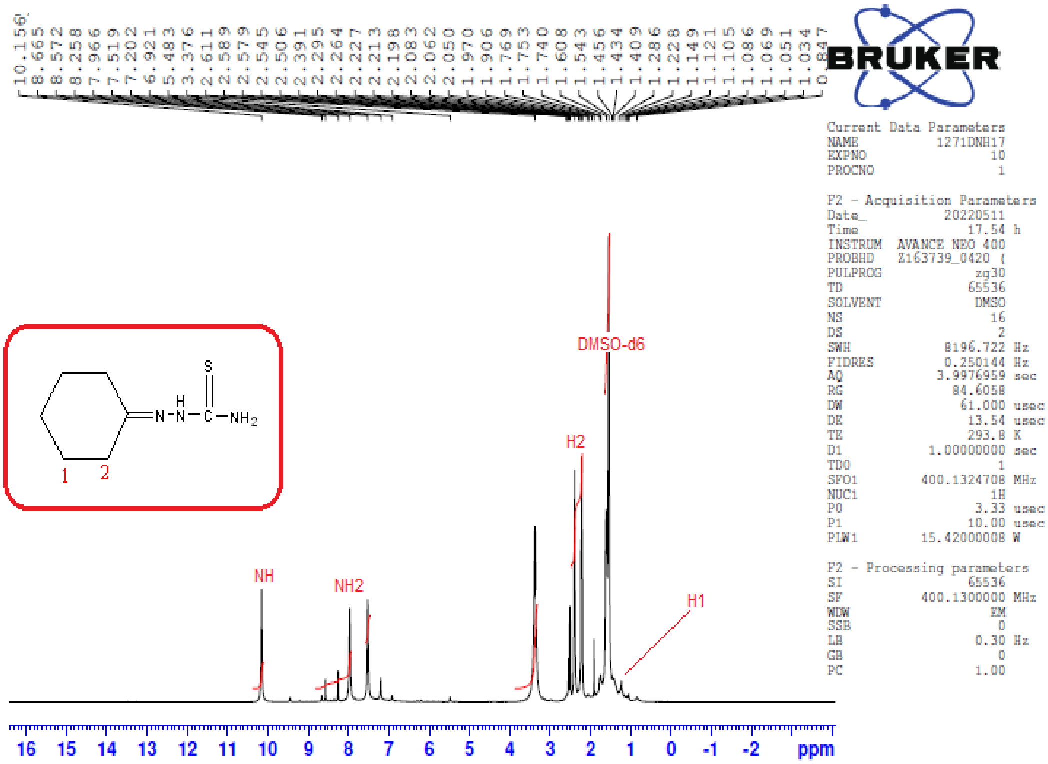
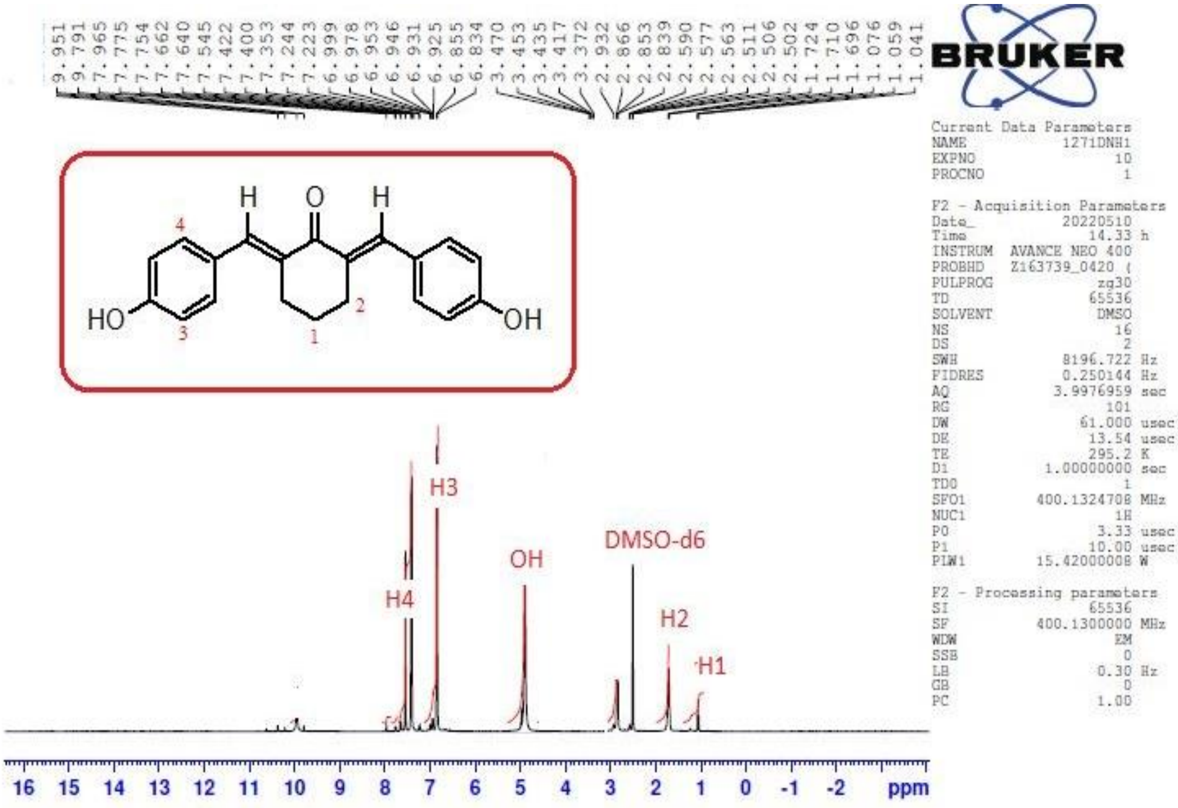


Figure 14. ^{1}HNMR spectrum of the compound (9)



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PROCNO                 1

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TD                 65536
SOLVENT             DMSO
NS                    16
DS                     2
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FIDRES          0.250144 Hz
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RG                   101
DW                61.000 usec
DE                 13.54 usec
TE                 295.2 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                  3.33 usec
P1                 10.00 usec
PLW1         15.42000008 W

F2 - Processing parameters
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SSB                    0
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GB                     0
PC                  1.00
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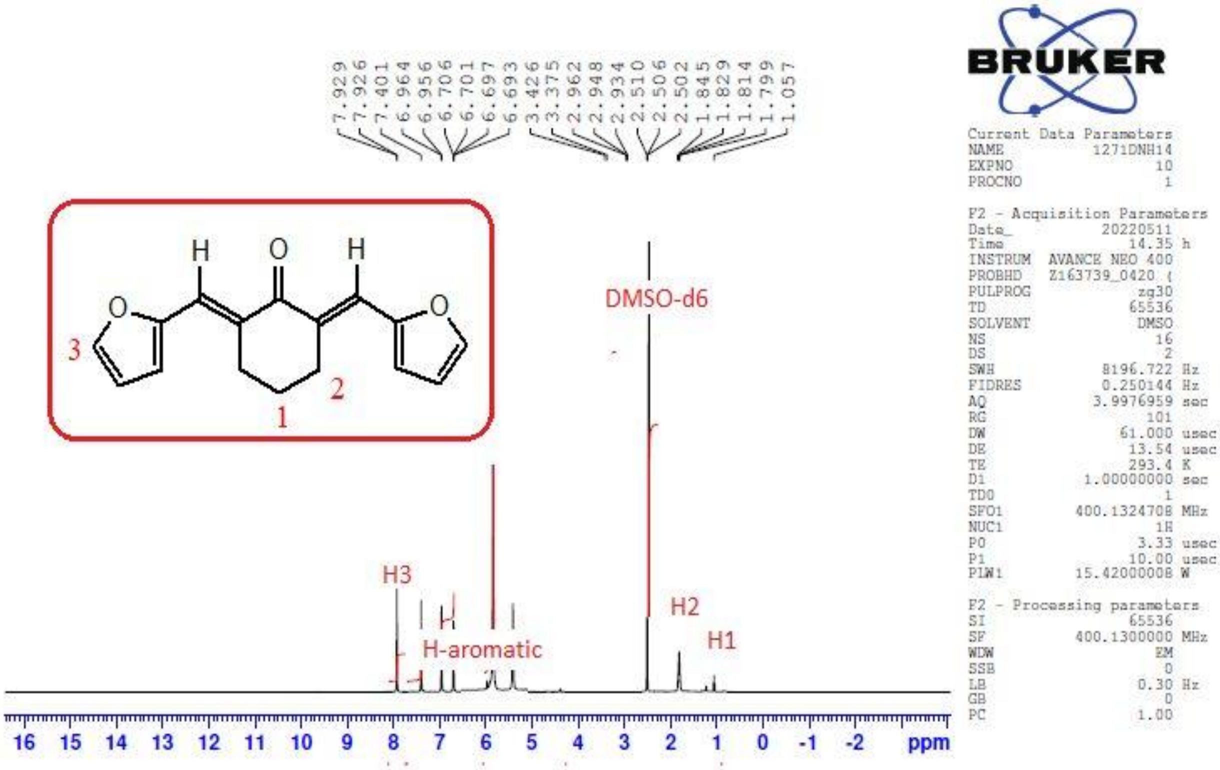
Figure 15. ^{1}HNMR spectrum of the compound (11)



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PROCNO                 1

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PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    16
DS                     2
SWH             8196.722 Hz
FIDRES          0.250144 Hz
AQ             3.9976959 sec
RG                   101
DW                61.000 usec
DE                 13.54 usec
TE                 293.4 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                  3.33 usec
P1                 10.00 usec
PLW1         15.42000008 W

F2 - Processing parameters
SI                 65536
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WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
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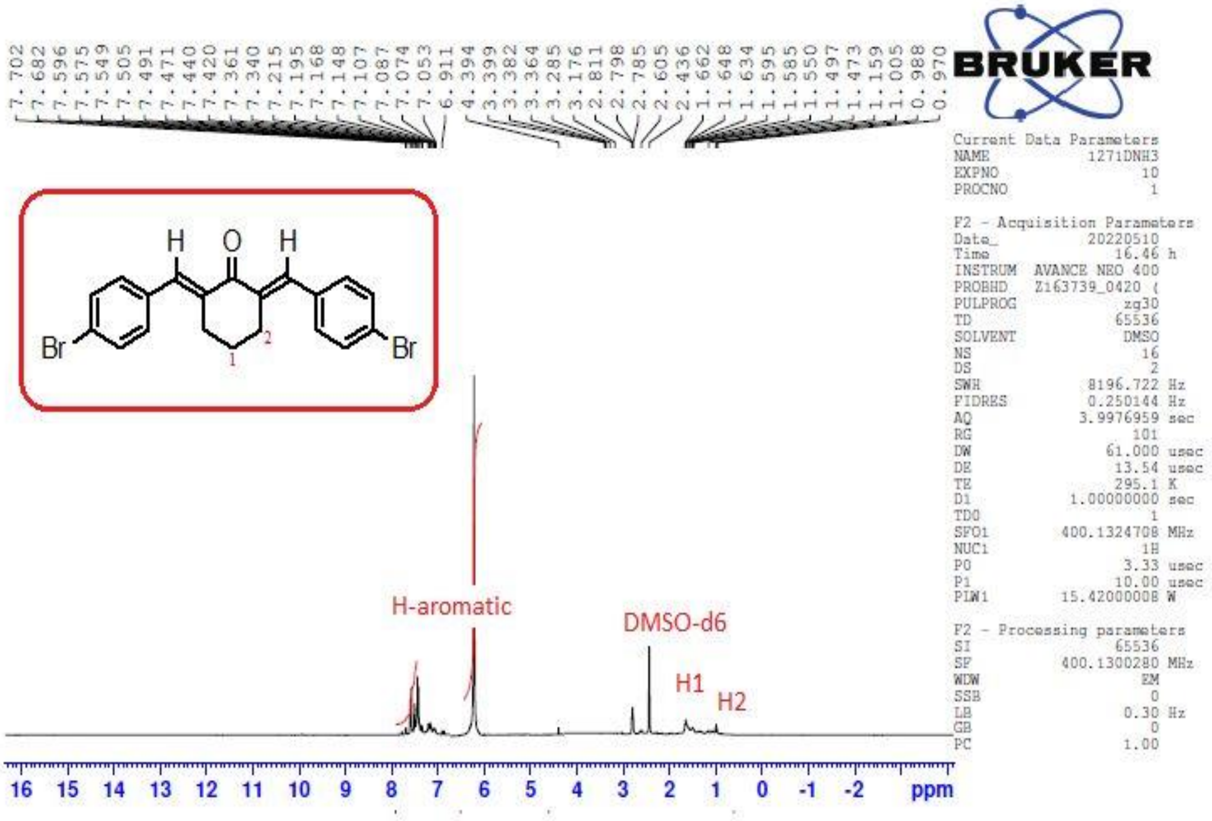
Figure 16. ^{1}HNMR spectrum of the compound (13)



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PROCNO                   1

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PULPROG               zg30
TD                   65536
SOLVENT               DMSO
NS                      16
DS                       2
SWH             8196.722 Hz
FIDRES          0.250144 Hz
AQ             3.9976959 sec
RG                     101
DW                61.000 usec
DE                 13.54 usec
TE                 295.1 K
D1            1.00000000 sec
TD0                      1
SFO1         400.1324708 MHz
NUC1                    1H
P0                  3.33 usec
P1                 10.00 usec
PLW1         15.42000008 W

F2 - Processing parameters
SI                   65536
SF           400.1300280 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
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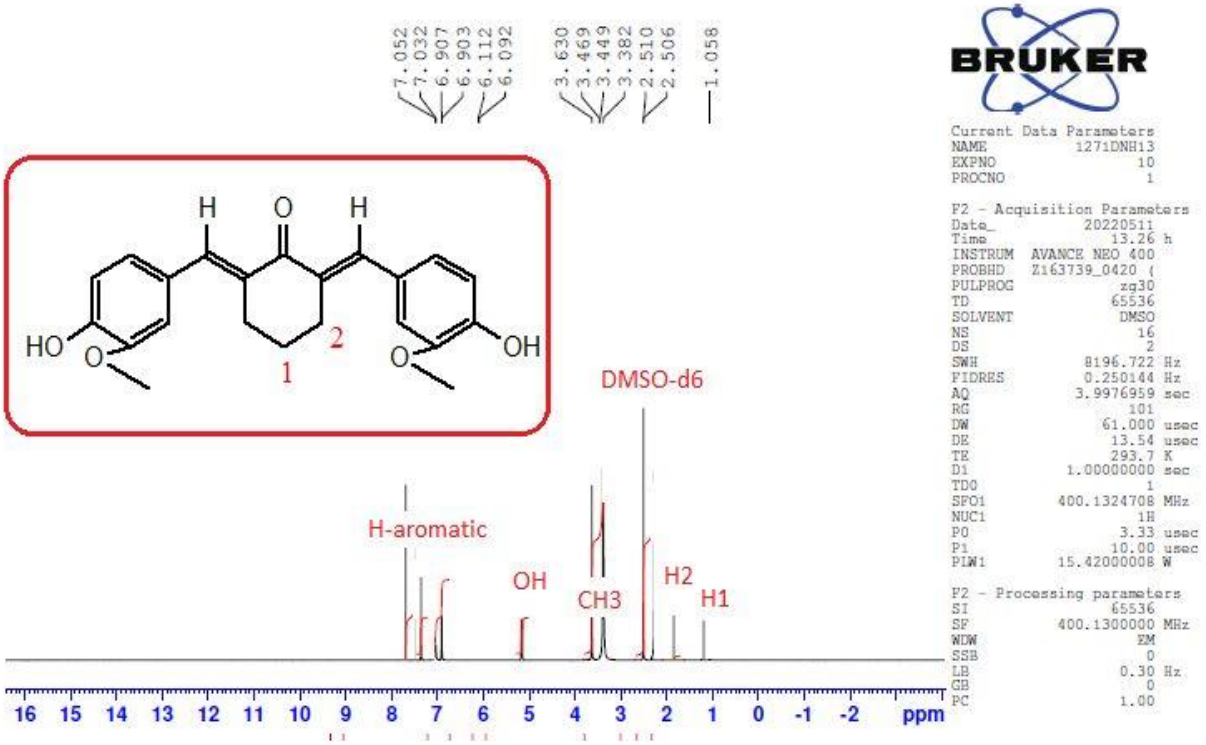
Figure 17. ^{1}HNMR spectrum of the compound (15)



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PROCNO                   1

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SOLVENT               DMSO
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DS                       2
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FIDRES          0.250144 Hz
AQ             3.9976959 sec
RG                     101
DW                61.000 usec
DE                 13.54 usec
TE                 293.7 K
D1            1.00000000 sec
TD0                      1
SFO1         400.1324708 MHz
NUC1                    1H
P0                  3.33 usec
P1                 10.00 usec
PLW1         15.42000008 W

F2 - Processing parameters
SI                   65536
SF           400.1300000 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
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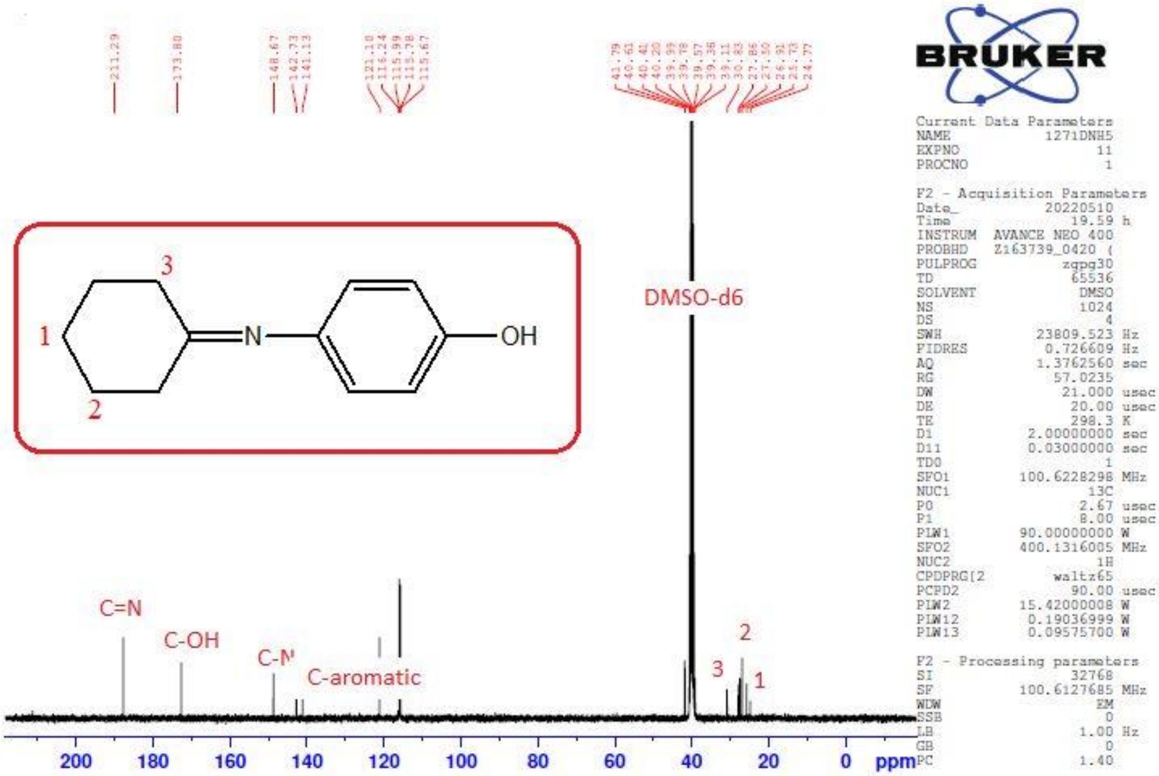
Figure 18. ^{1}HNMR spectrum of the compound (17)



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PROCNO                  1

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TD                  65536
SOLVENT              DMSO
NS                   1024
DS                      4
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FIDRES           0.726609 Hz
AQ              1.3762560 sec
RG                57.0235
DW                 21.000 usec
DE                  20.00 usec
TE                  298.3 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1
SFO1          100.6228298 MHz
NUC1                  13C
P0                   2.67 usec
P1                   8.00 usec
PLW1          90.00000000 W
SFO2          400.1316005 MHz
NUC2                   1H
CPDPRG[2          waltz65
PCPD2               90.00 usec
PLW2          15.42000008 W
PLW12          0.19036999 W
PLW13          0.09575700 W

F2 - Processing parameters
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PC                   1.40
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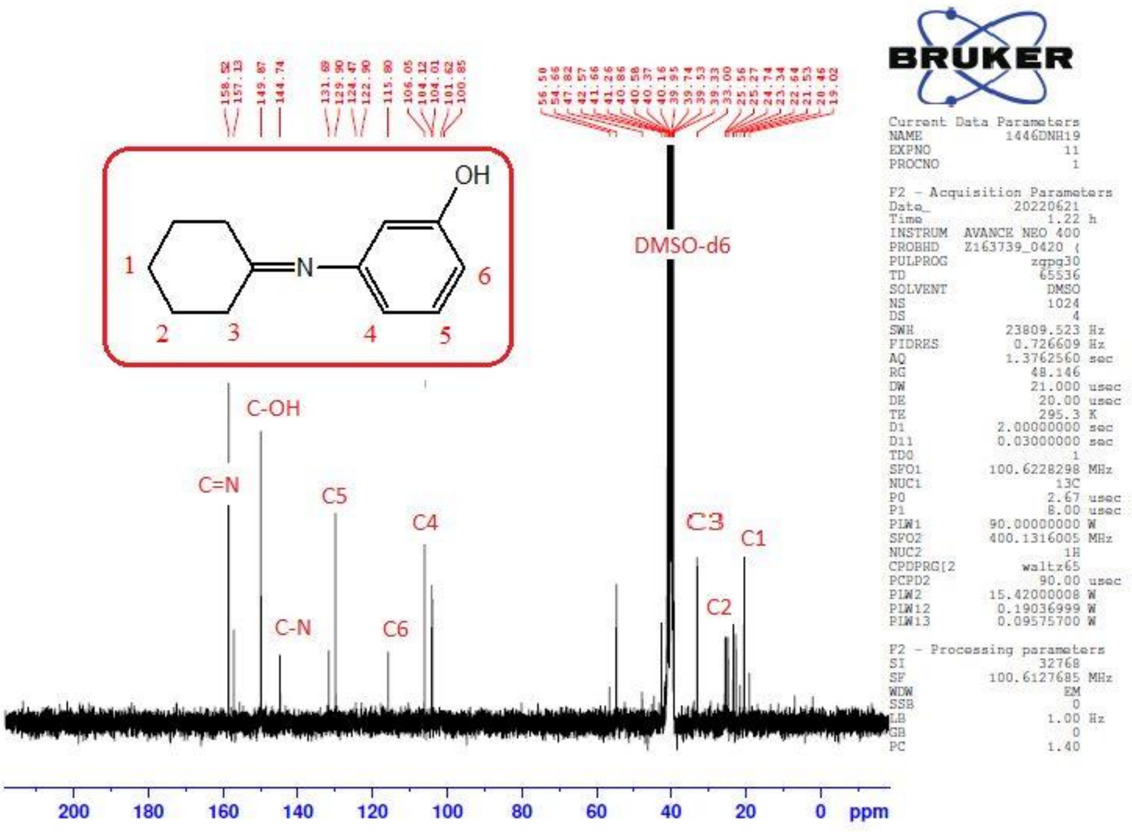
Figure 19. ^{13}C NMR spectrum of the compound (5)



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SOLVENT              DMSO
NS                   1024
DS                      4
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FIDRES           0.726609 Hz
AQ              1.3762560 sec
RG                 48.146
DW                 21.000 usec
DE                  20.00 usec
TE                  295.3 K
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D11            0.03000000 sec
TD0                     1
SFO1          100.6228298 MHz
NUC1                  13C
P0                   2.67 usec
P1                   8.00 usec
PLW1          90.00000000 W
SFO2          400.1316005 MHz
NUC2                   1H
CPDPRG[2          waltz65
PCPD2               90.00 usec
PLW2          15.42000008 W
PLW12          0.19036999 W
PLW13          0.09575700 W

F2 - Processing parameters
SI                  32768
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SSB                     0
LB                   1.00 Hz
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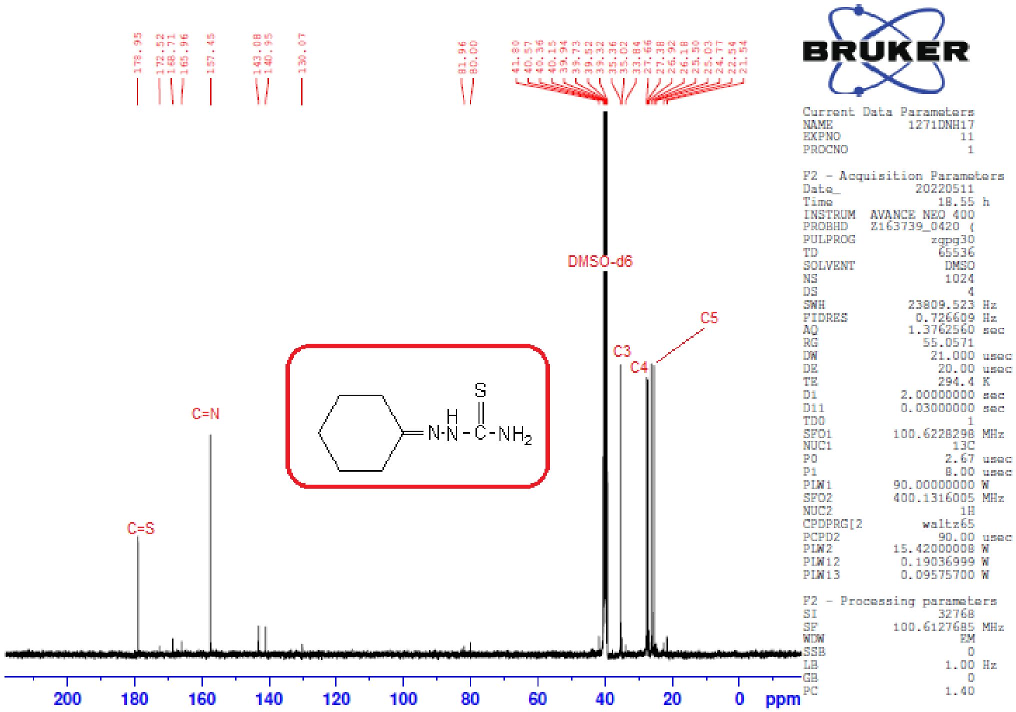
Figure 20. ^{13}C NMR spectrum of the compound (7)



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TD                65536
SOLVENT            DMSO
NS                 1024
DS                    4
SWH           23809.523 Hz
FIDRES         0.726609 Hz
AQ            1.3762560 sec
RG              55.0571
DW               21.000 usec
DE                20.00 usec
TE                294.4 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        100.6228298 MHz
NUC1                13C
P0                 2.67 usec
P1                 8.00 usec
PLW1        90.00000000 W
SFO2        400.1316005 MHz
NUC2                 1H
CPDPRG[2         waltz65
PCPD2             90.00 usec
PLW2        15.42000008 W
PLW12        0.19036999 W
PLW13        0.09575700 W

F2 - Processing parameters
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GB                    0
PC                 1.40
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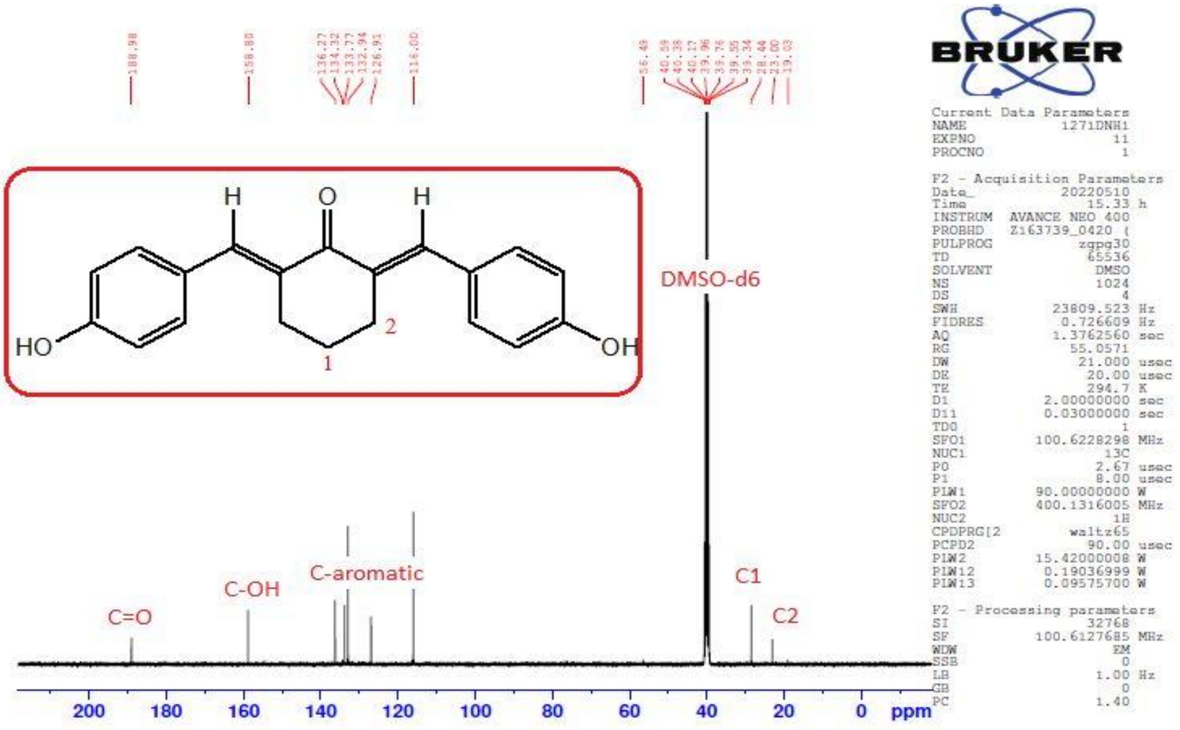
Figure 21. ^{13}C NMR spectrum of the compound (9)



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PROCNO                 1

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PULPROG          zgpg30
TD                65536
SOLVENT            DMSO
NS                 1024
DS                    4
SWH           23809.523 Hz
FIDRES         0.726609 Hz
AQ            1.3762560 sec
RG              55.0571
DW               21.000 usec
DE                20.00 usec
TE                294.7 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        100.6228298 MHz
NUC1                13C
P0                 2.67 usec
P1                 8.00 usec
PLW1        90.00000000 W
SFO2        400.1316005 MHz
NUC2                 1H
CPDPRG[2         waltz65
PCPD2             90.00 usec
PLW2        15.42000008 W
PLW12        0.19036999 W
PLW13        0.09575700 W

F2 - Processing parameters
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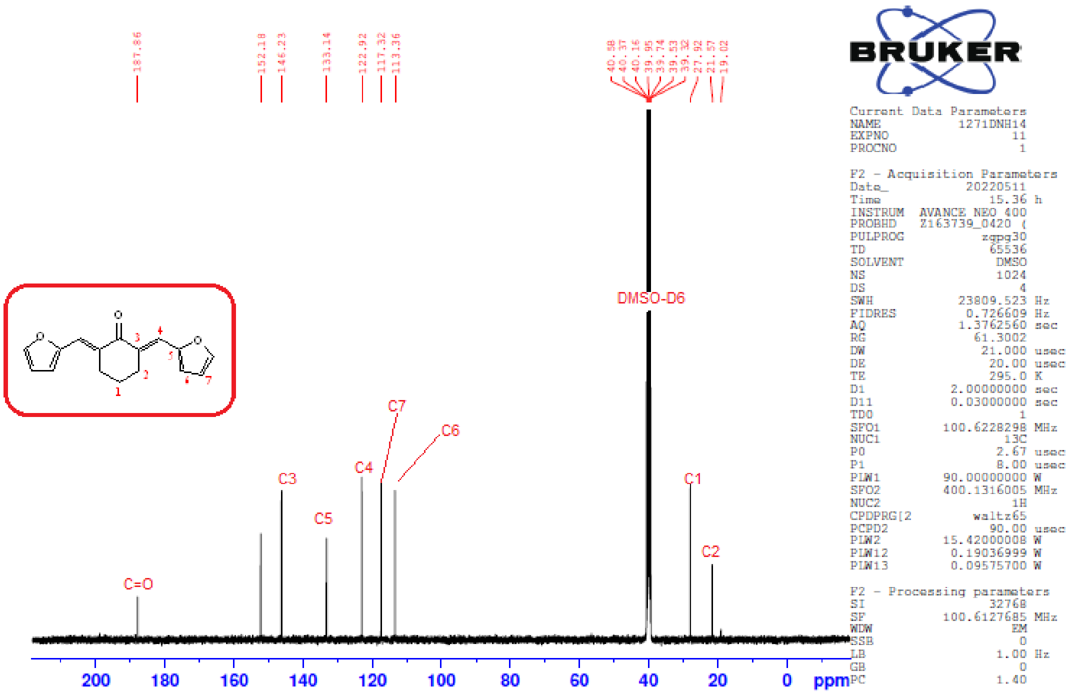
Figure 22. ^{13}C NMR spectrum of the compound (11)



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TD                   65536
SOLVENT               DMSO
NS                    1024
DS                       4
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FIDRES            0.726609 Hz
AQ               1.3762560 sec
RG                 61.3002
DW                  21.000 usec
DE                   20.00 usec
TE                   295.0 K
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D11             0.03000000 sec
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NUC1                   13C
P0                    2.67 usec
P1                    8.00 usec
PLW1           90.00000000 W
SFO2           400.1316005 MHz
NUC2                    1H
CPDPRG[2           waltz65
PCPD2                90.00 usec
PLW2           15.42000008 W
PLW12           0.19036999 W
PLW13           0.09575700 W

F2 - Processing parameters
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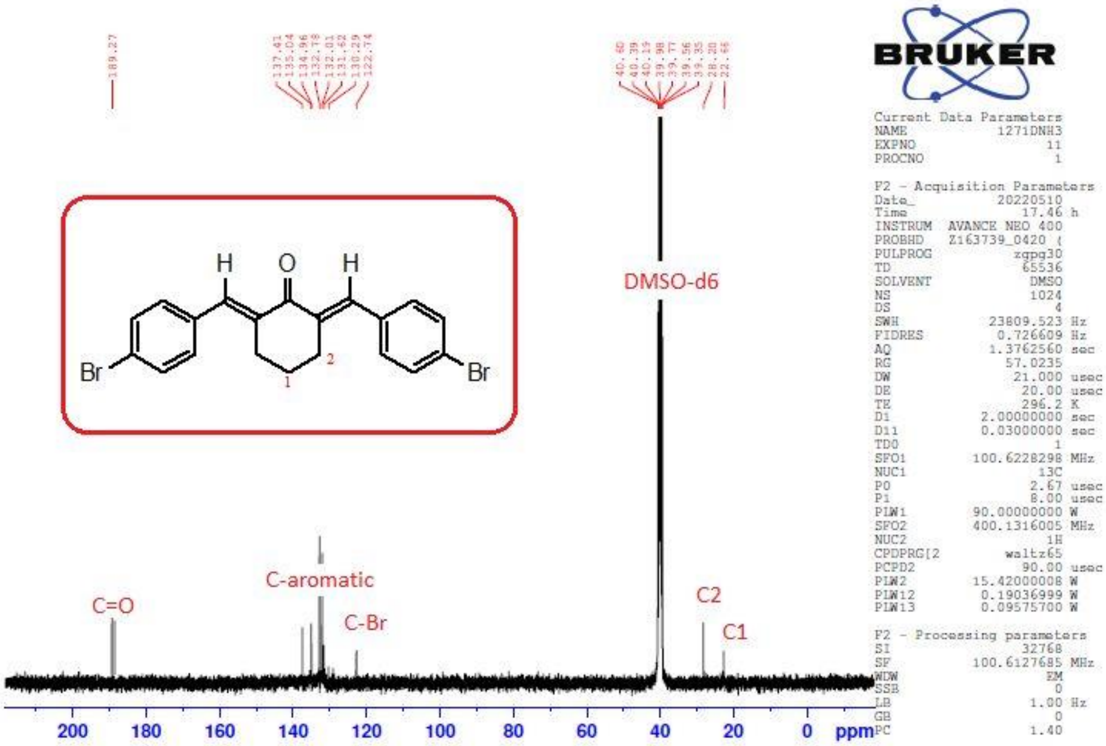
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.40
```

Figure 23. ^{13}C NMR spectrum of the compound (13)



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TD                   65536
SOLVENT               DMSO
NS                    1024
DS                       4
SWH              23809.523 Hz
FIDRES            0.726609 Hz
AQ               1.3762560 sec
RG                 57.0235
DW                  21.000 usec
DE                   20.00 usec
TE                   296.2 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                      1
SFO1           100.6228298 MHz
NUC1                   13C
P0                    2.67 usec
P1                    8.00 usec
PLW1           90.00000000 W
SFO2           400.1316005 MHz
NUC2                    1H
CPDPRG[2           waltz65
PCPD2                90.00 usec
PLW2           15.42000008 W
PLW12           0.19036999 W
PLW13           0.09575700 W

F2 - Processing parameters
SI                   32768
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WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.40
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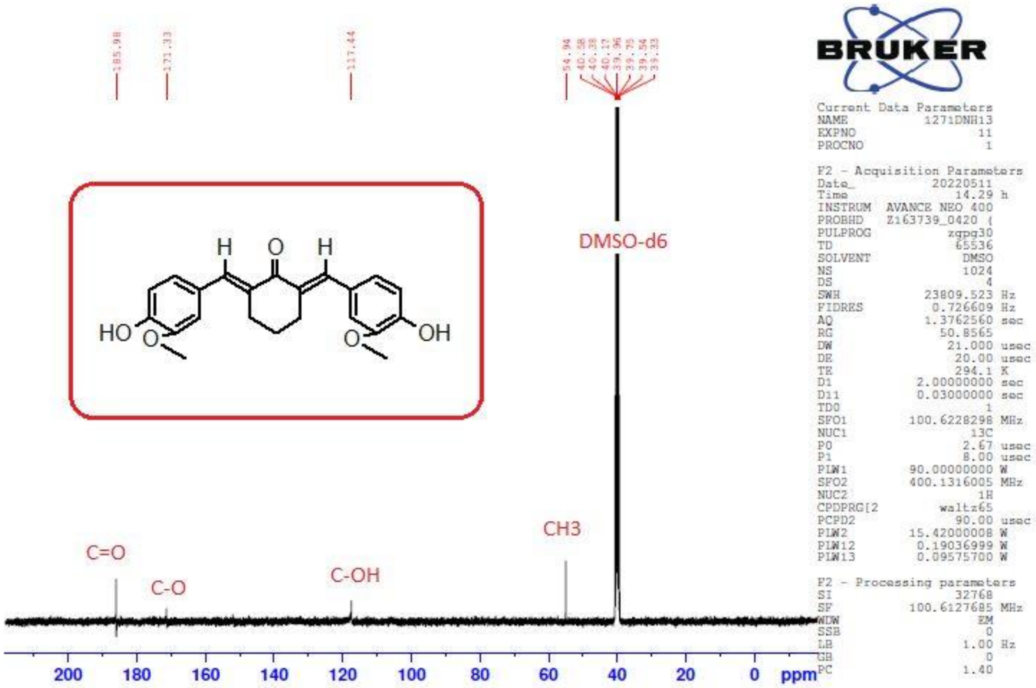
Figure 24. ^{13}C NMR spectrum of the compound (15)



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PROCNO                  1

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PULPROG            zgpg30
TD                  65536
SOLVENT              DMSO
NS                   1024
DS                      4
SWH             23809.523 Hz
FIDRES           0.726609 Hz
AQ              1.3762560 sec
RG                50.8565
DW                 21.000 usec
DE                  20.00 usec
TE                  294.1 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1
SFO1          100.6228298 MHz
NUC1                  13C
P0                   2.67 usec
P1                   8.00 usec
PLW1          90.00000000 W
SFO2          400.1316005 MHz
NUC2                   1H
CPDPRG[2          waltz65
PCPD2               90.00 usec
PLW2          15.42000008 W
PLW12          0.19036999 W
PLW13          0.09575700 W

F2 - Processing parameters
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SF            100.6127685 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
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Figure 25. ^{13}C NMR spectrum of the compound (17)