Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Synthesis, characterization of Diarylidenecyclohexanone derivatives as new anti-inflammatory pharmacophores exhibiting strong PGE2 and 5-LOX inhibition

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1. Instrumentation

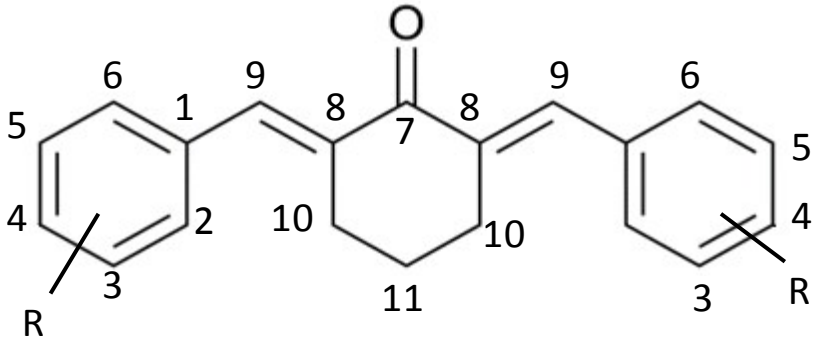
The melting points (MP) were determined using an open capillary apparatus and are uncorrected. Thermo-Nicolet Avatar 370spectrophotometer was employed for recording FT-IR using KBr pellets. The Shimadzu 2450 spectrophotometer was used for recording the UV–Vis spectra of the compounds in methanol between wavelength of 200 nm to 500 nm.VARIAN 400 MHz for the ^{1}H-NMR spectra and VARIAN 100 MHz for the ^{13}C-NMR spectra were employed using the internal standard TMS and the solvent$CDCl_3$. Mass spectra was obtained using AGILENT 6430 Triple Quad LC/MS and in cases of **Ib** and **IVa**SHIMADZU 2010 PLUSGC/MS. The spectral data of the synthesized compoundshave been provided below in section **3**.

2.Synthesis of various Diarylidenecyclohexanones

The diarylidenecyclohexanoneswere synthesized via the Claisen-Schmidt condensationreaction[1]. The procedure in brief: in a round bottom flask ethanol (50ml) and aqueous NaOH (10%, 50ml) were taken. A mixture of the corresponding aryl aldehyde (0.05 mol) and cyclohexanone (0.025 mol) was prepared separately and one half of the aldehyde-ketone mixture was added to the EtOH - aq. NaOH solution with continues stirring at room temperature. After 15 minutes, the remaining half of thealdehyde-ketone mixture was added to the round bottomed flask. The stirring of the

mixture was continuedtill the completion (checked by TLC).After completion, the contents of the round bottomed flask were filtered and then washed thoroughly with ice-cold water to remove any alkali present. The solid obtained thus was dried and wasrecrystallized.

3.Thespectral data of compounds:



3.1 ***Ia) 2,6-Bis(dibenzylidene)cyclohexanone:***

Yield:80 %.Light yellow solid. M.P:116.2^{0}C. ^{1}H NMR: δ 7.81 (H-9,s, 2H), δ 7.47 (H-6 and H-2, d, 4H, J=7.8Hz), δ 7.41 (H-5 and H-3,d, 4H, J=7.8Hz), δ 7.34 (H-4,t, 2H, J=7.8Hz), δ 2.94 (H-10**,** t, 4H, J=7Hz), and δ 1.79 (H-11,quintet, 2H, J=7Hz).^{13}C NMR**:** δ 190.40(C-7), δ 136.95(C-9),δ 136.18(C-8), δ 130.39 (C-6 and C-2), δ 128.60(C-4),δ 128.39(C-5 and C-3), δ 28.48 (C-10 ,2C), and δ 23.02 (C-11 ,1C). IR(KBr, cm^{-1}): 3059(Ar C-H stretch),2905(C-H stretch), 1660(),1606 (C=C stretch),1572,1554(Ar skeletal bands),1433 (C-H bend),716,694(mono-substituted phenyl ring).MS (*m/z*): 275[M + H]$^+$; UV: (MeOH): 330 nm.

3.2 ***Ib) 2,6-Bis(3-nitro-benzylidene)cyclohexanone:***

Yield: 8.6%.Yellow solid,Recrystalized with MeOH/$CHCl_3$. MP:188-190^{0}C. ^{1}H NMR: δ 8.31(H-2,s, 2H),δ 8.21 (H-4,d,2H ,J=8Hz) ,δ 7.80 (H-9**,**s, 2H), δ7.75(d, 2H,H-6, J=8Hz), δ7.61,(H-5, t, 2H, J=8Hz),δ 2.99 (H-10 **,**t, 4H,J=7Hz), and δ 1.86(H-11**,**m, 2H,J=7Hz). ^{13}C NMR**:**δ189.21(C=O),δ148.28(C-3,-NO_2), δ138.01(C-9), δ137.3(C-1),δ136.19(C-8),δ134.68(C-2),δ129.56(C-4),δ124.46(C-6), δ123.32(C-5), δ28.26(C-10), and δ22.57(C-11). IR(KBr, cm^{-1}):1664(), 1604 (C=C stretch), 1573(Ar C=C), 1521, 1325 (asymmetric and symmetric -NO_2 stretch), 808, 721, 678 (m-disubstituted benzene ring) 678, 621 (C-H oop).MS (*m/z*): 364[M]$^+$; UV: (MeOH): 224,313nm.

3.3 ***Ic) 2,6-Bis(2-chlorobenzylidene)cyclohexanone:***

Yield: 71%.Yellow flaky crystals . M.P:120-121^{0}C. ^{1}H NMR: δ 7.92 (H-9**,**s, 2H), δ 7.44(H-5,t, 2H, J=7.4Hz), δ 7.34 (H-6,d, 2H, J=7.4Hz), δ 7.28 (H-4 and H-3,multiplet, 4H)δ 2.80 (H-10 **,**t, 4H, J=6.4Hz), and δ 1.78(H-11**,**quintet, 2H, J=6.4Hz). ^{13}C NMR**:** δ 189.76(C=O), δ 137.73(C-8), δ 135.03 (C-2), δ 135.02(C-9) , δ 134.38(C-1),δ 130.52(C-4), δ 129.75 (C-6), δ 129.52(C-5) , δ 126.26(C-3) , δ 28.40 (C-10) , and δ 23.17 (C-11). IR(KBr, cm^{-1}): 3064(Ar C-H stretch), 2971 cm-

[1], 2941 cm^{-1}, 2917 cm^{-1} (sp^3 C-H stretch) 1663([redacted]),1601 (C=C stretch),1586,1575,1468(Ar C=C stretch), 1052 (C-Cl stretch),753(ortho di-substituted benzene ring). MS (*m/z*):342.9 $[M+H]^+$, 306.9 $[M - Cl]^+$, 270.9[M -2 Cl] $^+$; UV: (MeOH): 234,313nm.

3.4 ***Id) 2,6-Bis(3-chlorobenzylidene) cyclohexanone:***

Yield: 78%. Bright Yellow neddles . M.P:104-105^{0}C. ^{1}H NMR: , δ 7.71 (H-9**,**s, 2H), δ 7.43(H-2,s, 2H),δ 7.33 (H-4,H-5 and H-6,multiplet, 6H), δ 2.90 (H-10 **,**t, 4H, J=6.9Hz), and δ 1.81(H-11**,**quintet, 2H, J=6.9Hz). ^{13}C NMR**:** δ 189.74(C-7), δ 137.59(C-3), δ 137.02(C-8), δ 135.61(C-9) , δ 134.32(C-1), δ 129.90(C-2),δ 129.67(C-4), δ 128.62(C-5), δ 128.52 (C-6),δ 28.34 (C-10,2C) , and δ 22.76 (C-11 ,1C). IR(KBr, cm^{-1}): 3100(Ar C-H stretch), 2941 , 2866, 2842 (sp^3 C-H stretch) 1664([redacted]),1606 (C=C stretch),1579,1560,1473 (Ar C=C stretch) 1066 (C-Cl stretch)758(meta di-substituted benzene ring). MS (*m/z*):342.9 $[M+H]^+$, 308.9 $[M-Cl]^+$, 272 $[M-2Cl]^+$;UV: (MeOH): 234,323nm.

3.5 ***Ie) 2,6-Bis(4-chlorobenzylidene) cyclohexanone:***

Yield: 35.58%.Bright yellow solid ,Recrystalized with EtOH. M.P:144-146^{0}C. ^{1}H NMR: δ 7.63 (H-9**,**s, 2H), δ 7.29(H-2,H-6,d, 4H, J=7.4Hz), δ 7.27 (H-3,H-5 ,d, 4H, J=7.4Hz), δ 2.80 (H-10 **,**t, 4H, J=6.8Hz), and δ 1.72 (H-11**,**quintet, 2H, J=6.8Hz). ^{13}C NMR**:** δ 190.44(C-7), δ 137.15(C-4) , δ 136.36(C-9) , δ 135.22(C-1**),** δ 134.92(C-8), δ 132.15(C-3,C-5), δ 129.27 (C-2,C-6), 28.96 (C-10),and δ 23.11 (C-11) . IR(KBr, cm^{-1}):1666([redacted]), 1606 (C=C stretch),1575(Ar C=C stretch),1091 (C-Cl), 837 (P- disubstituted benzene ring) 707, 632 (C-H oop). MS (*m/z*):342.9 $[M+H]^+$, 308.9, $[M-Cl]^+$, 272 $[M-2Cl]^+$; UV: (MeOH): 349,240 nm.

3.6 ***If) 2,6-Bis-(4-methoxybenzylidene) cyclohexanone:***

Yield:22.96%.Yellow needles, Recrystalized with EtOH . M.P:160-162^{0}C. ^{1}H NMR: δ7.76(s, 2H,H-9), δ7.45(d, 4H, H-2,H-6, J=7.6Hz), δ6.93(d, 4H, H-3,H-5, J=7.6Hz),δ3.84(s,6H,-OCH_3), δ2.92(4H, t,H-10, J=6.5Hz),and δ1.81(H-11,quintet, 2H,J=6.5Hz).^{13}CNMR**:**δ190.81(C=O), δ160.52(C-4),δ137.1(C-9),δ134.96 (C8),δ132.82(C-2,C-6), δ129.37(C-1), δ114.50(C-3,C-5), δ59.93(–OCH_3), δ29.12(C-10),andδ23.64(C-11). IR(KBr, cm^{-1}):1658([redacted]), 1593 (C=C stretch), 1556, 1508(Ar C=C stretch), 1247 (Ar C-O stretch), 835(P- disubstituted benzene ring),663(C-H, oop). MS (*m/z*):335 $[M+H]^+$, 214 [M- H_3CO-C_6H_4-CH + H] $^+$; UV: (MeOH): 240,362nm.

3.7 ***Ig) 2, 6-Bis-(4-iso-propylbenzylidene) cyclohexanone:***

Yield: 26.50%.Yellow needles, Recrystalized with EtOH. M.P:142-144^{0}C. ^{1}H NMR: δ7.79(s,2H,H-9),δ7.42(d,4H,H-2,H-6,J=8Hz), δ7.27(d,4H,H-3,H-5,J=8Hz), δ2.94(m, 6H, H-10 and-C<u>H</u>-$(Me)_2$), and δ1.27(d, 12H,-CH–2C<u>H</u>$_3$,J=6Hz). ^{13}C NMR**:** δ 190.45(C=O), δ136.92(C-8),δ135.52 (C-9), δ133.62(C-3 and C-5),δ130.63(C-1), δ126.53(C-2 and C-6), δ34.05(C-4),δ28.57(C-10),δ23.87 (-<u>C</u>H-$(Me)_2$)andδ23.08(C-11). IR(KBr, cm^{-1}):1668([redacted]), 1610 (C=C stretch), 1566, 1583(Ar C=C

stretch) 970 (C-H bend), 825 (para di-substituted benzene ring), 731(C-H oop), 669. MS (*m/z*):359 $[M+H]^+$; UV: (MeOH):235, 339 nm.

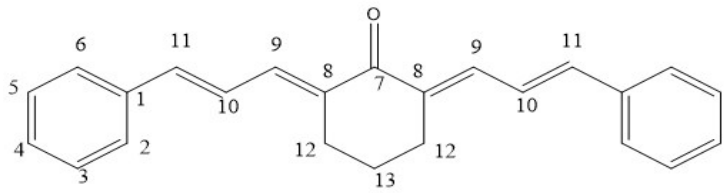
3.8 ***Ih) 2,6-bis((E)-4-(dimethylamino)benzylidene)cyclohexanone:***

Yield: 58%. Orange crystals. Recrystalized from MeOH. M.P:183-184.1^{0}C.^{1}H NMR:7.76(s, 2H, H-9), 7.45(d, 4H , J=8.8Hz, H-2, H-6), 6.72(d, 4H, J=8.8Hz, H-5, H-3), 3.02(s, 12H, -N$(CH_3)_2$), 2.93(t, 4H, J=5.6Hz, H-10), and 1.81(quintet, 2H, J=5.6Hz, H-11).^{13}C NMR**:**δ 190.03(C=O), 150.32(C-4), 136.98 (C-9), 132.39 (C-1), 132.38(C-2 and C-6), 124.26 (C-8), 111.62(C-3 and C-5), 40.12(C-NMe_2), 28.72(C-10) and 23.18 (C-11).IR(KBr, cm^{-1}):3010 (sp^3C-H stretch), 2922(asymmetric C-H), 1643(C=O), 1608(C=C stretch), 1577, 1518 (Ar skeletal bands), 1155 (sp^3 C-N stretch), 1355 (sp^2 C-N stretch), and 817(ArC-H(oop)). MS (*m/z*):362 $[M]^+$, 369; UV: (MeOH):282, 470nm

3.9 ***Ii) 2, 6-Bis(4-methylthiobenzylidene)cyclohexanone:***

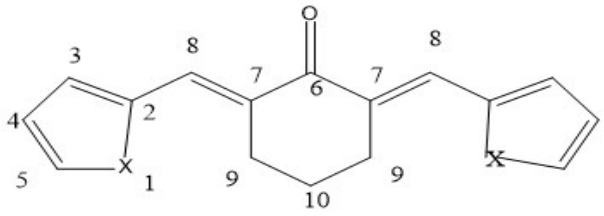
Yield: 46%. Yellow amorphous solid. Recrystalized from $CHCl_3$. M.P:183-184.1^{0}C.^{1}H NMR:δ7.74 (s, H-8), δ7.41 (d,4H, J= 8Hz, H-2,H-6), δ 7.25 (d, 4H, J= 8Hz, H-3, H-5), δ2.92 (t,4H, J= 6 Hz, H-11), δ 2.51 (s,6H,S-CH3), and δ1.04(quintet, 2H, J= 6Hz, H-12).^{13}C NMR**:**δ 190.023 (C=O), δ 139.89(2C, C-9), δ136.38(C-8), δ 135.49(2C, C-4**)**, δ 130.87 (4C, C-2, C-6), δ 132.465(2C, C-1), δ 125.65(4C, C-3, C-5), δ 22.89 (1C, C-12), δ 28.51 (2C, C-11), δ 15.09(2C, C-7).IR(KBr, cm^{-1}):3060(ArC-H stretch), 3050(olefinic C-H stretch), 2921 (SP^3C-H stretch), 1659 (C=O), 1586,1492($\upsilon_{Ar\ C=C}$), 1429(C-H bending), 817,96(ArC-Hoop). MS (*m/z*):367 $[M+H]^+$, 369 $[M+2+H]^+$,338$[M-C_2H_4]^+$, 338 $[M-C=O]^+$; UV: (MeOH):258, 376nm

3.10 ***Ij) 2, 6-Bis-(cinnamylidine) cyclohexanone:***



Yield: 96.5%.Orange-yellow solid, Recrystalized with MeOH . M.P:158-160^{0}C.^{1}H NMR:δ7.50(d,6H,H-9 , H-6 and H-2, J=7.2Hz),δ7.37(t, 2H,H-4, J=7.2Hz), δ7.36(t, 4H,H-5 and H-3, J=7.2Hz),δ 7.07(t,2H, H-10),δ 6.97(d,2H,J=15.6Hz, H-11), δ 2.8(t, 4H,H-12, J=7Hz), and δ1.8(quintet, 2H,H-13, J=7Hz). ^{13}C NMR**:** δ188.89(C=O),δ140.78(2C,C-9), δ136.34(2C,C-11), δ135.38(2C,C-8),δ129.19(C-4),δ128.85(2C,C-2 and C-6), δ128.80(2C and C-3,C-5) δ123.68(2C,C-10), δ26.64(2C,C-12), and δ22.07(C-13). IR(KBr, cm^{-1}): 3032 (Ar C-H stretch), 2935 (sp^3 C-H),

1652 ( ), 1610 (C=C stretch), 1581, 1552(Ar C=C stretch), 690,744(C-H, oop). MS: m/z: 327 $[M+H]^+$, 236$[M-C_3H_5-CH]^+$;UV: (MeOH): 272,388nm.



3.11 ***IIa) 2, 6-Bis-(2-furanylidene)cyclohexanone (X=O):***

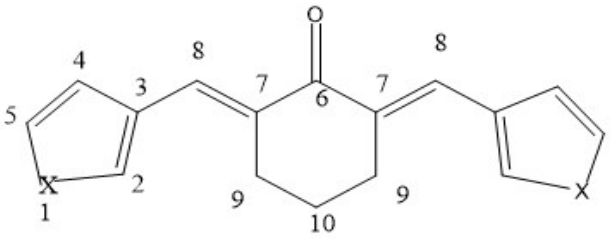
Yield: 31%. Yellow solid. Recrystalized with EtOH . M.P:138-140^{0}C. ^{1}H NMR: δ7.55(d, 2H, H-5, J=3.5Hz), δ7.54(s, 2H,H-8), δ6.65(d, 2H, H-3, J=3Hz), δ6.50(dd, 2H, H-4, J=3.5Hz,3.0Hz),δ3.0(t, 4H, H-9, J=6.5Hz), andδ1.88(quintet, 2H, H-10, J=6.5Hz).^{13}C NMR**:** δ189.06(C=O), δ152.79(C-2),δ144.54(C-5),δ133.03(C-7),δ123.38(C-8),δ116.10(C-3),δ112.34(C-4), δ27.99(C-9), and δ21.67(C-10). IR(KBr, cm^{-1}):1643( ), 1593 (C=C stretch),1546 (Ar C=C stretch), 1471 (CH_2 bend), 1281(C–O–Casymmetric), 750, 657,613 (C-H oop). MS (*m/z*):254$[M+H]^+$, 240$[M-CH]^+$, 226 $[M- 2CH_2]^+$, 212 $[M- 3CH_2]^+$; UV: (MeOH): 246,377nm.

3.12 ***IIb) 2,6-Bis-(2-pyrrolylidene) cyclohexanone (X=NH):***

Yield: 8.4%. Maroon flaky crystals. Recrystalized with EtOH . M.P:142-144^{0}C. ^{1}H NMR: δ10.45(d(br), 2H, H-1), δ7.70(s, 2H,H-8), δ6.91(dd, 2H, H-5, J=3.5Hz,2.5Hz), δ6.54(d, 2H, H-3, J=3.5Hz), δ6.24(m, 2H, H-4), δ2.77(t, 4H, H-9, J=6.5Hz), and δ1.82(quintet, 2H, H-10, J=6.5Hz).^{13}C NMR**:** δ189.1(C=O),δ130.6(C-2),δ129.6(C-8), δ126.3(C-7), δ121.58(C-5), δ117.73(C-3),δ110.4(C-4), δ28.42(C-9),and δ22.9(C-10). IR(KBr, cm^{-1}): 3469 (N-H stretch), 1643( ),1591 (C=C stretch),1492(Ar C=C stretch), 742 , 663,619 (C-H oop). MS (*m/z*):253$[M+H]^+$; UV: (MeOH): 250,418,436 nm.

3.13 ***IIc) 2,6-Bis-(2-thienylidene) cyclohexanone(X=S):***

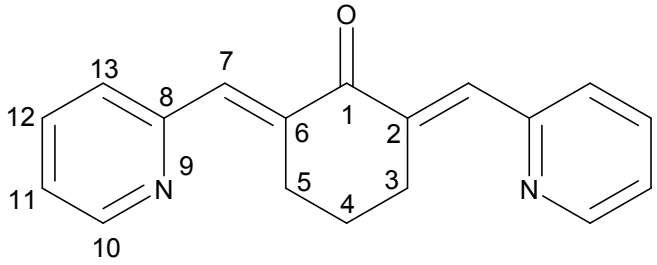
Yield: 88.57%. Yellow solid. Recrystalized with EtOH . M.P:149-152^{0}C. ^{1}H NMR:δ7.98(s, 2H,H-8), δ7.54(d, 2H, H-5, J=5.0Hz), δ7.38(d, 2H, H-3, J=3.5Hz), δ7.15(dd, 2H, H-4, J=5.0Hz, J=3.5Hz), δ2.98(t, 4H, H-9, J=6.5Hz), and δ1.87(quintet, 2H, H-10, J=6.5Hz).^{13}C NMR**:** δ190.60(C=O),δ138.31(C-8), δ135.2(C-2), δ131.07(C-7), δ130.01(C-5), δ128.62(C-3),δ126.23(C-4), δ29.04(C-9), andδ22.34(C-10). IR(KBr, cm^{-1}): 1649( ), 1587 (C=C stretch), 1548(Ar C=C stretch), 730, 633(C-H, oop), 617. MS (*m/z*):287 $[M+H]^+$, 288$[M+2]^+$ (sulphur),259, 175 and 123; UV: (MeOH): 255,374 nm.



3.14 ***IIIa) 2,6-Bis-(3-thienylidene) cyclohexanone(X=S):***

Yield: 10%. Brownish yellow solid. Recrystalized with EtOH . M.P:142-144^{0}C. ^{1}H NMR:δ7.76(s, 2H,H-8), δ7.51(d, 2H, H-2,J=2.5Hz), δ7.36(dd, 2H, H-5,J=5Hz,2.5Hz), δ7.29(dd, 2H, H-4, J=5Hz,1.5Hz),δ2.98(t, 4H, H-9,J=6.5Hz), andδ1.87(quintet, 2H, H-10 , J=6.5Hz).^{13}C NMR**:** δ190.60(C=O),δ138.31(C-8), δ135.2(C-3),δ131.07(C-7),δ130.01(C-2), δ128.62(C-5), δ126.23(C-4), δ29.04(C-9), andδ22.34(C-10). IR(KBr, cm^{-1}):1662( ), 1604 (C=C stretch), 1570, 1508 (Ar C=C stretch), 991, 856(C-H oop), 788, 732 . MS (*m/z*):287 [M+H] $^+$, 288 [M +2] , 259, 175 and 123; UV: (MeOH): 312,345 nm.

3.15 ***IVa) 2,6-Bis(pyridin-2-ylmethylene)cyclohexan-1-one:***



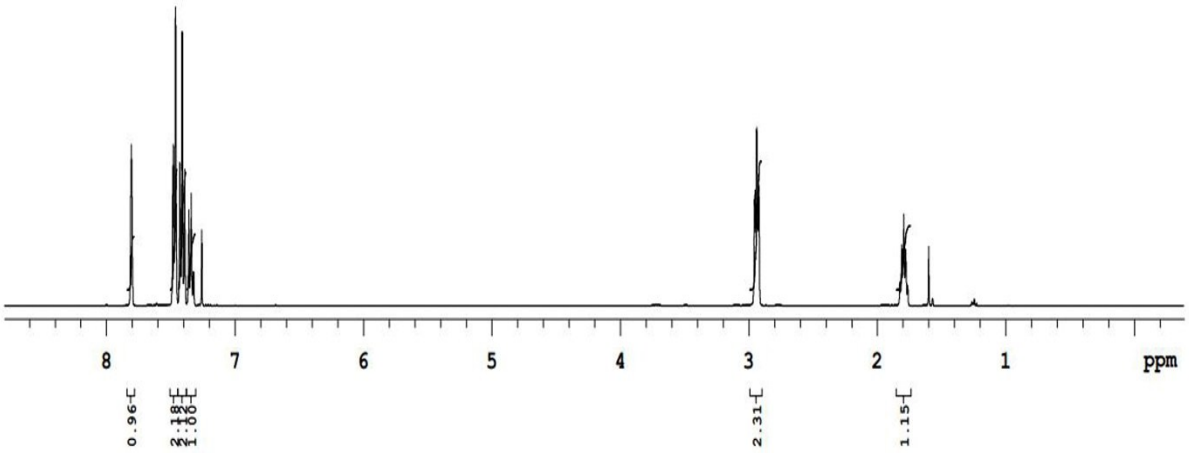
Yield: 60%. Pale white solid. Recrystalized with $CHCl_3$-MeOH. ^{1}H NMR:δ8.70 (d, 2H, H-10, J=4.4 Hz), δ7.71 (t, 2H, H-12, J=7.6Hz), δ7.69 (s, 2H, H-7), δ7.44(d, 2H, H-13, J=7.6),7.11(m, 2H, H-11), δ3.31(t, 4H, H-3 and H -5, J=6.4Hz), andδ1.28(quintet, 2H, H-4, J=6.4Hz).^{13}C NMR**:** δ191.39(C=O), δ155.52 (C-8), δ149.52 (C-10),δ140.11 (C-2 and C-6),δ136.14 (C-12), δ134.02 (C-7), δ127.13 (C-13), 122.46 (C-11), δ28.47 (C-3 and C-5), andδ22.24 (C-4). IR(KBr, cm^{-1}):1705( ), 1604 (C=C stretch), 1583, 1465, 1437 (ring stretching bands in pyridine), 991, 856(C-H oop). MS (*m/z*):276 [M] $^+$; UV: (MeOH): 265, 364 nm.

(^{1}H and ^{13}C NMR spectra of these compounds are provided at the end of this document)

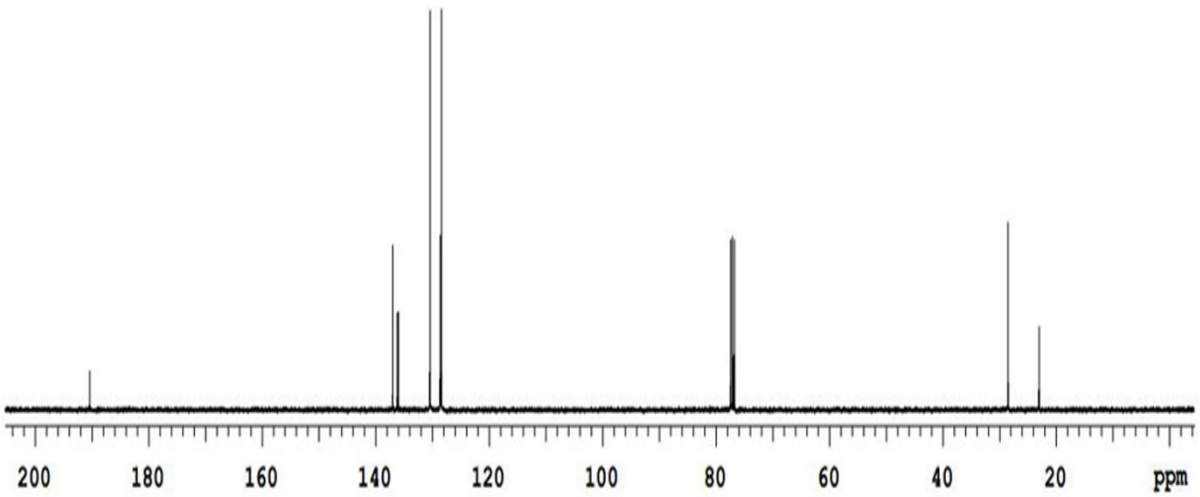
4.References:

1) A.I. Vogel, B.S. Furniss, Vogel's Textbook of Practical Organic Chemistry, 5thedn., Longman, Harlow, 1996

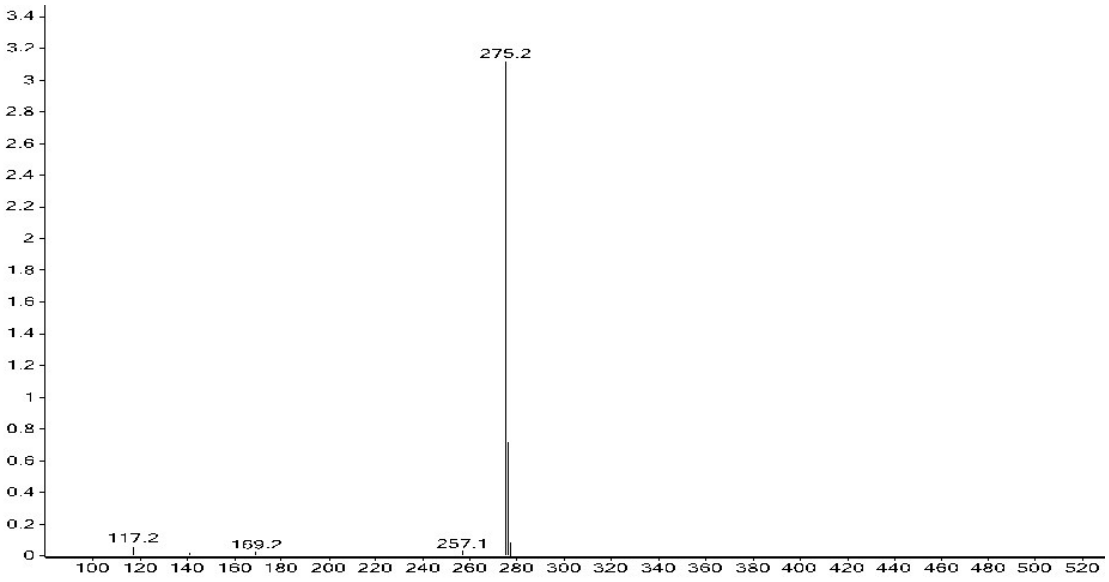
PMR spectrum of2, 6-(Dibenzylidene)cyclohexanone(Ia):



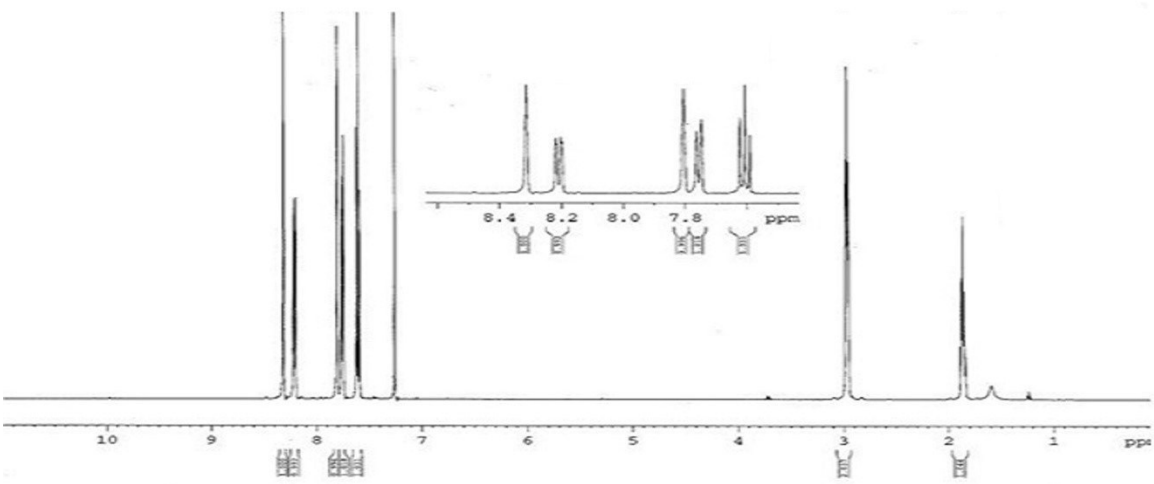
^{13}C NMR spectrum of 2,6-(Dibenzylidene)cyclohexanone (Ia):



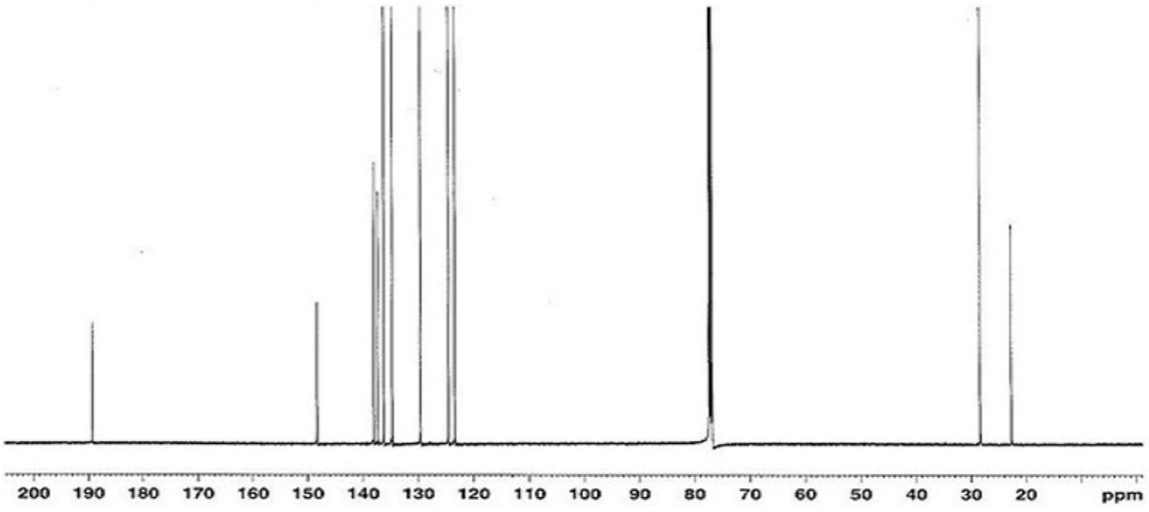
Mass spectrum of2, 6-(Dibenzylidene)cyclohexanone(I a):



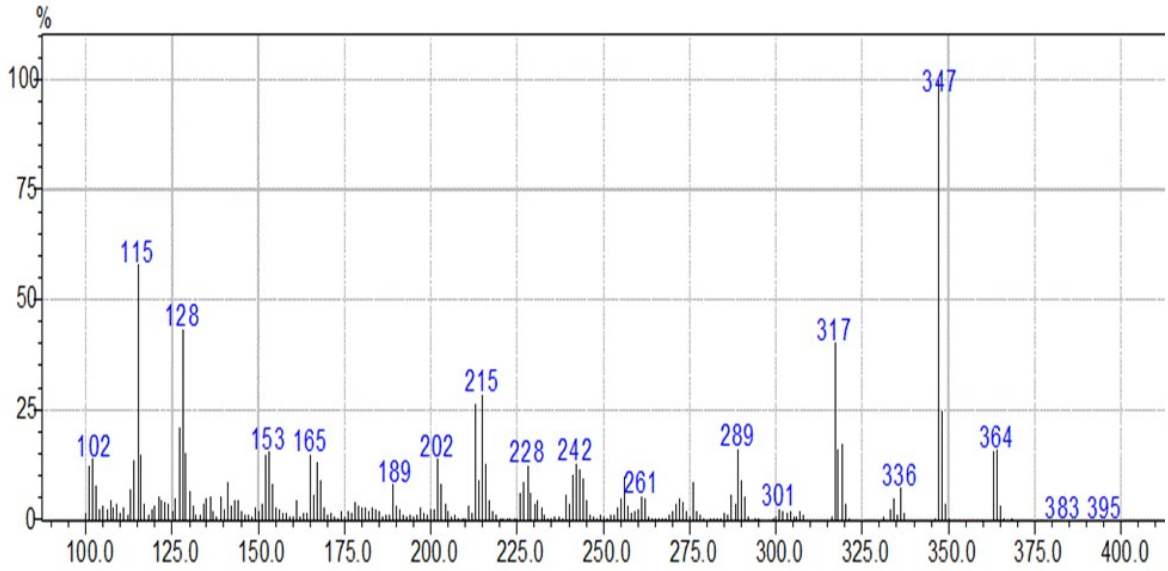
PMR spectrum of 2,6-Bis(3-nitro-benzylidene)cyclohexanone (Ib):



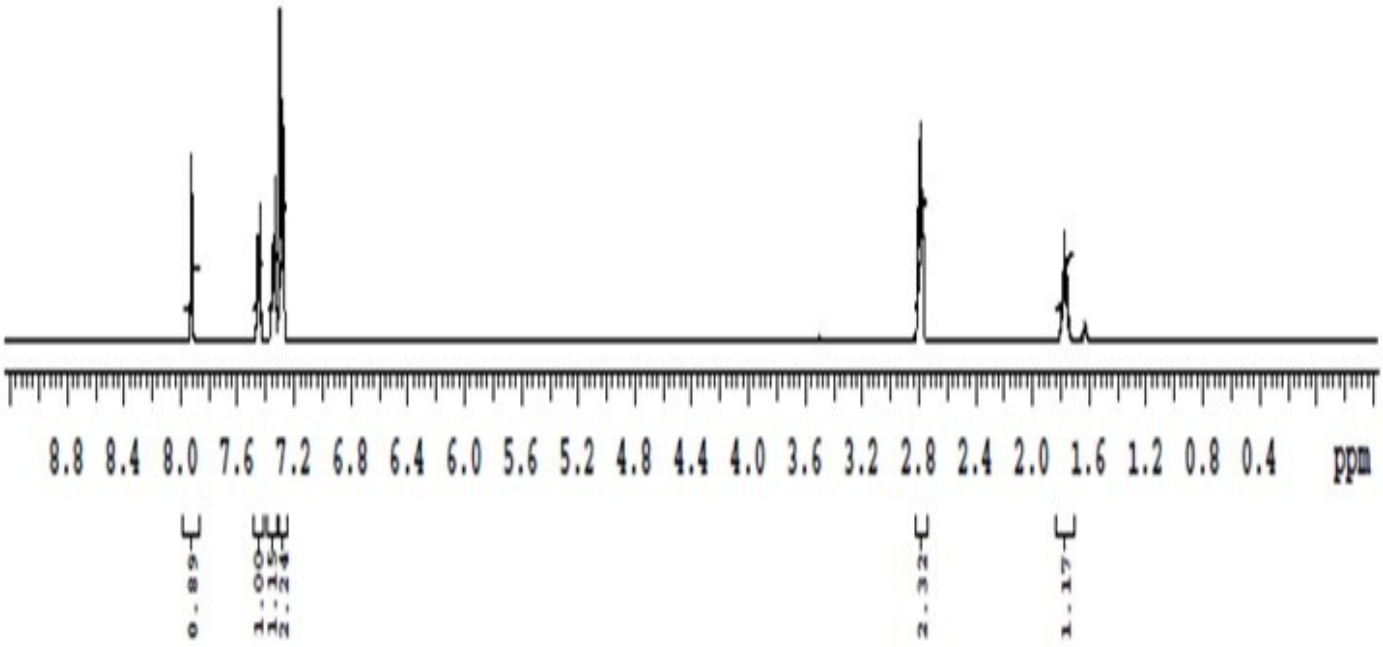
^{13}C NMR spectrum of 2,6-Bis(2-hydroxybenzylidene)cyclohexanone(Ib):



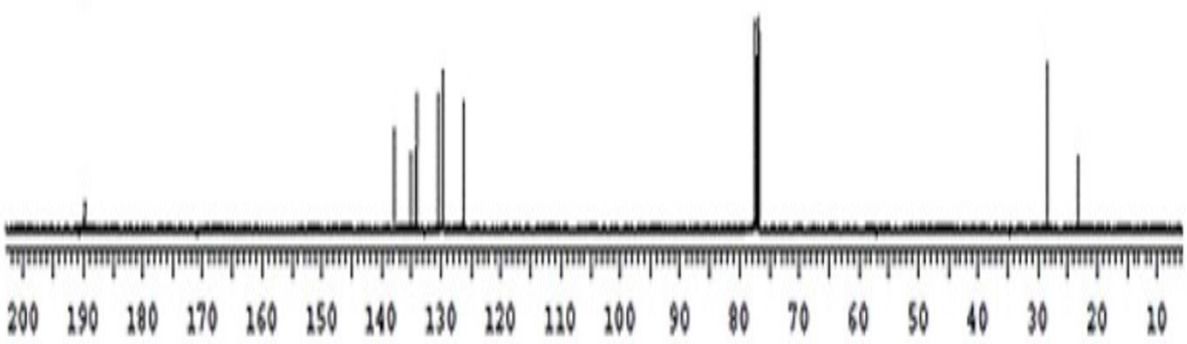
Mass spectrum of 2,6-Bis(3-nitro-benzylidene)cyclohexanone (I b):



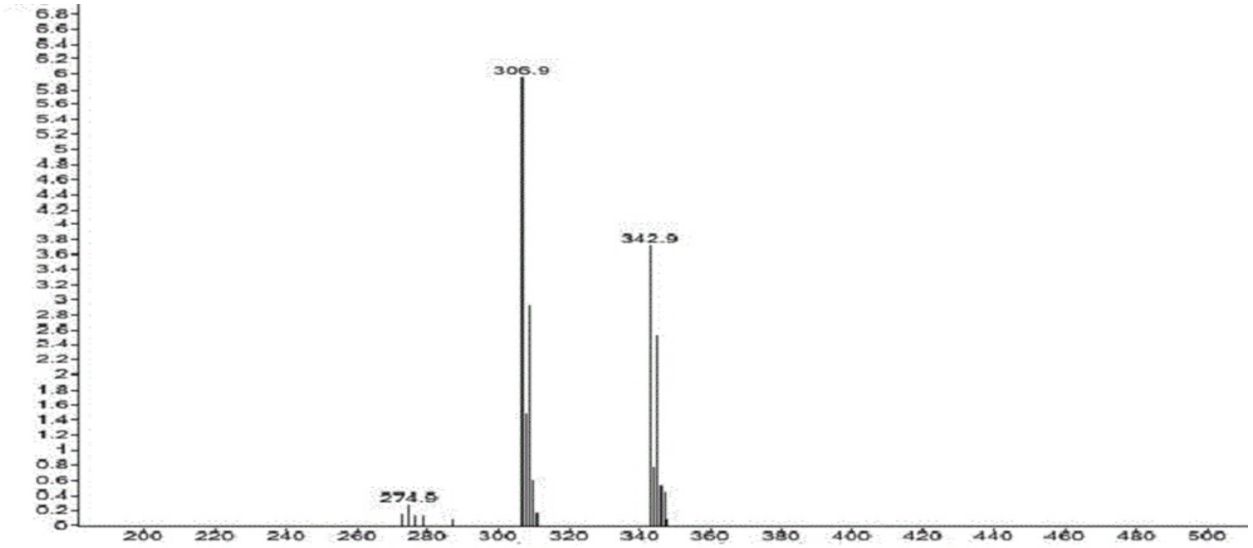
PMR spectrumof2,6-Bis(2-chlorobenzylidene)cyclohexanone(Ic):



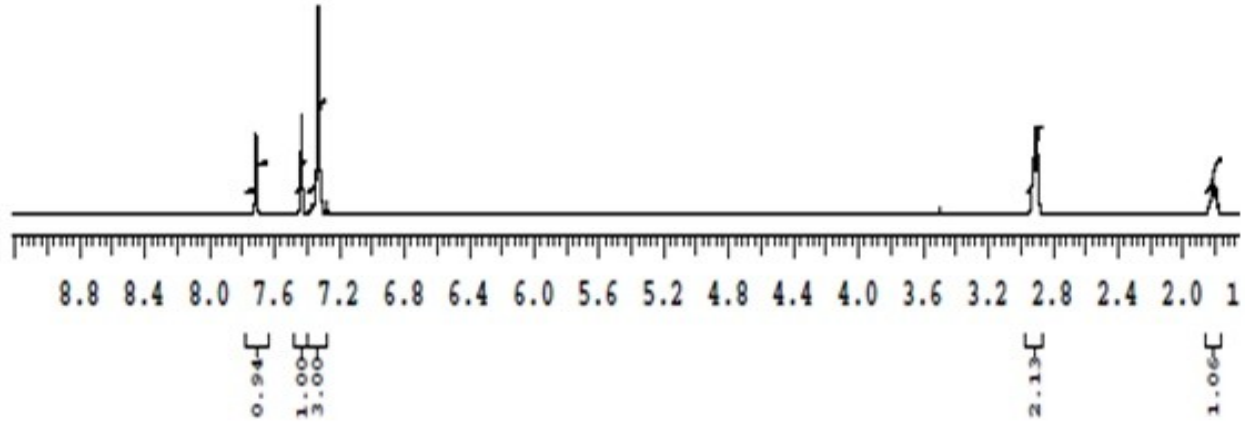
^{13}CNMR spectrumof2,6-Bis(2-chlorobenzylidene)cyclohexanone(Ic):



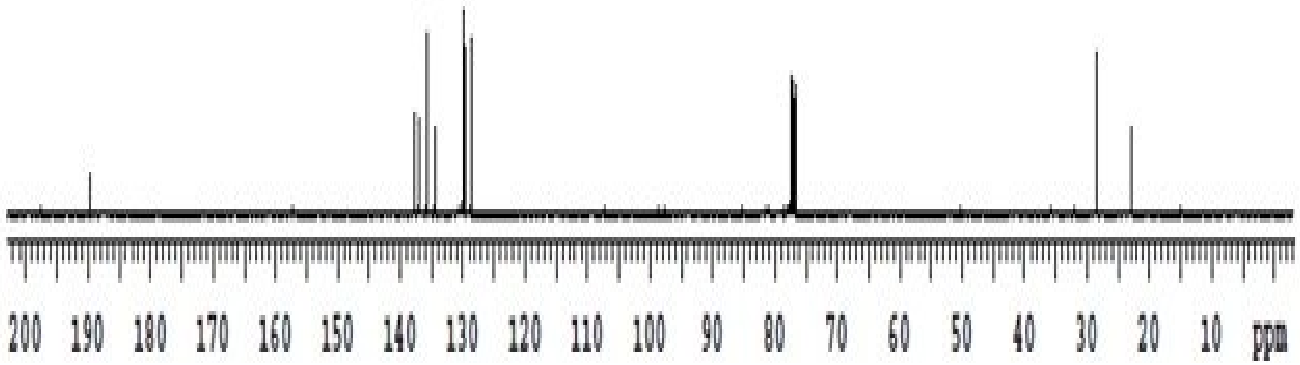
Mass spectrumof2,6-Bis(2-chlorobenzylidene)cyclohexanone(I c):



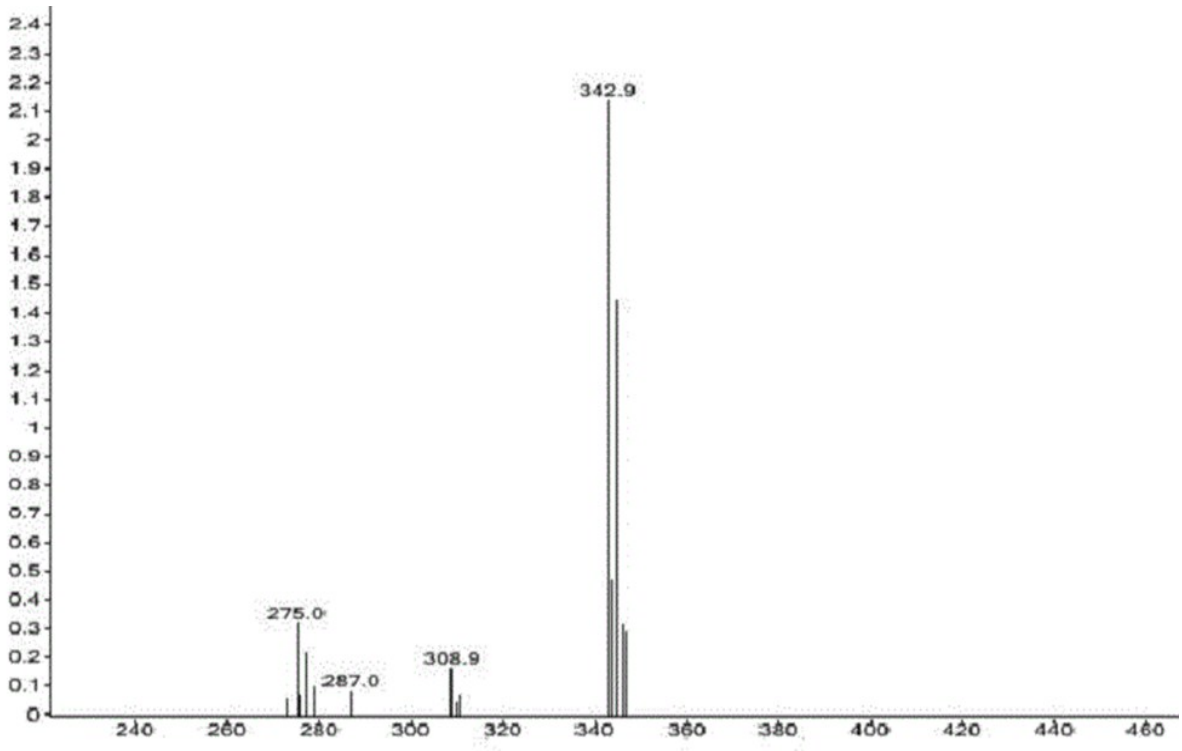
PMR spectrum of 2,6-Bis(3-chlorobenzylidene)cyclohexanone (Id):



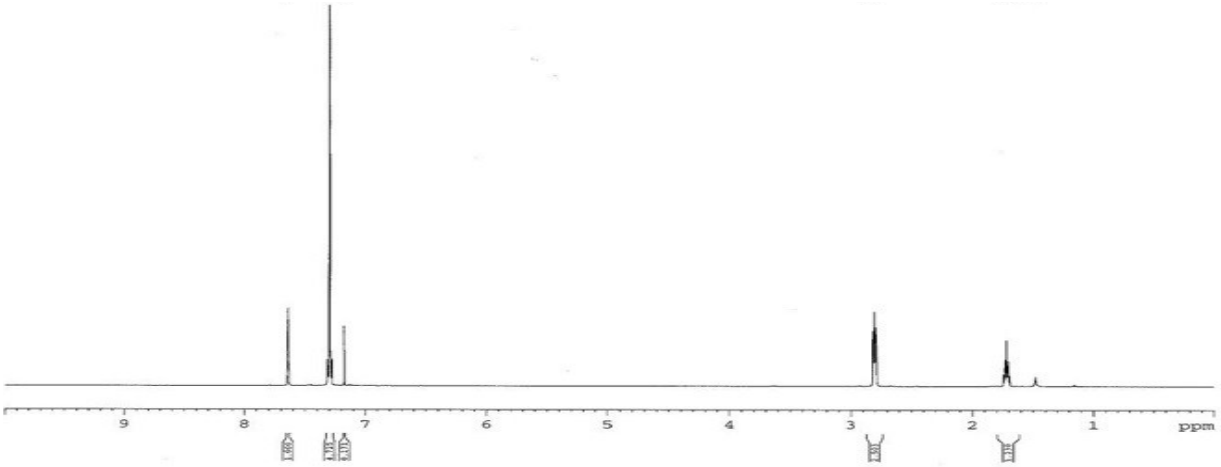
^{13}CNMR spectrum of 2,6-Bis(3-chlorobenzylidene)cyclohexanone (Id):



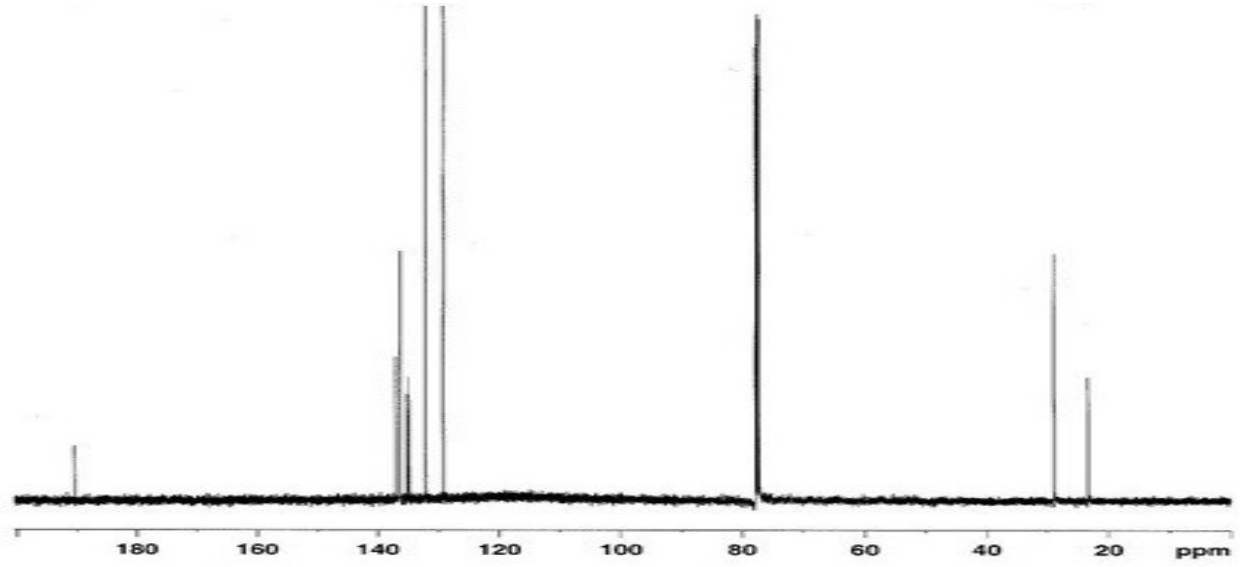
Mass spectrum of 2,6-Bis(3-chlorobenzylidene)cyclohexanone (I d):



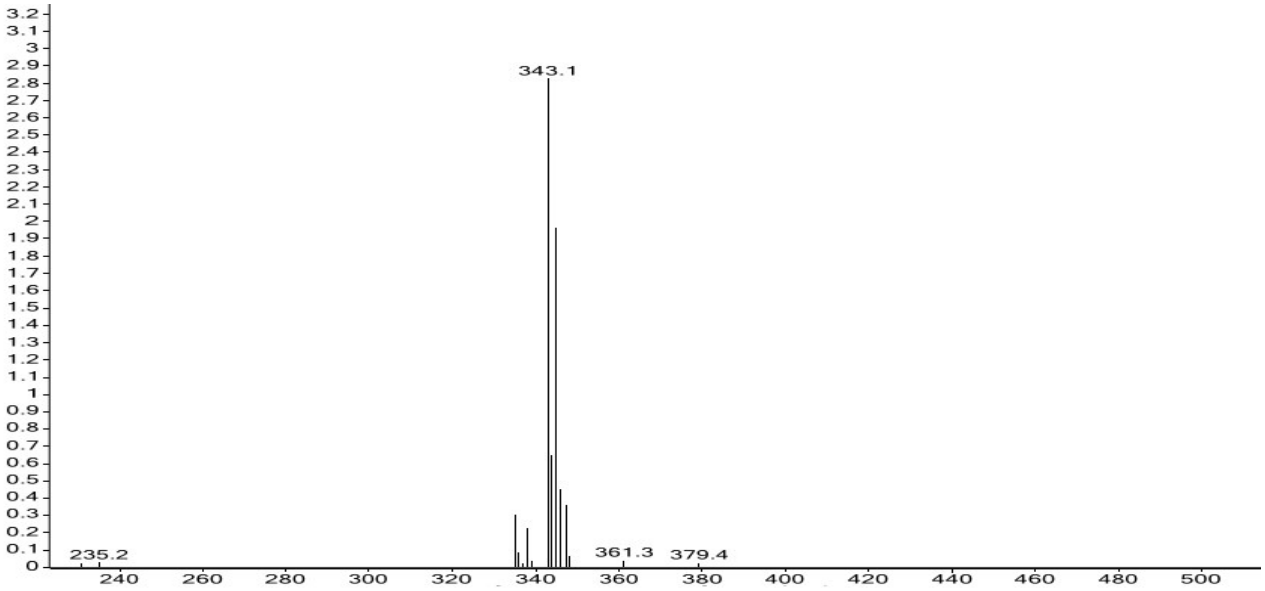
PMRspectrum of 2,6-Bis(4-chlorobenzylidene) cyclohexanone(Ie):



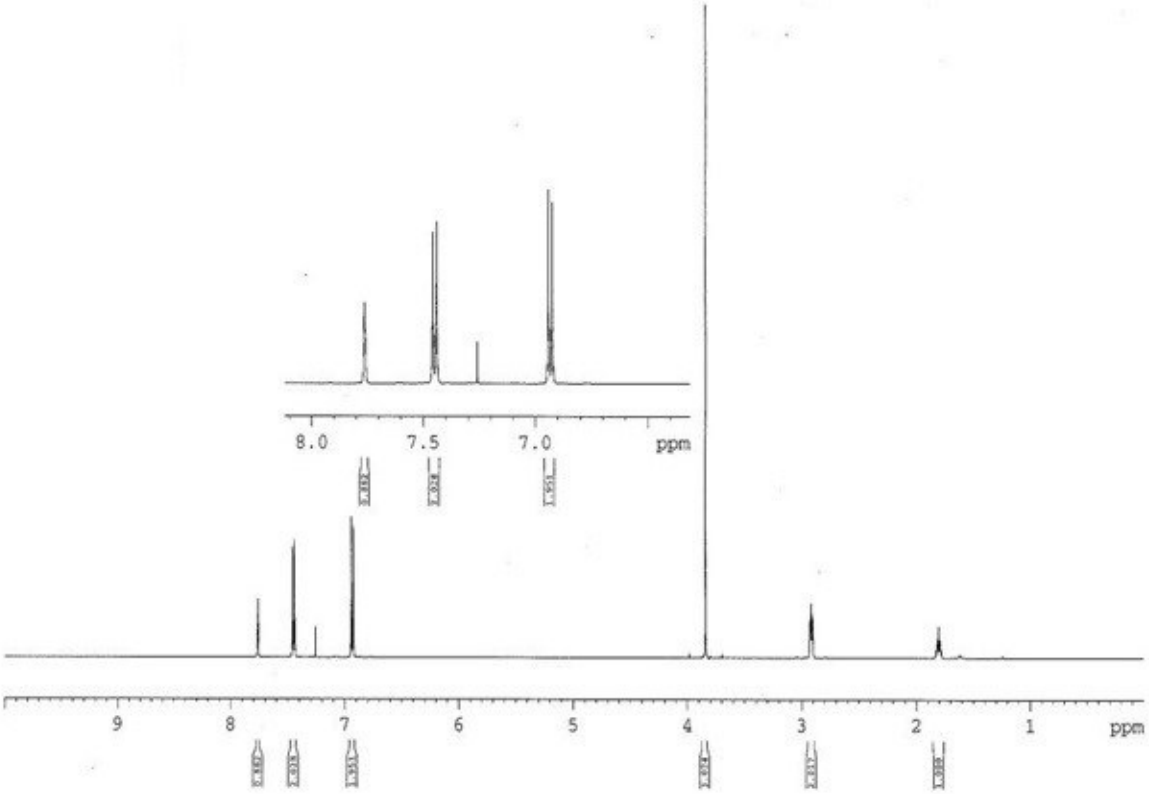
^{13}CNMRspectrum of 2,6-Bis(4-chlorobenzylidene) cyclohexanone(Ie):



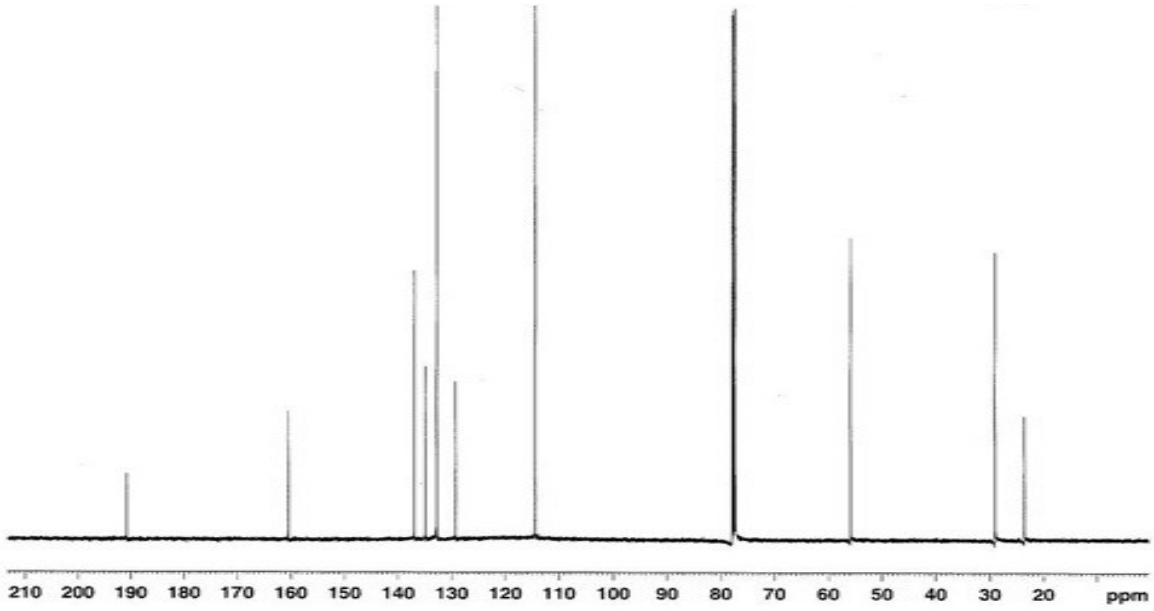
Mass spectrum of 2,6-Bis(4-chlorobenzylidene) cyclohexanone(I e):



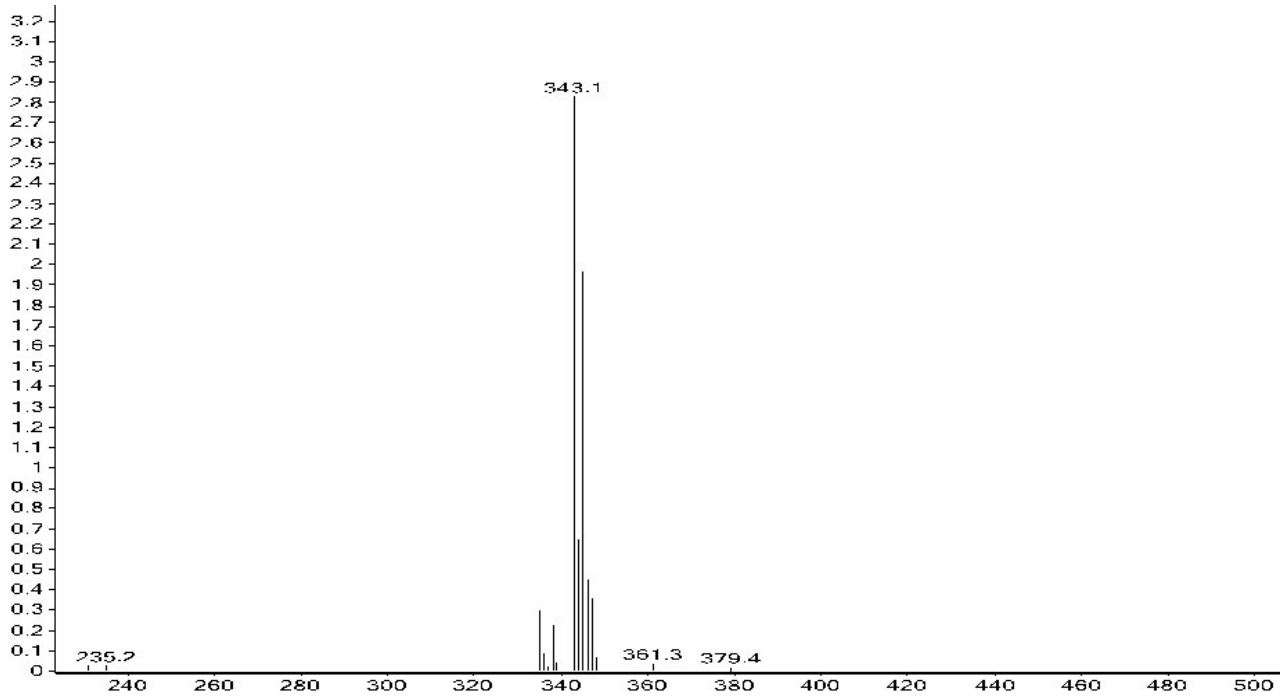
PMR spectrum of 2,6-Bis-(4-methoxybenzylidene) cyclohexanone (If):



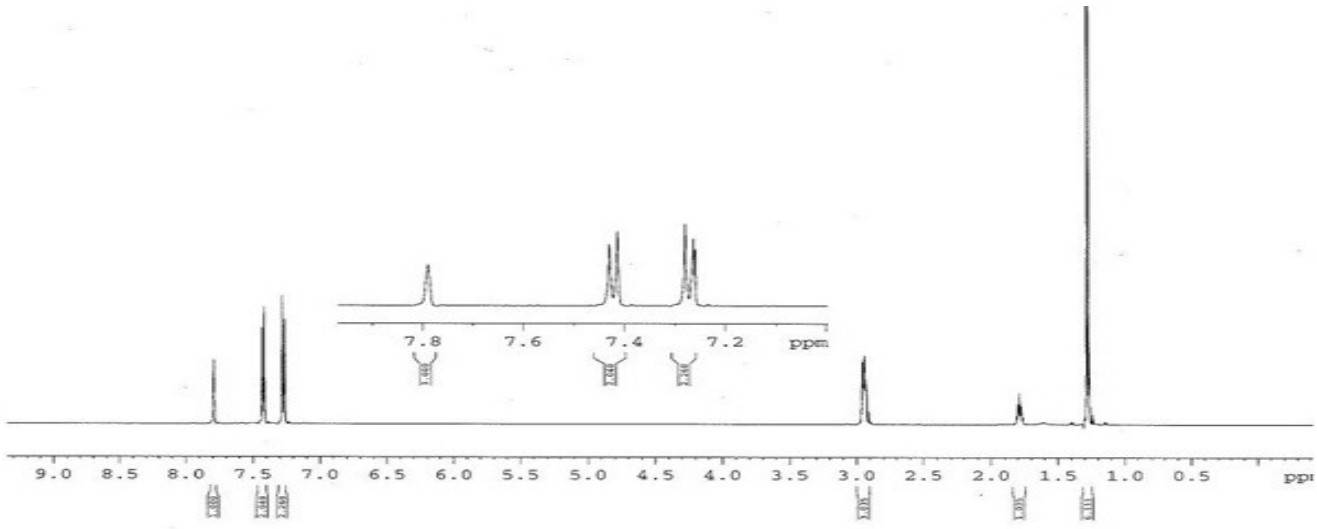
^{13}CNMRspectrum of 2,6-Bis-(4-methoxybenzylidene) cyclohexanone (If):



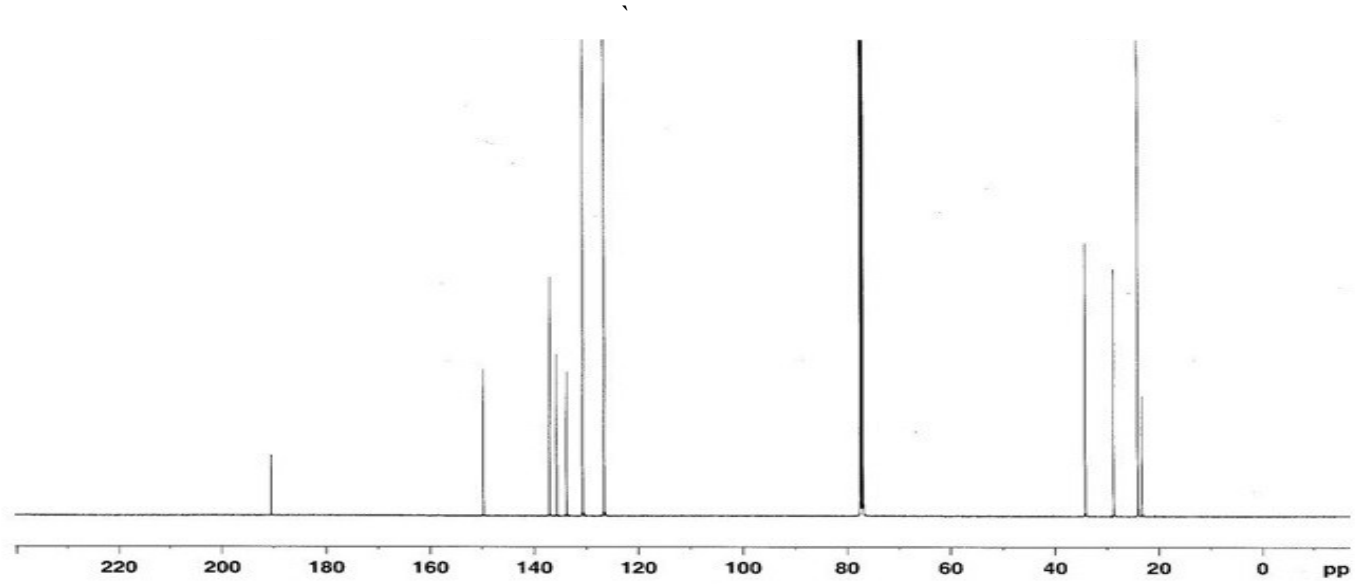
Mass spectrum of 2,6-Bis-(4-methoxybenzylidene) cyclohexanone (I f):



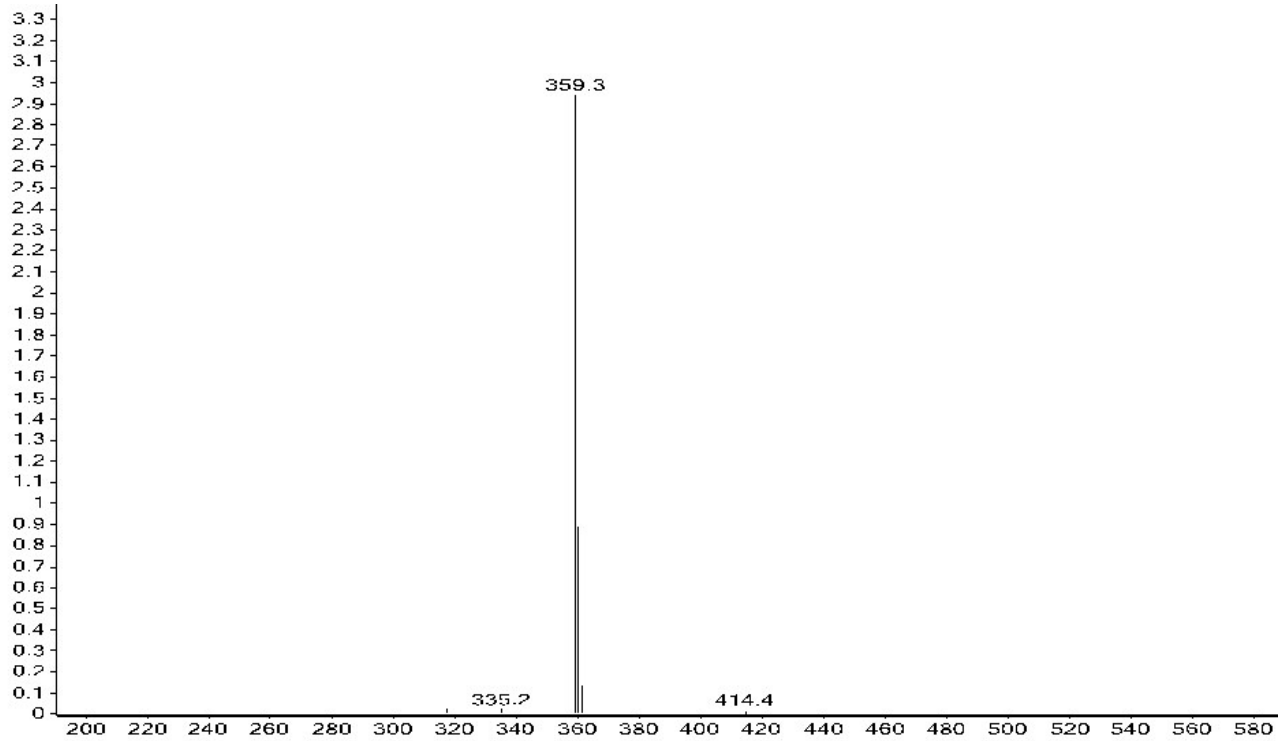
PMR 2, 6-Bis-(4-iso-propylbenzylidene) cyclohexanone (Ig):



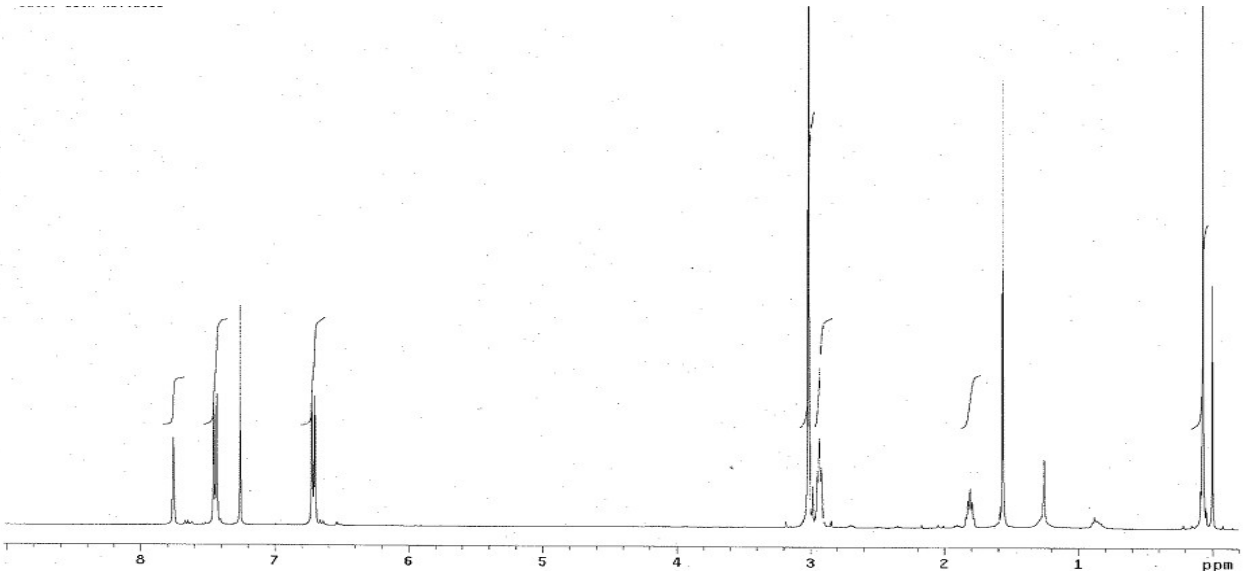
^{13}CNMR2, 6-Bis-(4-iso-propylbenzylidene) cyclohexanone (Ig):



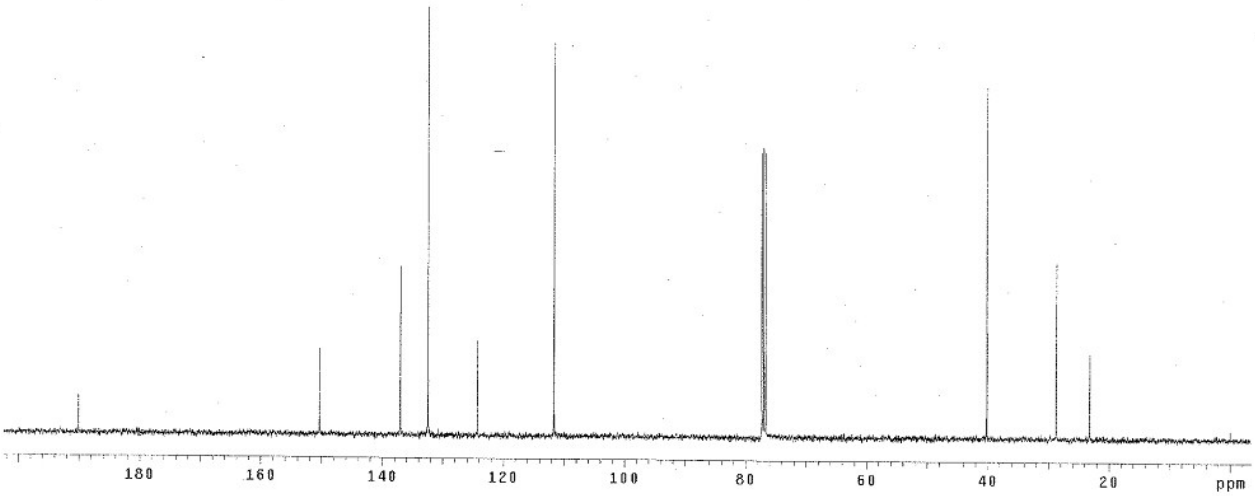
Mass spectrum2, 6-Bis-(4-iso-propylbenzylidene) cyclohexanone (I g):



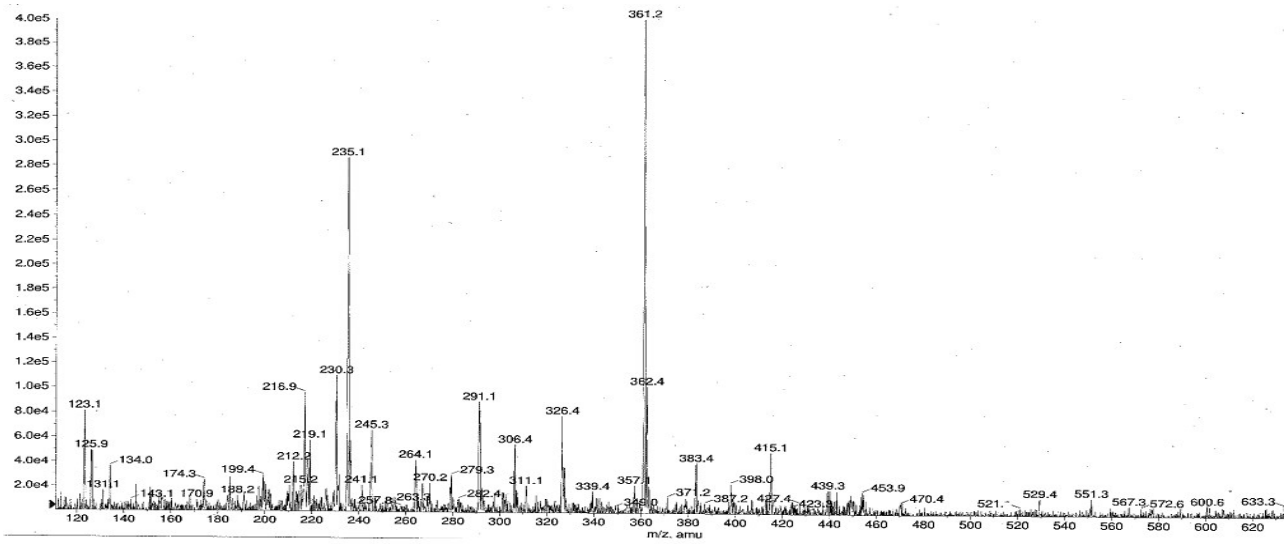
PMR2,6-bis((E)-4-(dimethylamino)benzylidene)cyclohexanone (Ih)



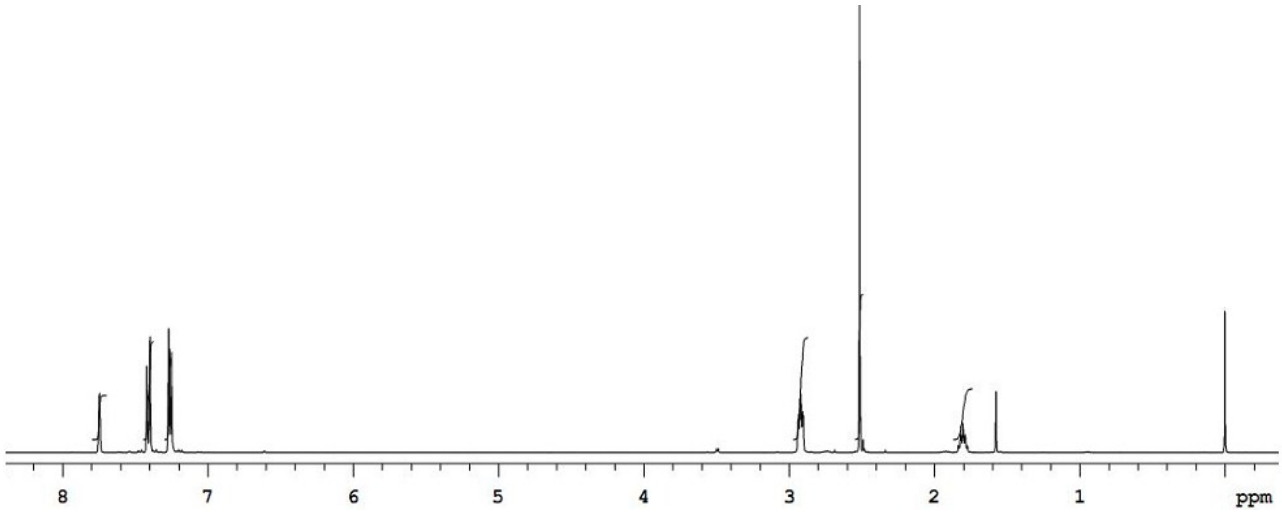
^{13}C NMR2,6-bis((E)-4-(dimethylamino)benzylidene)cyclohexanone (Ih)



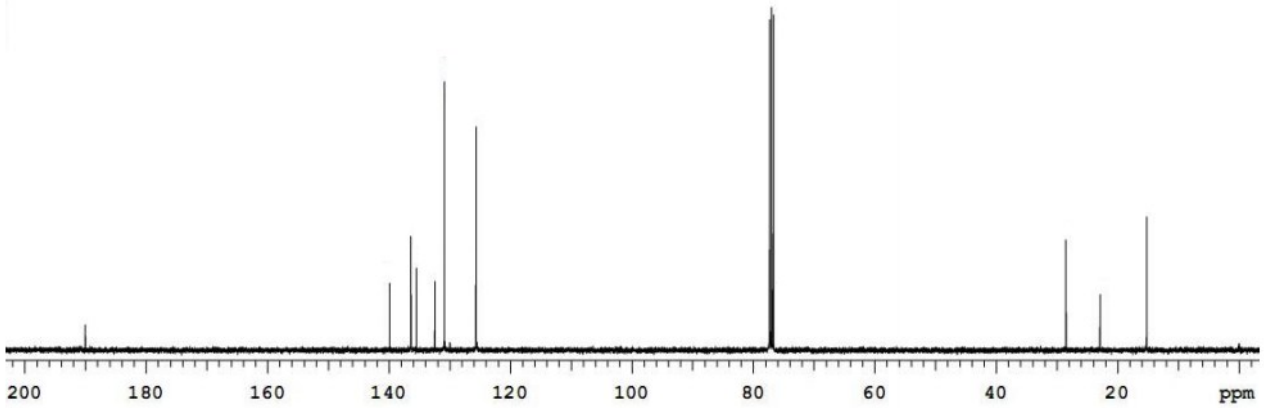
Mass spectrum of2,6-bis((E)-4-(dimethylamino)benzylidene)cyclohexanone (Ih)



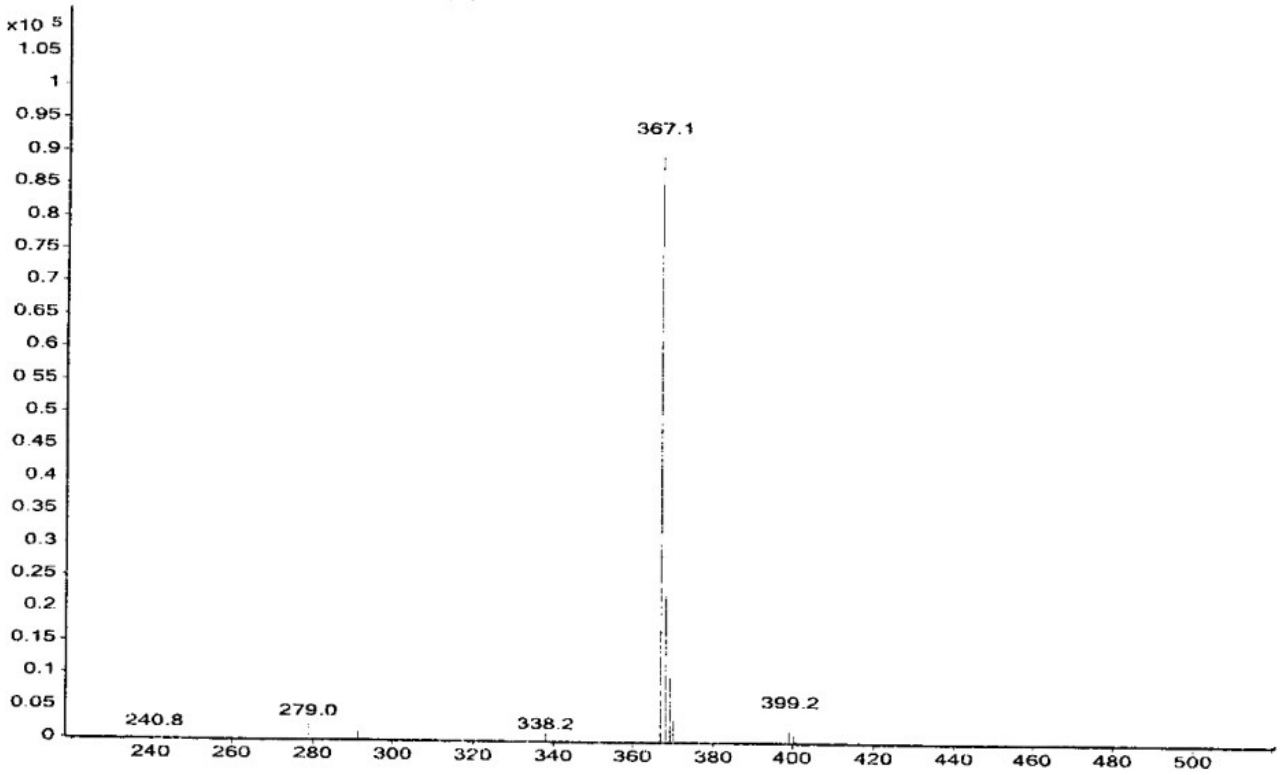
PMR2, 6-Bis(4-methylthiobenzylidene)cyclohexanone (Ii)



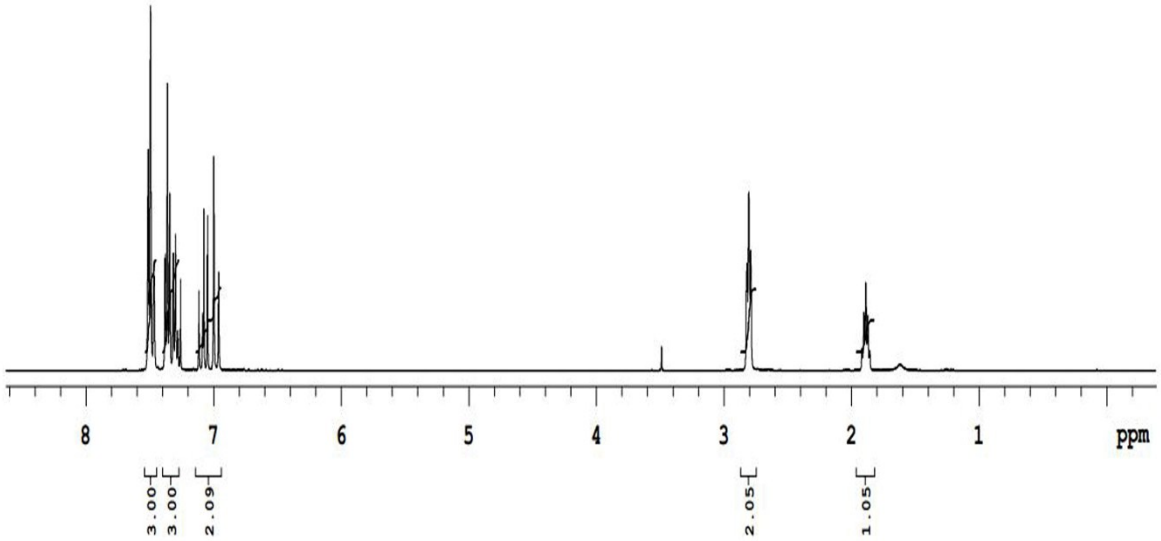
^{13}C NMR2, 6-Bis(4-methylthiobenzylidene)cyclohexanone (Ii)



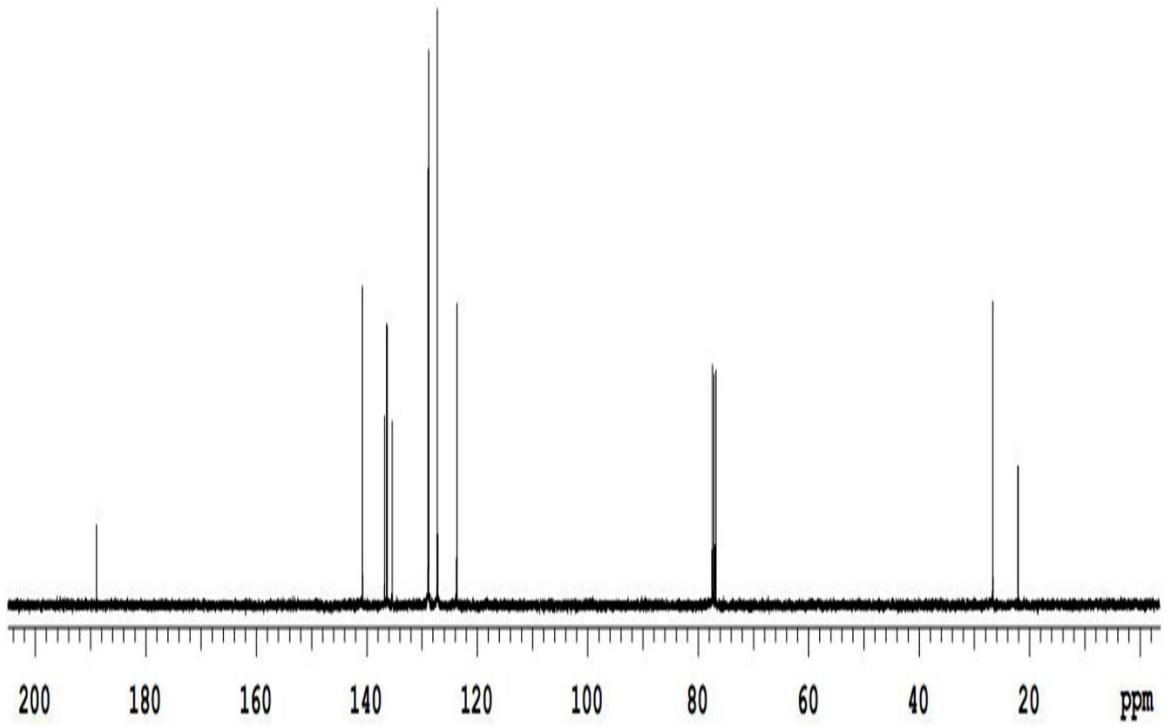
Mass spectrum of2, 6-Bis(4-methylthiobenzylidene)cyclohexanone (Ii)



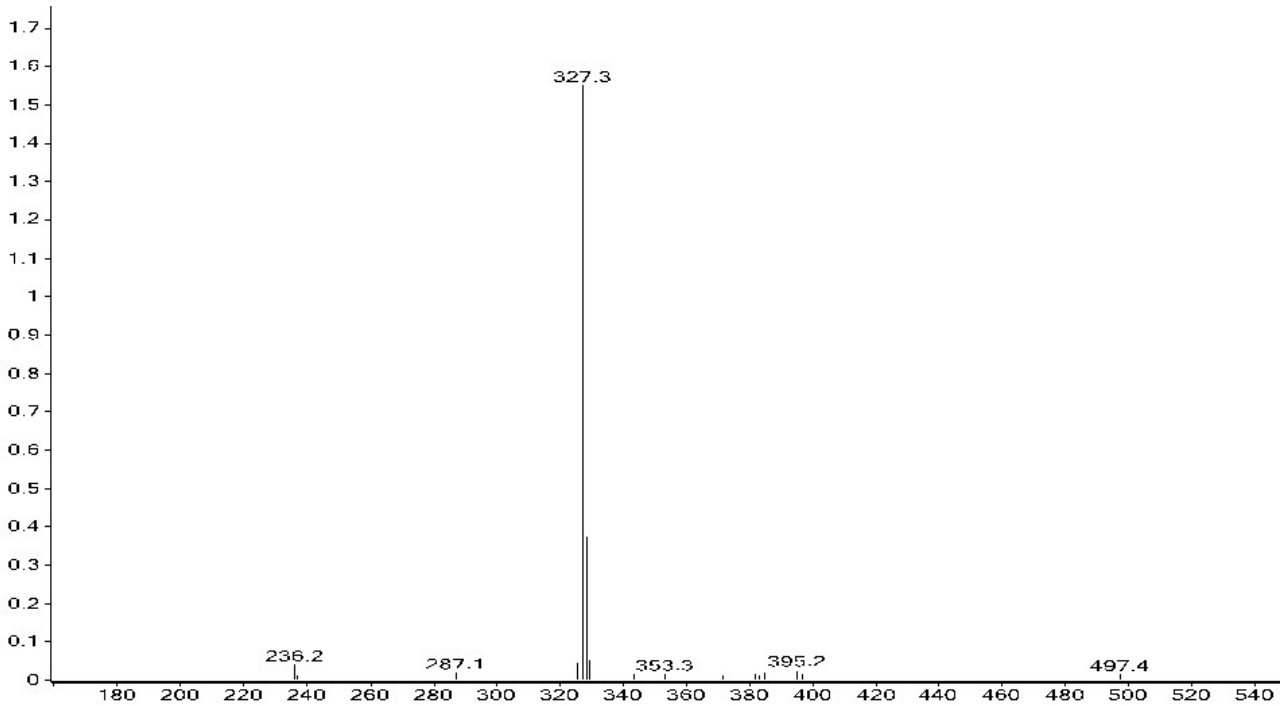
PMRspectrum of 2, 6-Bis-(cinnamylidine) cyclohexanone (Ij):



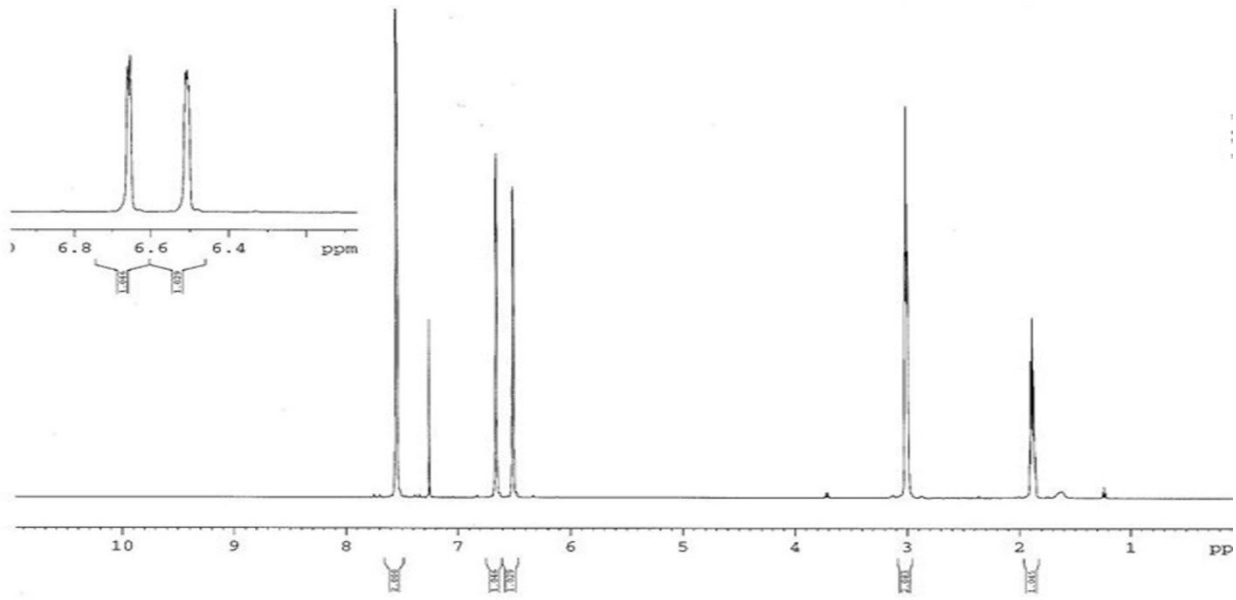
^{13}CNMR spectrum of 2, 6-Bis-(cinnamylidine) cyclohexanone (Ij):



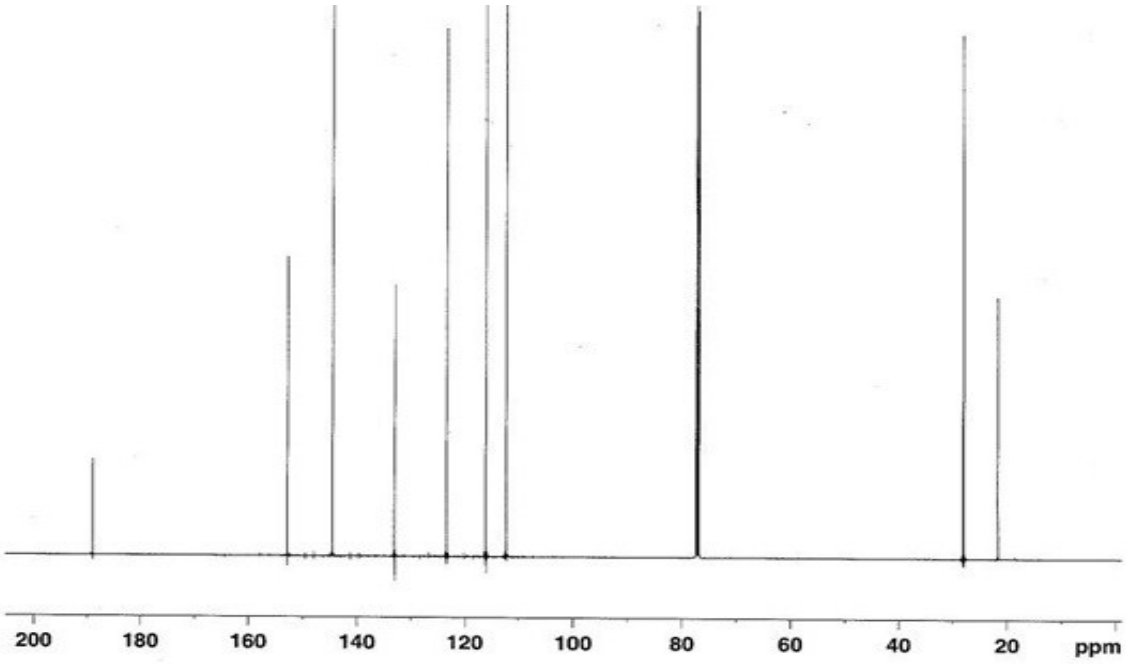
Mass spectrum of 2, 6-Bis-(cinnamylidine) cyclohexanone (Ij):



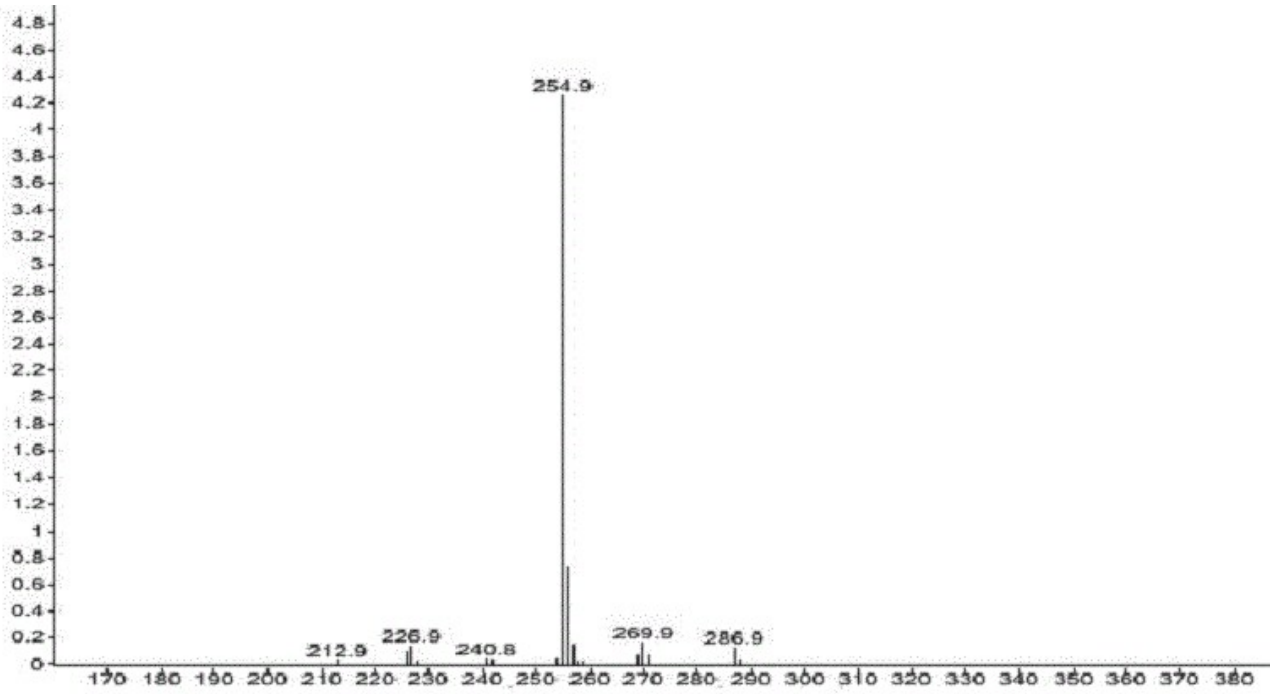
PMR spectrum of 2, 6-Bis-(2-furanylidene) cyclohexanone (IIa):



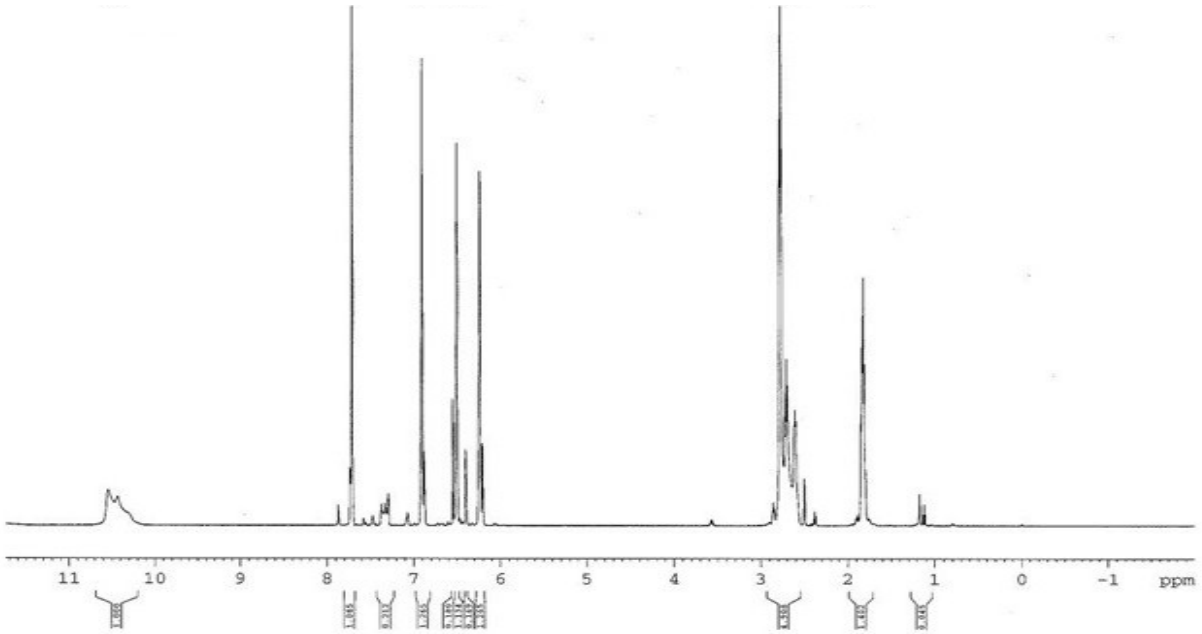
^{13} CNMRspectrum of 2, 6-Bis-(2-furanylidene) cyclohexanone (IIa):



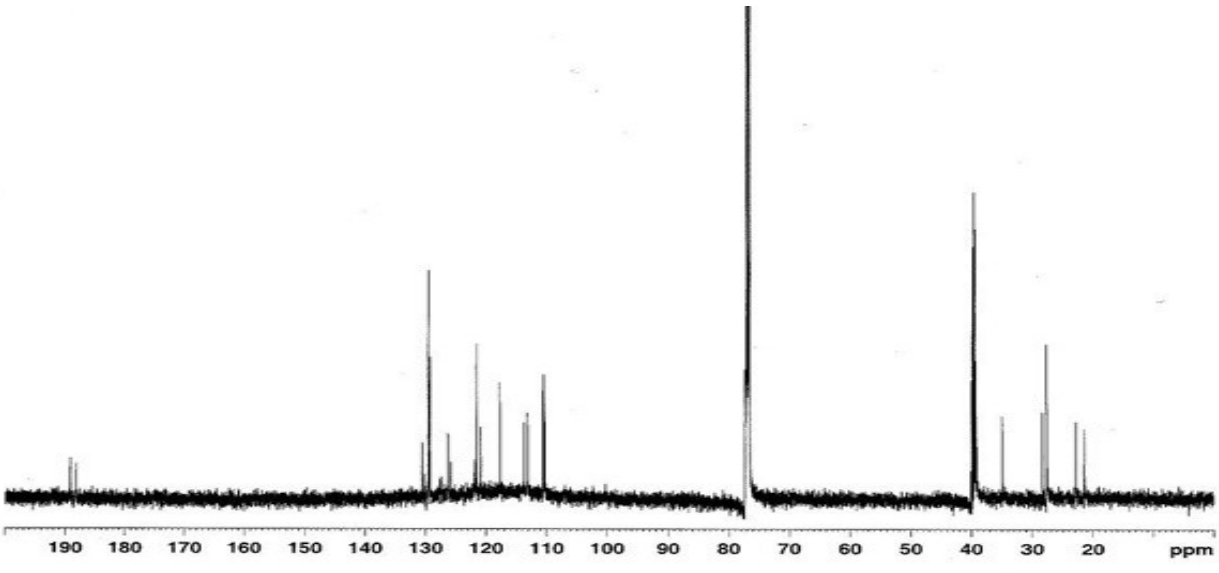
Mass spectrum of 2, 6-Bis-(2-furanylidene) cyclohexanone (II a):



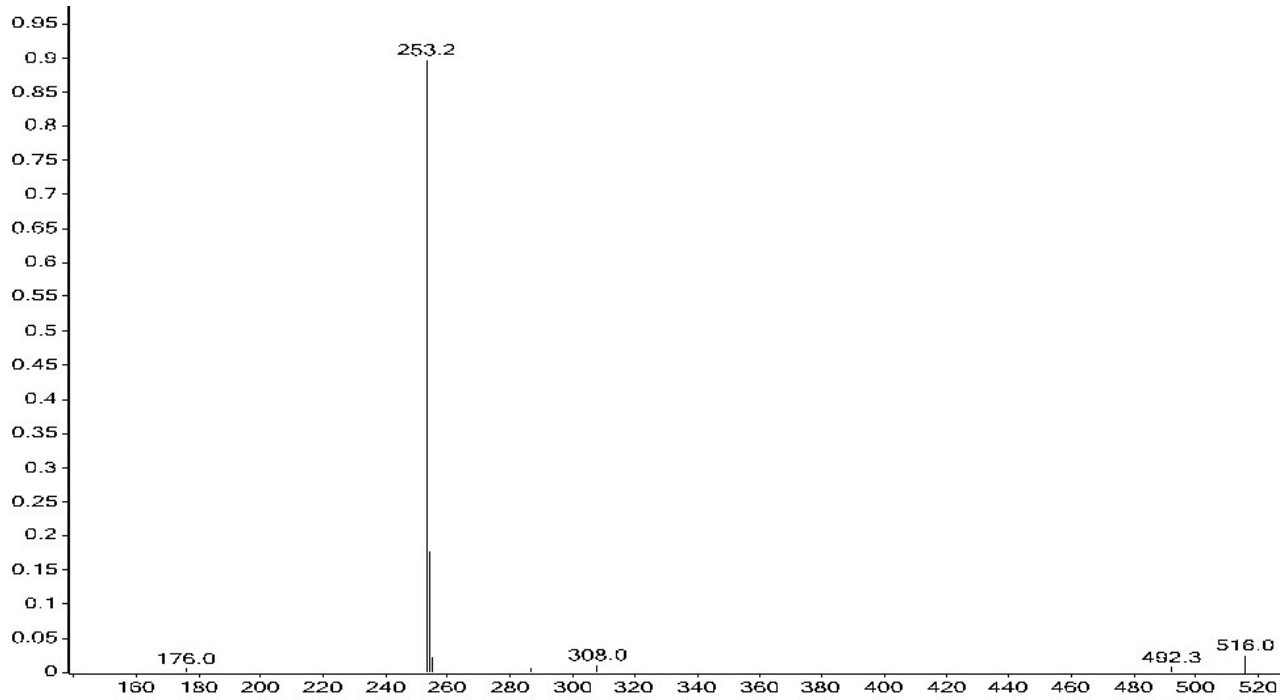
PMR spectrum of 2,6-Bis-(2-pyrrolylidene) cyclohexanone (IIb):



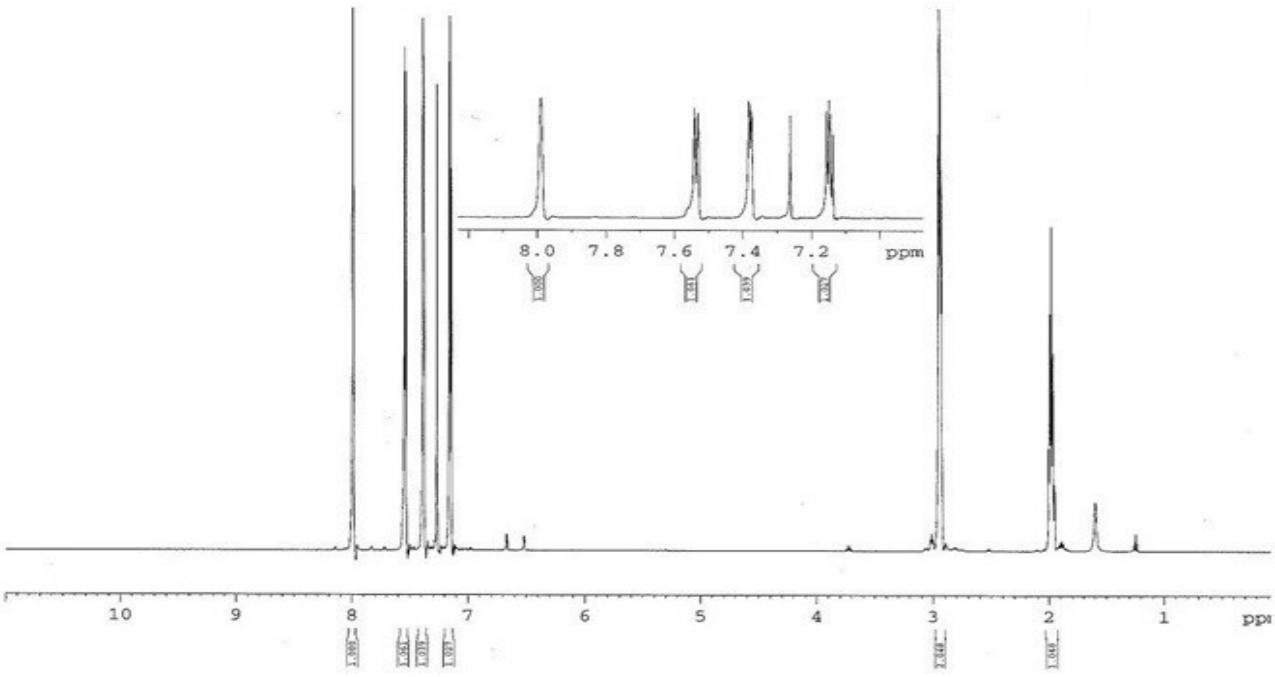
^{13} CNMR spectrum of 2,6-Bis-(2-pyrrolylidene) cyclohexanone (IIb):



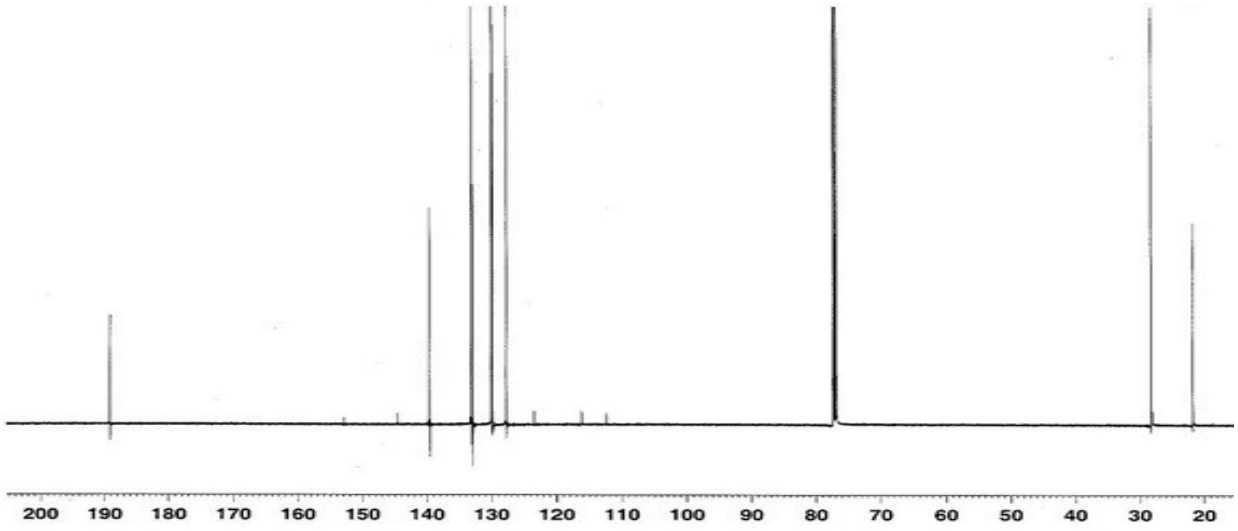
Mass spectrum of 2,6-Bis-(2-pyrrolylidene) cyclohexanone (lI b):



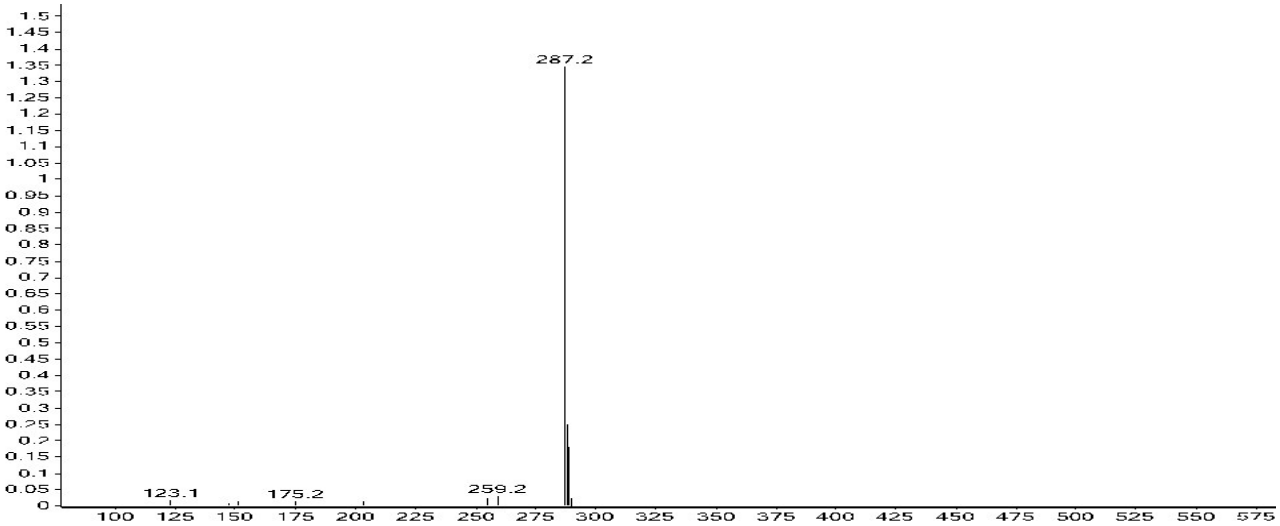
PMR spectrum of 2,6-Bis-(2-thienylidene) cyclohexanone(IIc):



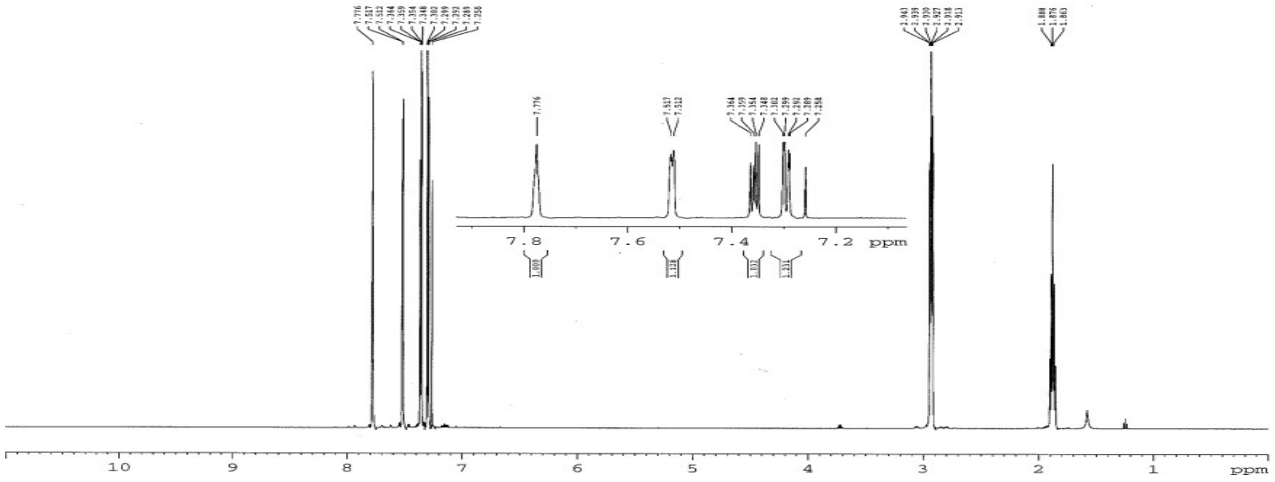
^{13} CNMR spectrum of 2,6-Bis-(2-thienylidene) cyclohexanone(IIc):



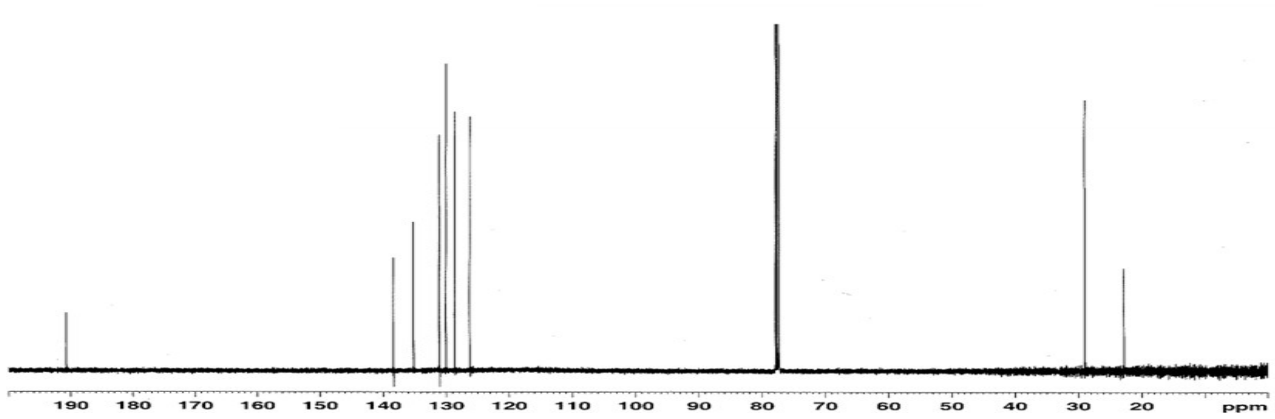
Mass spectrum of 2,6-Bis-(2-thienylidene) cyclohexanone(II c):



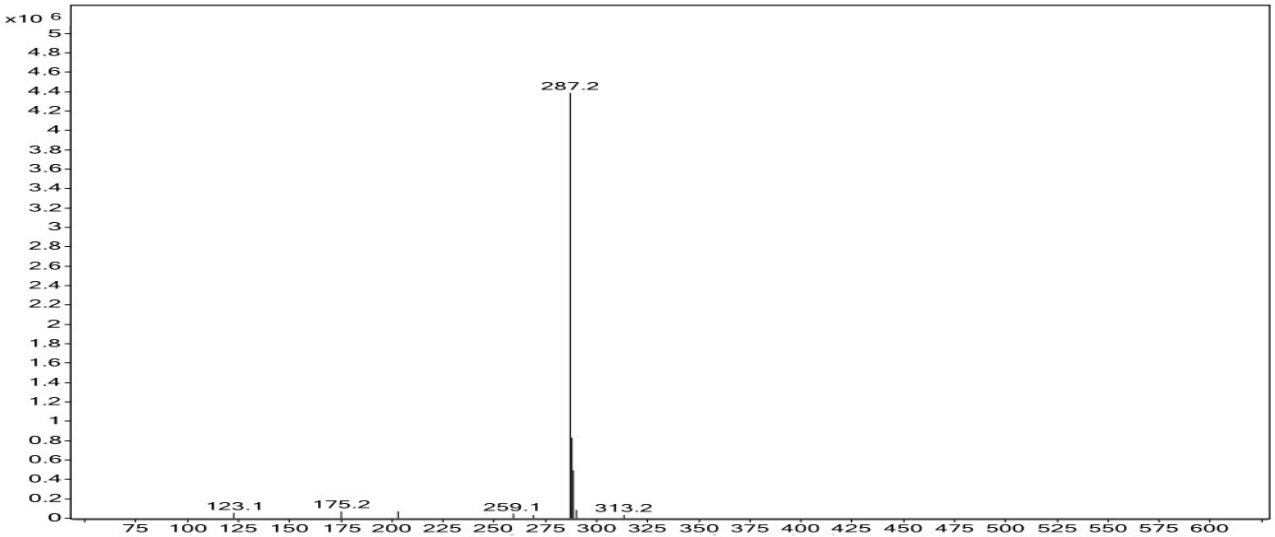
PMR spectrum of 2,6-Bis-(3-thienylidene) cyclohexanone(IIIa):



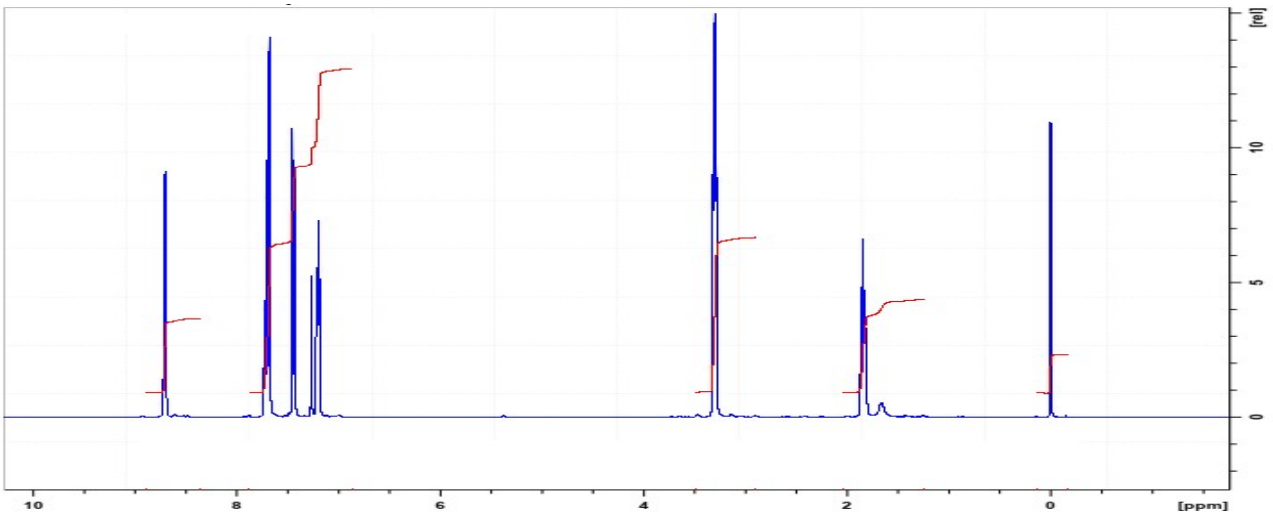
^{13}CNMR spectrum of 2,6-Bis-(3-thienylidene) cyclohexanone(IIIa):



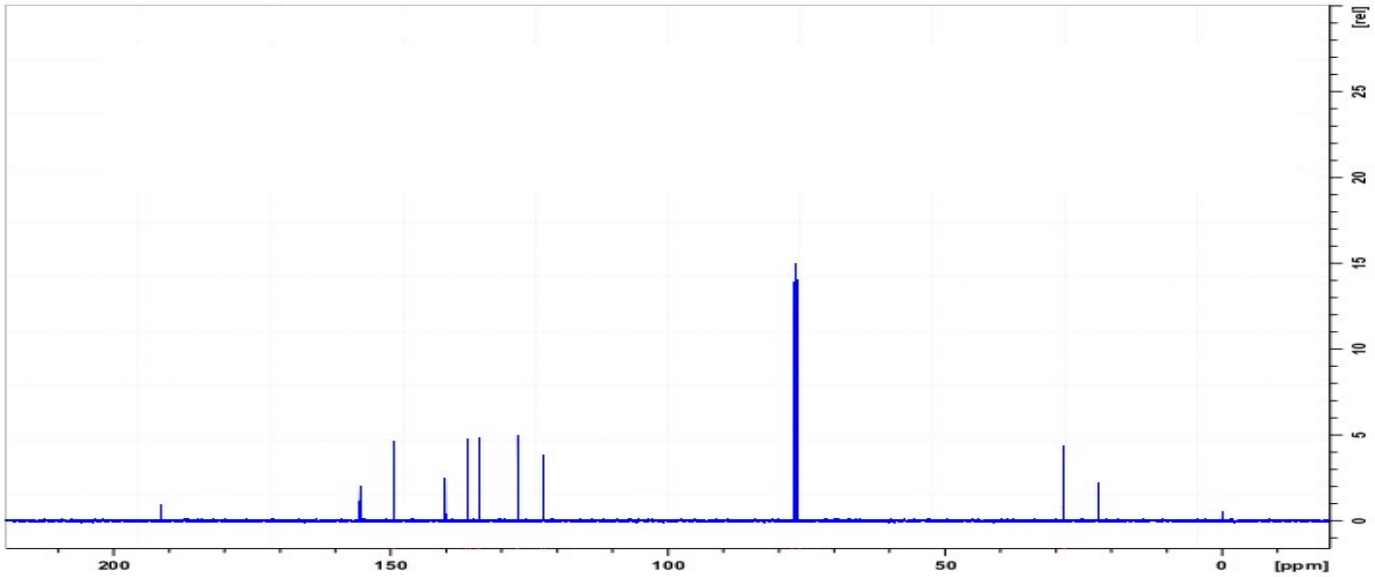
Mass spectrum of 2,6-Bis-(3-thienylidene) cyclohexanone(III a):



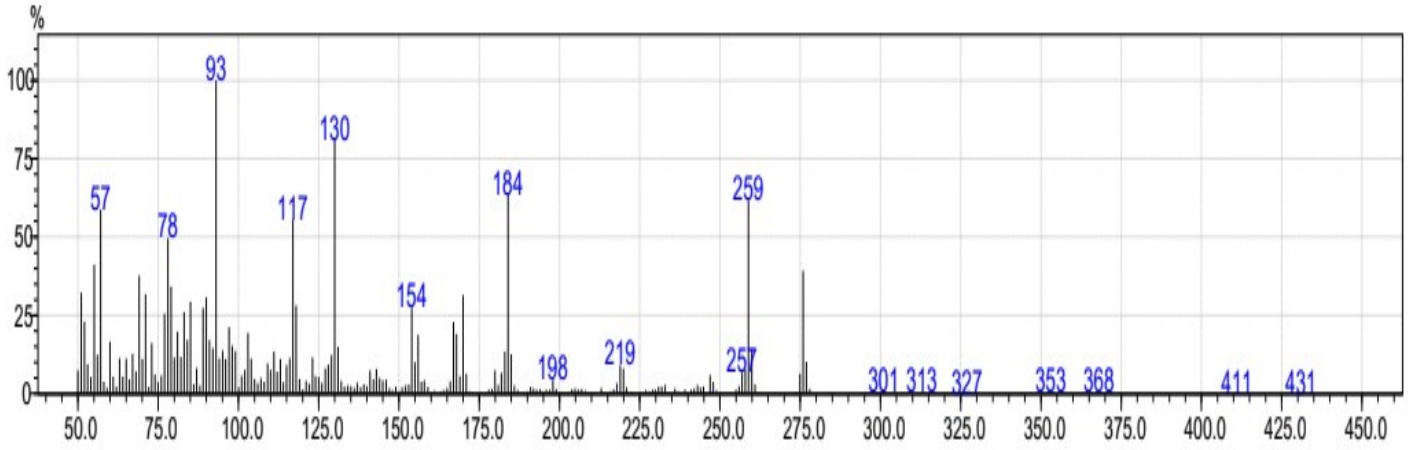
PMR spectrum of 2,6-Bis(pyridin-2-ylmethylene)cyclohexan-1-one(IVa):



^{13}CNMR spectrum of 2,6-Bis(pyridin-2-ylmethylene)cyclohexan-1-one(IVa):

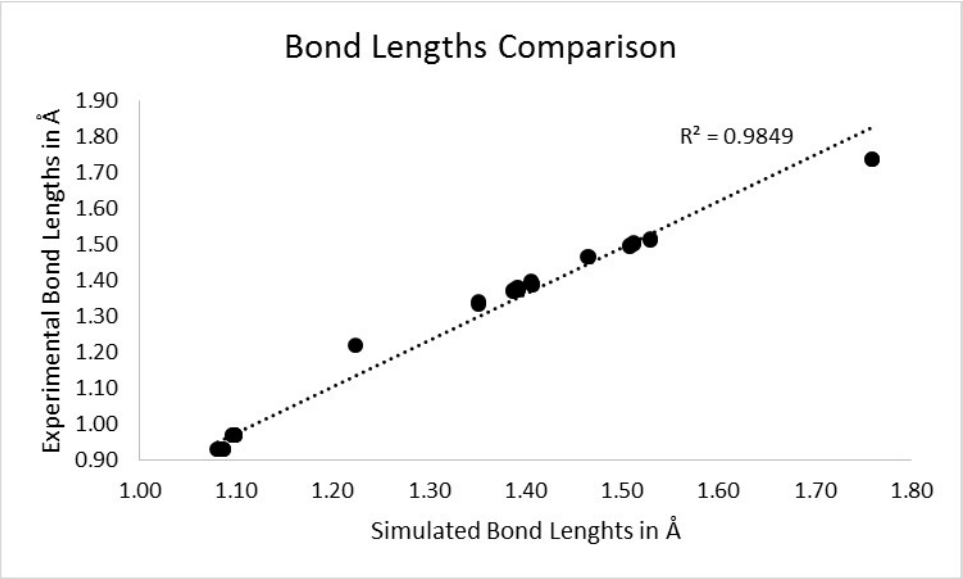


Mass spectrum of 2,6-Bis(pyridin-2-ylmethylene)cyclohexan-1-one(IVa):



SD Table Ia: Bond lengths (Å) comparison

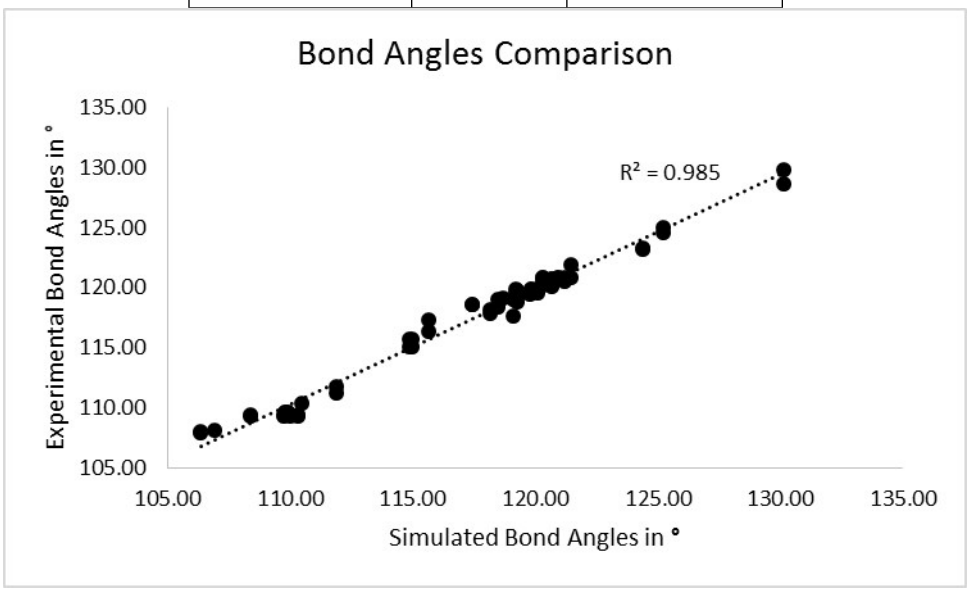
ATOMS	Gaussian	Experimental
Cl1 C10	1.76	1.74
Cl2 C19	1.76	1.74
O1 C1	1.22	1.22
C7 C6	1.35	1.33
C7 C8	1.47	1.46
C7 H7	1.09	0.93
C14 C2	1.35	1.34
C14 C15	1.47	1.46
C14 H14	1.09	0.93
C20 C19	1.39	1.37
C20 C15	1.41	1.39
C20 H20	1.08	0.93
C15 C16	1.41	1.40
C9 C10	1.39	1.37
C9 C8	1.41	1.39
C9 H9	1.08	0.93
C6 C1	1.51	1.50
C6 C5	1.51	1.50
C2 C1	1.51	1.50
C2 C3	1.51	1.50
C4 C3	1.53	1.51
C4 C5	1.53	1.52
C4 H4A	1.10	0.97
C4 H4B	1.10	0.97
C3 H3A	1.10	0.97
C3 H3B	1.10	0.97
C10 C11	1.39	1.38
C13 C12	1.39	1.38
C13 C8	1.41	1.39
C13 H13	1.08	0.93
C5 H5A	1.10	0.97
C5 H5B	1.10	0.97
C19 C18	1.39	1.38
C16 C17	1.39	1.38
C16 H16	1.08	0.93
C11 C12	1.39	1.38
C11 H11	1.08	0.93
C17 C18	1.39	1.37
C17 H17	1.08	0.93
C18 H18	1.08	0.93
C12 H12	1.08	0.93


Bond Lengths Comparison
Experimental Bond Lengths in Å
Simulated Bond Lenghts in Å
R² = 0.9849
1.90
1.80
1.70
1.60
1.50
1.40
1.30
1.20
1.10
1.00
0.90
1.00
1.10
1.20
1.30
1.40
1.50
1.60
1.70
1.80

SD Table Ib: Bond angles (°) comparison

ATOMS	Gaussian	Experimental
C6 C7 C8	130.12	128.64
C6 C7 H7	114.86	115.70
C8 C7 H7	115.00	115.70
C2 C14 C15	130.13	129.80
C2 C14 H14	114.86	115.10
C15 C14 H14	114.99	115.10
C19 C20 C15	120.31	120.20
C19 C20 H20	119.84	119.90
C15 C20 H20	119.85	119.90
C20 C15 C16	118.17	117.90
C20 C15 C14	124.38	123.33
C16 C15 C14	117.41	118.60
C10 C9 C8	120.30	120.80
C10 C9 H9	119.84	119.60
C8 C9 H9	119.86	119.60
C7 C6 C1	115.63	117.32
C7 C6 C5	125.24	124.98
C1 C6 C5	119.08	117.64
C14 C2 C1	115.63	116.32
C14 C2 C3	125.24	124.55
C1 C2 C3	119.09	119.08
O1 C1 C6	120.65	120.06
O1 C1 C2	120.65	120.76
C6 C1 C2	118.69	119.18
C3 C4 C5	110.48	110.38
C3 C4 H4A	109.81	109.60
C5 C4 H4A	109.80	109.60
C3 C4 H4B	109.88	109.60
C5 C4 H4B	109.88	109.60
H4A C4 H4B	106.92	108.10
C2 C3 C4	111.89	111.72
C2 C3 H3A	109.76	109.30
C4 C3 H3A	110.30	109.30
C2 C3 H3B	109.99	109.30
C4 C3 H3B	108.39	109.30
H3A C3 H3B	106.35	107.90
C9 C10 C11	121.45	120.80
C9 C10 Cl1	119.27	119.81
C11 C10 Cl1	119.28	119.40
C12 C13 C8	120.65	120.20
C12 C13 H13	119.19	119.90

C8 C13 H13	120.11	119.90
C9 C8 C13	118.17	118.20
C9 C8 C7	117.42	118.57
C13 C8 C7	124.38	123.20
C6 C5 C4	111.88	111.21
C6 C5 H5A	109.77	109.40
C4 C5 H5A	110.30	109.40
C6 C5 H5B	109.99	109.40
C4 C5 H5B	108.39	109.40
H5A C5 H5B	106.35	108.00
C20 C19 C18	121.45	121.90
C20 C19 Cl2	119.27	118.85
C18 C19 Cl2	119.28	119.23
C17 C16 C15	120.65	120.70
C17 C16 H16	119.19	119.60
C15 C16 H16	120.12	119.60
C10 C11 C12	118.48	119.00
C10 C11 H11	120.33	120.50
C12 C11 H11	121.18	120.50
C18 C17 C16	120.91	120.90
C18 C17 H17	119.32	119.50
C16 C17 H17	119.77	119.50
C17 C18 C19	118.48	118.40
C17 C18 H18	121.18	120.80
C19 C18 H18	120.33	120.80
C11 C12 C13	120.91	120.80
C11 C12 H12	119.32	119.60
C13 C12 H12	119.77	119.60



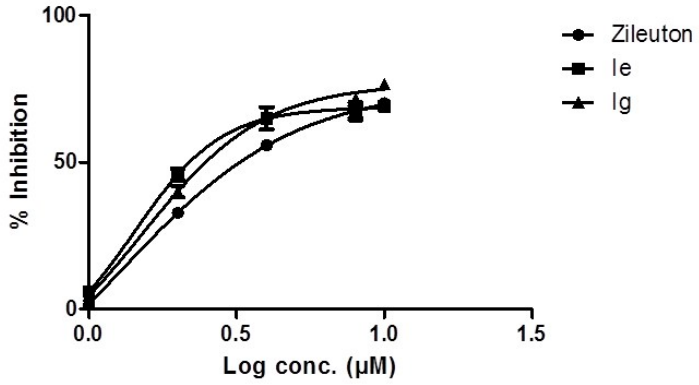


Fig 1. Dose response curve for **Ie, Ig** and **Zileuton** against enzyme 5-LOX.

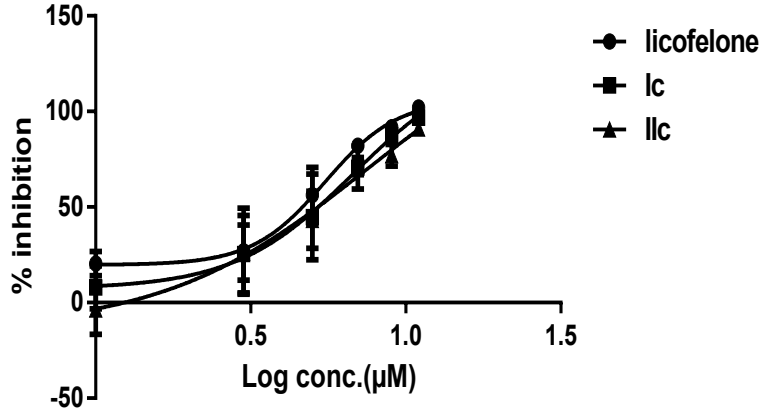


Fig 2. Dose response curve for **Ic, IIc** and **Licofelone** against enzyme COX2/mPGES1.