CHAPTER III

ONE-POT SYNTHESIS

OF

ACETOXY-2,4-

CYCLOHEXADIENONES

III.1 ABSTRACT

One-pot method for oxidative acetylation of some substituted phenols is described for the synthesis of corresponding acetoxy-2,4-cyclohexadienones. A novel triacetate or bis(4-acetoxy-3,5-dimethylphenyl)methyl acetate **(30)** has also been prepared using the present method from tetramethyl bisphenol-F **(29)**. The structures of all compounds were deduced from their various spectral and elemental analyses.

III.2 INTRODUCTION AND OBJECTIVES

Polyquinane is a generic name given to carbocyclic frames composed of fused five membered rings, which constitutes an important class of sesquiterpenoids. Since their discovery, polyquinane natural products have generated a worldwide interest among organic chemists due to their unique and fascinating molecular architecture and promising biological activity.[1,2] Literature survey [3] reveals over hundred such natural products isolated from plants,[4] marine organisms, [5] fungi and insects.[6,7]

Compounds containing three cyclopentane rings fused together are known as "triquinanes" and amongst the natural polyquinanes they are the most abundant.[8] The triquinanes natural products embody the two C_{11} tricyclopentanoid skeleta **(1)** and **(2)** **(Figure III.1)** incorporating three linearly and angularly fused five member rings respectively as the fundamental ring system. Three families of C_{11}-carbocyclic skeleta based on **(1)** are known. They are (I) Hirsutane family, (II) Capnellane family and (III) Pleurotellane family. Whereas, five families based on **(2)** are known, namely (I) Isocomene family, (II) Pentalenene family, (III) Silphinene family, (IV) Silphiperfolene family and (V) subergorgic acid family.[9]

The class of linearly fused tricyclopentanoids is further divided in to two different classes depending upon the mode of fusion of the third cyclopentane ring "C". Different two isomers as shown in **Figure III.1** are *cis-anti-cis* **(3)** and *cis-syn-cis* **(4)**.

Osawa and co-workers [10] reported that the *cis-anti-cis* **(3)** is more stable compared to the hindered fold form, *cis-syn-cis* isomer **(4)** due to its chair like conformation.[11] The *cis-anti-cis* isomer has received greater attention because it constitutes the basic carbocyclic framework of biologically important sesquiterpenoids like hirsutic acid, coriolin, capnellene and hirsutene **(Figure 2)** [12,13]

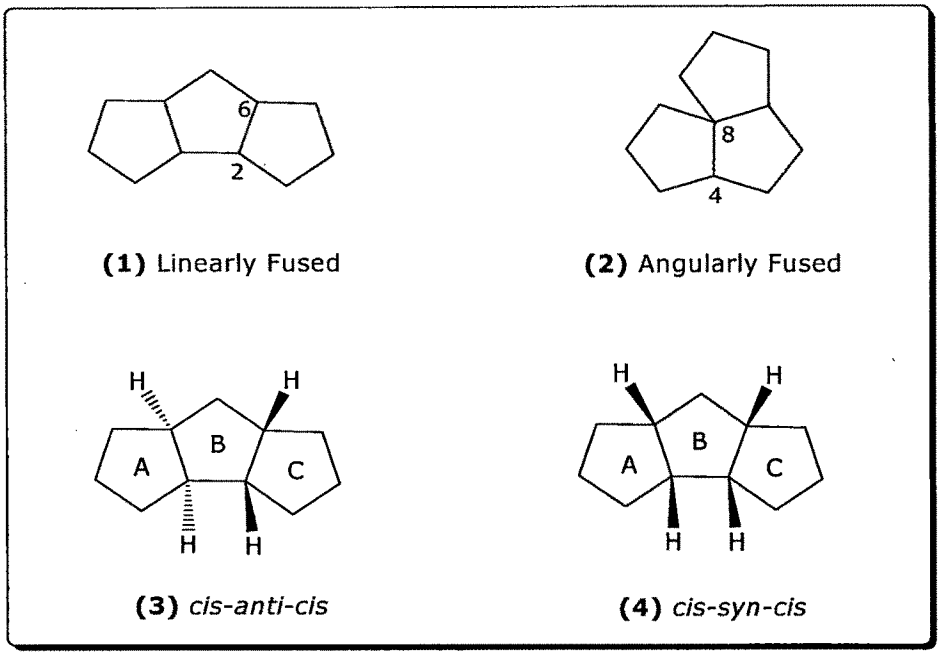


Figure III.1

The fact that polyquinanes exhibit diverse biological activity has generated a flurry of activity in their chemistry. For example, coriolin **(5, Figure III.2)** shows antitumour and antibacterial activitiy, [7] capnellene **(6)** and its congeners have been suggested to act as a chemical defense agent to inhibit the growth of microorganisms and to prevent larval settlement, [14, 15] hirsutic acid (7) possesses antibiotic properties [16] etc.

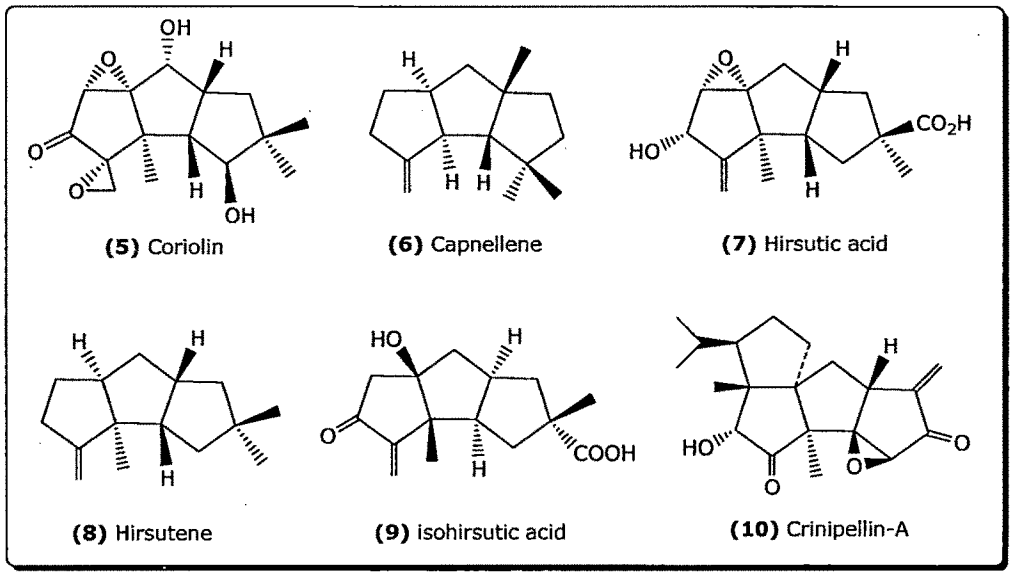
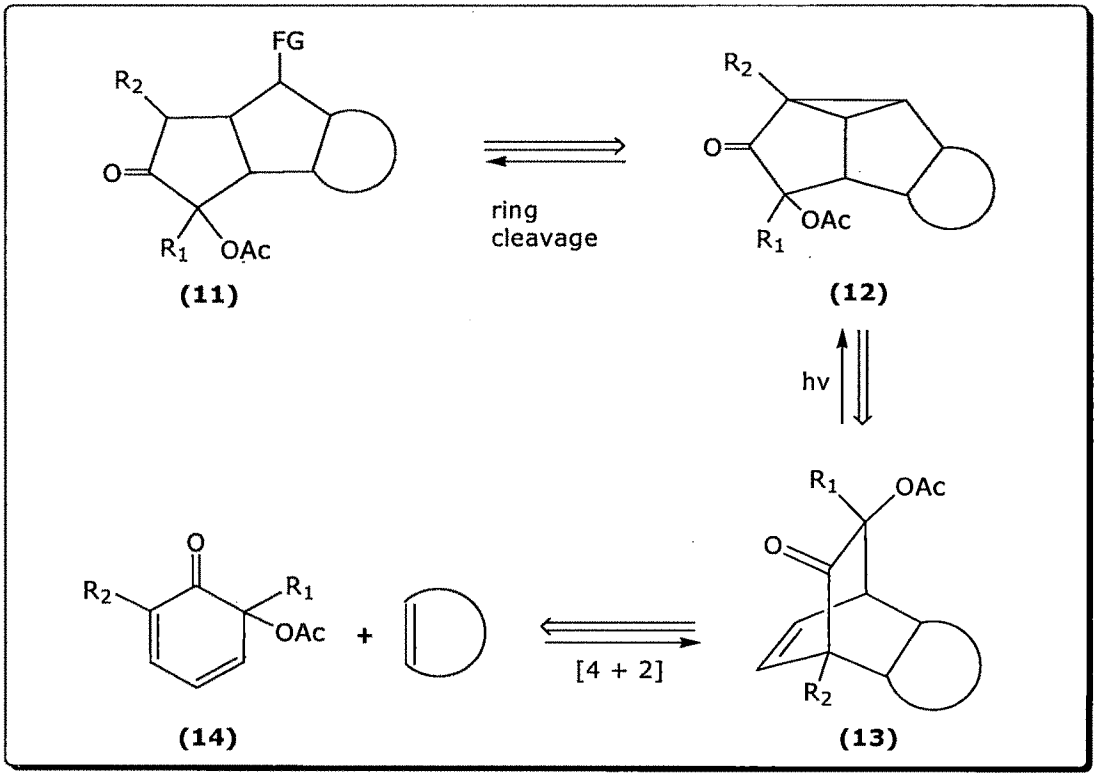


Figure III.2

Though a variety of methods have been developed for the construction of tricyclopentanoid framework, most of them are target specific, lacking adaptability and involve multi-step sequences.[17, 18]

In this context, Singh *et al* reported a unified approach towards the synthesis of linearly fused triquinanes [19] of the type **(9)** via a peripheral ring cleavage of the tetracyclic intermediate **(10)**, which is easily obtainable from the key intermediate **(11)** via photochemical oxa-di-π-methane rearrangement.[20] The chromophoric system **(11)** was assembled via an inverse electron demand $\pi^{4s} + \pi^{2s}$ cycloaddition between a cyclohexa-2,4-dienone of the type **(12)** and a suitable dienophile **(Scheme 1)**.



Scheme 1

Above mentioned approach is highly dependent on the easy availability of the key intermediate, acetoxycyclohexadienone **(12)**, via a high yielding process.

Though, 2,4-cyclohexadienones (o-quinol) such as **(12)** are well known intermediates in the literature, only a few methods are reported for their preparation.[21] o-Quinols and their derivatives are among the least investigated cyclohexadienones among the other types and its chemistry is again dominated by a propensity toward dimerization.[21] In addition, o-quinols with specific functionality undergo a few other problematic reactions. For example, in alkaline medium acetate or hydroxyl groups containing o-

quinols undergo ring-opening reactions. Wessely,[22] Van Dongen,[23] and Bugg [24] have reported that some unusual products emerges when o-quinols and their corresponding acetates are subjected to alkaline conditions.

Figure III.3 shows the strategies for preparing o-quinols and their derivatives. These include (i) oxidation of the ortho-alkylated phenol **(13)** in the presence of an oxygen nucleophile; [25-30] (ii) oxidation of the ortho-alkoxy phenol **(14)** in the presence of a carbon nucleophile; [31-35] (iii) [4+2] cycloaddition of an oxy-diene to an o-quinone **(15)**, [36-38] (iv) single addition of a carbon nucleophile to an o-quinone, [39-45] such as **(16)**; and (v) rearrangement of an aryl ether **(17)**.[46-50] In addition, transition metal carbene-mediated couplings and carbon-insertion processes also have been used.[51,52] Among all these processes, the prevailing method usually involves oxidation of phenols **(13)** with intramolecular delivery of a oxygen nucleophile.

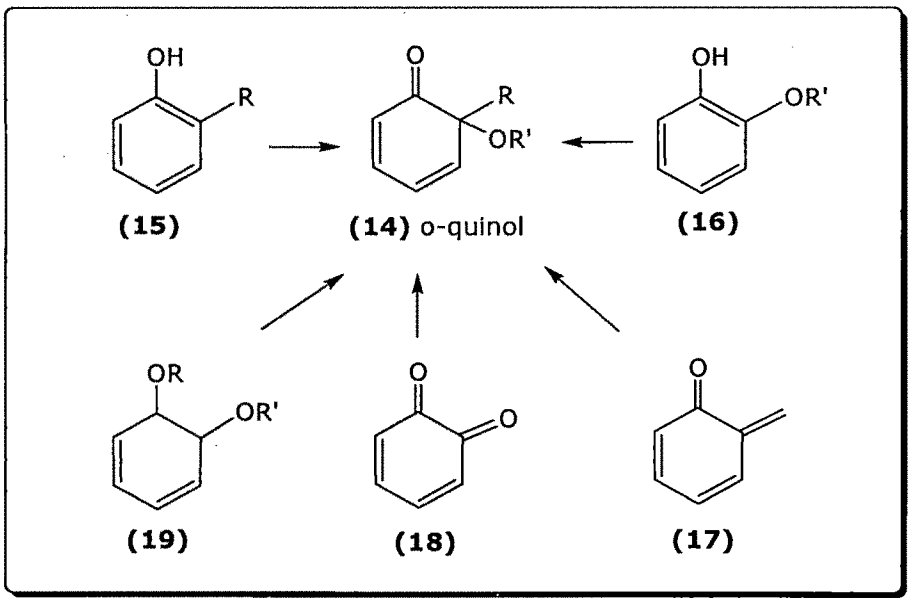
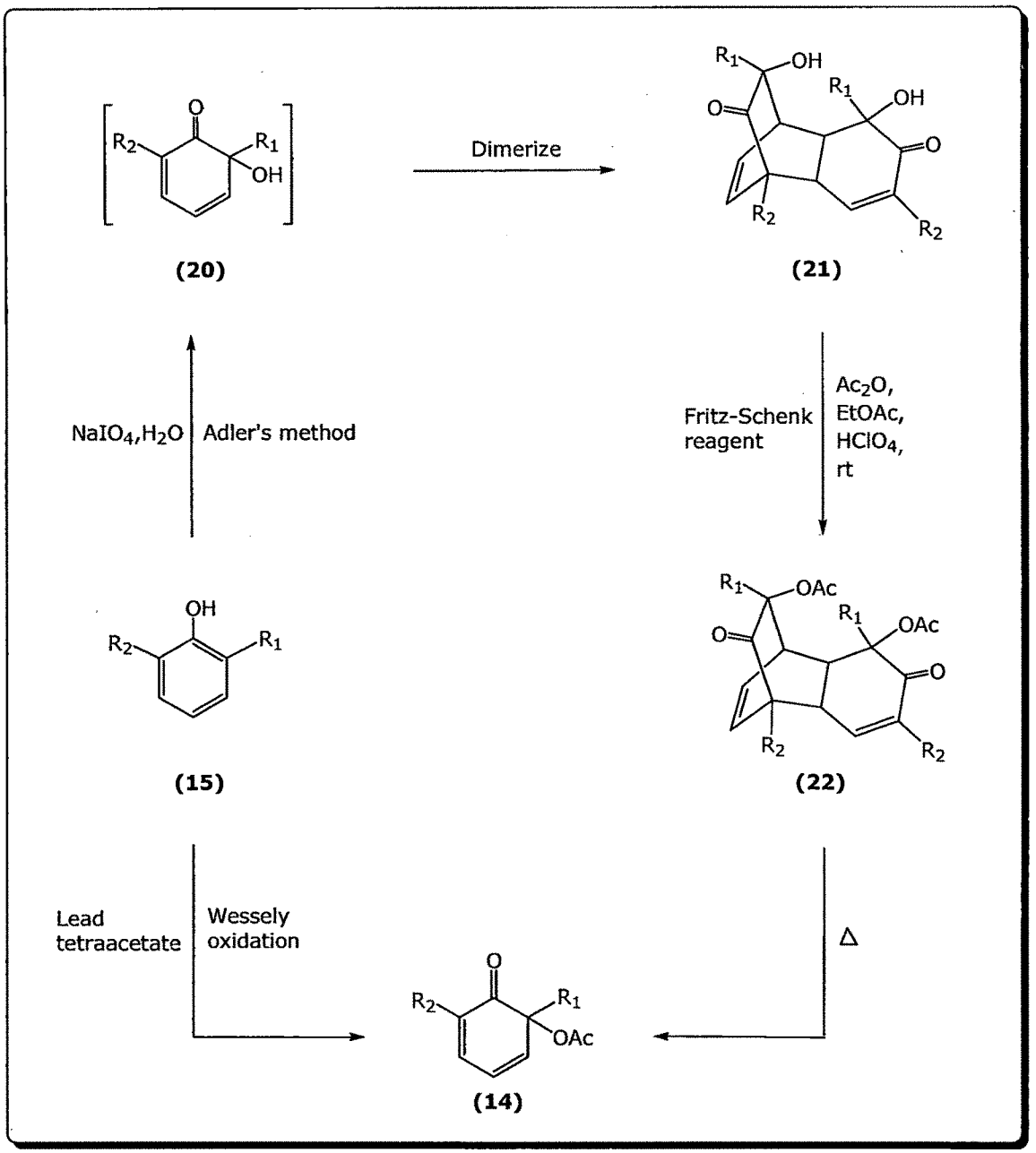


Figure III.3

Wessely oxidation is a generally used method for the preparation of acetoxy-cyclohexadienone **(12)** involves oxidation of phenols **(13)** with lead-tetraacetate.[53] Pinhey [54] and Thomas [55] have investigated the mechanism of the Wessely oxidation[53,56] of electron-rich o-alkylated phenols and reported that it involves an intramolecular oxidative delivery of acetate from an intermediary $ArOPb(OAc)_3$ complex. However, it often proceeds in low yields and furnishes a mixture of products depending upon the nature of the substituents on the aromatic ring.[53] Furthermore, it requires rather excess quantities of the expensive and toxic oxidant. Alternatively, it can also be prepared from diol-dimeric

form by the periodate oxidation of phenols in water, as investigated by Adler *et al.*[57] followed by acetylation of the 3°-hydroxy groups using Fritz-Schenk reagent.[58] Occasionally, diacyl peroxide [59] and trifluoro-peroxyacetic acid [60, 61] have also been used for their preparation.



Scheme 2

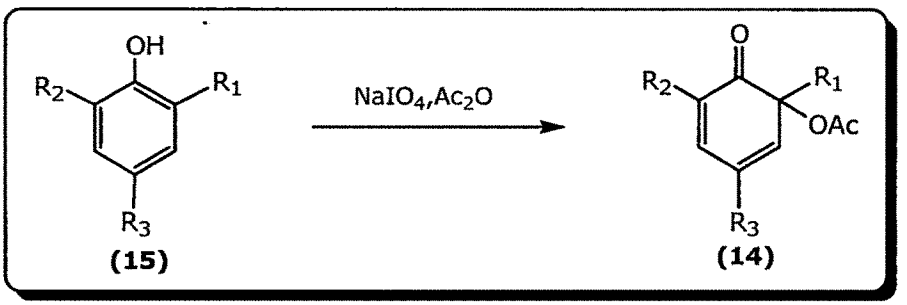
Wessely oxidation gives acetoxycyclohexadienones (**14, Scheme 2**) in one step but gives low yield. On the other hand, Adler's method gives relatively better yields but results in the formation of a diol-dimeric compound (**20**), which needs to be acetylated to

furnish corresponding diacetate dimer (**22**) using Fritz-Schenk reagent. The dimeric diacetate requires being pyrolzed to furnish the corresponding acetoxy-cyclohexadienone (**14**), which results in lower overall yield. **Scheme 2** shows the comparison of these two methods.

Perumal[25], Coleman[62], Hunter[63] and Pinhey[54] have all extensively investigated the Wessely oxidations of various types of phenols.

Though Adler's method seemed satisfactory to proceed on towards the total synthesis of the triquinane natural products, we continued our search for a shorter and convenient preparation of acetoxy-cyclohexadienone (**14**) with moderate to high yielding procedure.

During search for a better method, our group explored the reaction of alkyl substituted phenols (**15**) with sodium metaperiodate in acetic anhydride medium at room temperature.[64] It was thought that the oxidative acetylation of phenol would give the corresponding acetoxy-cyclohexadienone (**14**), as depicted in **Scheme 3**. In continuation with this endeavour we have attempted to generalize the procedure for other phenols having various types of reactive/sensitive functional groups and structural variations like, aldehyde, anilide, lactone, etc. Thus, Vanillin, 4-methyl-7-hydroxy coumarin, 4-hydroxy-4'-chlorobenzophenone, 4-hydroxy butyranilide, tetramethyl bisphenol-F [bis(3,5-dimethyl-4-hydroxyphenyl)methane] etc, were treated with sodium metaperiodate in acetic anhydride at different temperatures to obtain corresponding acetoxy-cyclohexadienones in good tomoderate yields.



Scheme 3

III.3 RESULTS AND DISCUSSION

The results obtained from the oxidative acetylation of the phenols having alkyl group at different position on the ring with periodate in acetic anhydride medium prompted us to generalize this reaction for the phenol containing sensitive functional groups rather than alkyl groups on the ring. Towards accomplishing the objective, Vanillin(4-Hydroxy-3-methoxy benzaldehyde) (**23, Figure III.4**, 1 mole) in acetic anhydride was treated with sodium metaperiodate (1.2 equi.) added in portions, with stirring for 5 h at 60 °C, which gave (**24**) in 59 % yields after usual workup and chromatography. Vanillin has aldehyde and methoxy groups on first and third position on the ring. It was thought that the aldehyde group would undergo oxidation and get converted into the carboxylic acid but ^{1}H NMR spectrum of the product (**24**) exhibited singlet at δ_H 9.91 indicating the presence of the aldehyde group. The structure of the acetate dienone (**24**) was fully discernible from its UV, FTIR, ^{1}H NMR, ^{13}C NMR, mass spectra and elemental analysis. It showed a strong band at 1757 cm^{-1} in addition to the characteristic conjugated carbonyl absorptions at 1690 cm^{-1} and 1678 cm^{-1} in its IR spectrum.[65] It showed a band at 300 nm in its UV spectrum, which clearly exhibited the features of a conjugated cyclic ketone molecular framework. Its ^{1}H NMR spectrum exhibited singlets at 3.88, indicating the presence of methoxy groups among other signals. The presence of an α,β-unsaturated system was further confirmed by the characteristic signals at δ_H 7.48 (s, 1H at C_2), 7.44 (d, J = 6 Hz, 1H at C_4) and 7.21 (d, J = 6 Hz, 1H at C_5) for the olefinic protons along with the signal at δ_H 2.32 (sharp s, 3H, -COC<u>H</u>$_3$). Its ^{13}C NMR showed separate signals at δ_c 20.36 (-OCOC<u>H</u>$_3$), 55.87 (OC<u>H</u>$_3$), 110.57 (tetra subst., -O-<u>C</u>-O- type), 135, 144, 151, 168 (four olefinic C), 190.8, 191.2, 206.5 (three carbonyls). Its Mass spectrum showed m/z: (M^+) at 210 along with 196, 168, 154, 104, 97, 89 and 80. Elemental analysis of (**24**) was in good agreement with the required one. Found C; 57.21 %, H; 4.68 % requires C; 57.14 %, H; 4.76 % for $C_{10}H_{10}O_5$.

Encouraged by these results, we attempted this method on other phenol having fused lactone system, 4-methyl-7-hydroxy coumarin (**25**) which was treated in similar way at 85 °C to give rise to only one regioisomer (**26**) it was confirmed by its ^{1}H PMR. Its IR spectrum showed an absorption band at 1765 cm^{-1} for the presence of carbonyl group in a α-keto ester and strong bands at 1726 cm^{-1} and 1713 cm^{-1} for the presence of a conjugated carbonyl group. It showed a band at 280 nm in its UV

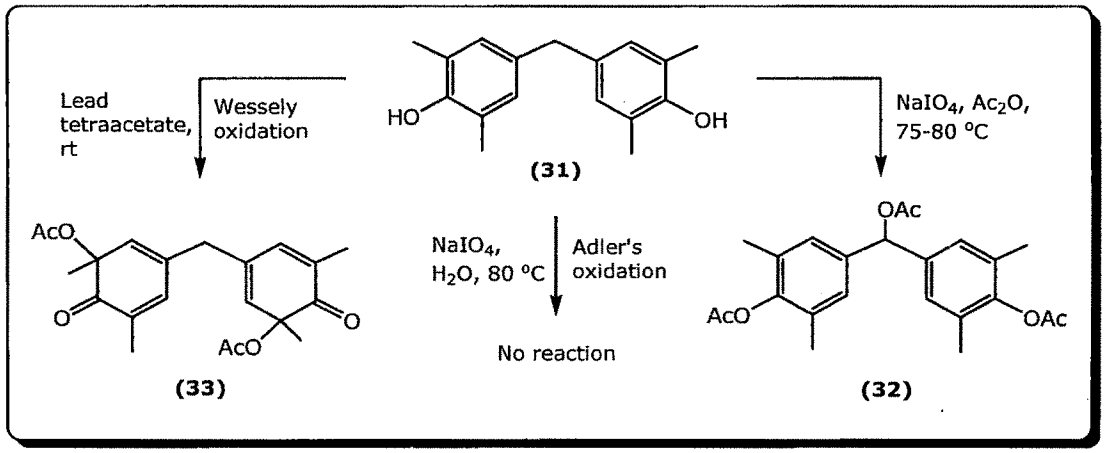
spectrum, which clearly exhibited the features of a conjugated cyclic ketone. It exhibited a doublet at δ_H 7.59 (1H at C_5) and sharp singlet at δ_H 7.10 (1H at C_8) for one olefinic proton each in its ^1H NMR spectrum confirmed the presence of only one regioisomer (**26**), and ruling out the possibility of other isomers. The olefinic proton on C_3 appeared as singlet at δ_H 6.25 along with the other signals δ_H 2.42 (sharp s, 3H, -COC<u>H</u>$_3$), 2.33 (sharp s, 3H, olefinic -C<u>H</u>$_3$), 1.72 (broad s, 1H at C_6). Its ^{13}C NMR showed separate signals at δ_c 20.9 (-OCOC<u>H</u>$_3$), 63.6 (olefinic -<u>C</u>H$_3$), 96.4 (C_6), 110.4, 114.4, 118.0, 125.4, 132.2, 140.3 [six olefinic C (sp^2 type)], 154.1, 160.5, 168.8 (three carbonyls). Mass spectra showed, m/z: 234 (M^+), 217, 207, 192, 175, 165, 100 and 77. Elemental analysis: Found C; 60.98 %, H; 4.19 % requires C; 61.53 %, H; 4.27 % for $C_{12}H_{10}O_5$.

4-Hydroxy-4'-chlorobenzophenone (**27**) furnished 3-(4-chlorobenzoyl)-6-oxocyclohexa-2,4-dienyl acetate (**28**) in 60 % yield under similar reaction conditions at 70 °C. The IR spectrum of (**28**) showed an absorption band at 1757 cm^{-1} for the presence of carbonyl group in a α-keto ester and strong bands at 1694 cm^{-1} and 1683 cm^{-1} for the presence of a conjugated carbonyl group. It showed a band at 300 nm in its UV spectrum, clearly exhibited the features of a conjugated cyclic ketone. Its ^1H NMR showed different signals at δ_H 7.79 (d, J = 8 Hz, aromatic ring p-substituted), 7.82 (d, J = 8 Hz, aromatic ring p-substituted), 7.45 (d, J = 8 Hz, 2H at C_4 & C_2), 7.49 (merged with signal of C_2-olefinic proton), 7.24 (d, J = 12 Hz, 1H at C_5), 2.35 (sharp s, 3H, - COC<u>H</u>$_3$), and 1.63 (sharp s, 1H at C_6). Its ^{13}C NMR showed δc 21.1 for the ($OCOCH_3$), 65.1 for C_6, 101.9, 121.4, 121.6, 121.9 for the four different olefinic carbons, 128.9, 131.3, 131.8, 134.7, 135.8, 138.9 for the six aromatic carbons and 154.1, 168.9, 194.3 for the three carbonyl carbons. The mass spectrum of (**26**) displayed a base peak at M-140, which suggested loss of the $C_6H_4ClCO^+$ ion, among other characteristic signals. m/z: M^+ = 292.6, M+2 = 294.6 (of 1/3 intensity of M^+), and M-60 (M-CH_3COOH). Elemental analyses were in good agreement with the required for the $C_{15}H_{11}O_4Cl$. Found C; 61.88 %, H; 3.83 % requires C; 61.96 %, H; 3.78 % for $C_{15}H_{11}O_4Cl$.

Oxidation of phenol having anilde group on the ring (4-hydroxy butyranilide) (**29**) also led to similar observation producing (**30**) at room temperature, whose IR spectrum showed an absorption band at 1763 cm^{-1} presence of carbonyl group in a α-keto ester. It showed a band at 300 nm in its UV spectrum, which clearly exhibited the

features of a conjugated cyclic ketone. Its ^{1}H NMR spectrum revealed a doublet at δ_H 1.60 (1H at tetra substituted carbon) for single proton in addition to other signals. The three olefinic protons appeared at δ_H 7.55 (d, 1H at C_2), 7.15 (d, 1H at C_4) and 7.00 (d, 1H at C_5). Sharp singlet appeared at δ_H 7.30 for (1H, NHCO) along with δ_H 2.35 (t, merged with $-OCOCH_3$ signal, 2H, $NHCOCH_2$-), 2.30 (s, 3H, $-OCOCH_3$), 1.75 (m, 2H, $-CH_2-CH_3$) and 1.00 (t, 3H, $-CH_3$). Its ^{13}C NMR showed different signals at δ_c 13.3, 18.4, 21.2, 39.3 for the methyl and methylene carbons, δ_c 97.4 for tetra substituted carbon, δ_c 121.1, 122.0, 135.8, 146.6 for four olefinic carbons. Mass spectrum shows m/z: 237 (M^+), 220, 178. Elemental analysis for $C_{12}H_{15}NO_4$ **(28)**: Found C; 50.69 %, H; 6.28 %, N; 6.10 % requires C; 50.53 %, H; 6.33 %, N; 5.90 % for $C_{12}H_{15}NO_4$.

In continuation with this study, when tetramethyl bisphenol-F [bis(3,5-dimethyl-4-hydroxyphenyl)methane] **(31)** was subjected to oxidation, it's reaction gave different products with different methods, as shown in **Scheme 4.** Tetramethyl bisphenol-F **(31)** was obtained by the reaction between 2,6 dimethyl phenol and formaldehyde in aqueous alkaline medium. The bisphenol-F **(31)** was treated with sodium metaperiodate in acetic anhydride medium at 75-80 °C for 5 h to furnish the novel triacetate as a white crystalline solid **(32)** in 51% yield. It showed the formation of the unusual product instead of the biscyclohecadienone. Structure of triacetate **(32)** was fully established through its spectral and analytical data. It showed a characteristic band at 1749 cm^{-1} for the carbonyl absorption in its IR spectrum. It also displayed singlets for methyl group at δ_H 2.14 (12H) along with δ_H 2.15 (3H) and δ_H 2.26 (6H). Its ^{13}C NMR spectrum showed signals at δ_C 170.1 and 168.9 for acetate carbonyls along with 21.6 and 20.7 for acetate methyls. The mass spectrum of **(32)** showed a molecular ion peak at 398 and a base peak at 339 (loss of acetic acid) in addition to other diagnostic signals. It was evident that acetylation of the two phenolic OH groups and at the benzylic position led to the formation of the novel triacetate **(32)**. Elemental analysis was also in good agreement with its proposed structural formula. Elemental analysis: Found C; 68.93 %, H; 6.43 %; requires C; 69.34 %, H; 6.53 % for $C_{23}H_{26}O_6$.



Scheme 4

Unexpected results prompt us to carry out the reaction of tetramethyl bisphenol-F (**31, Scheme 4.**) with LTA in dry benzene at room temperature. After usual workup and chromatography over silica gel furnished the bis(3,5-dimethyl-3-acetoxy-4-oxocyclohexa-1,5-dienyl)methane (**33**) in 45% yield. Structure of the compound (**33**) was confirmed through its spectral and analytical characteristics. The biscyclohexadienone (**33**) showed a characteristic band at 1669 cm^{-1} in its IR spectrum for cyclohexadienones. Its ^{1}H NMR spectrum displayed signals at δ_H 1.37, 1.92, and 2.06 each for 6H along with singlets at 3.05 (2H) and 5.86 (2H) for methylene and olefinic protons respectively. The ^{13}C NMR spectrum of (**33**) was also consistent with the structure and exhibited resonances at δ_C 15.90, 21.07, and 24.63 for methyl carbons and a signal at 40.51 for the methylene carbon in addition to other characteristic signals. Its mass spectrum showed a molecular ion peak at 372 and a base peak at 313 (M-59) indicating loss of acetate ion and was correctly analyzed for $C_{21}H_{24}O_6$. It was interesting to observe that both the aromatic rings participated in the oxidation leading to the bis-cyclohexadienone (**33**). It is also noteworthy that although the oxidative acetylation of tetramethyl bisphenol-F could lead in principle to the formation of several addition products through inter- and intramolecular modes of cycloaddition, the reaction only furnished a single product. To study its possible intra- as well as intermolecular cycloaddition reactions, the bis-dienone (**33**) was also heated under reflux in o-xylene for 5 h with stirring. We observed that the bis-dienone (**33**) was stable under the reaction conditions and remained unchanged. The tetramethyl bisphenol-F (**31**) was found to be stable toward oxidation with $NaIO_4$ in water even at 80 °C and did not yield any cyclohexadienone.

4-Methoxy phenol, eugenol, cardnol and o-, m-, p-cresols gave rise to complex mixtures, while 2-hydroxy benzoic acid, 4-hydroxy benzoic acid, 4-hydroxy acetophenone, 4-hydroxy diphenyl gave only acetylated products under similar reaction conditions with periodate due to the presence of the electron withdrawing group. Here all the substituted phenols underwent reaction by varying temperature (ambient to 90 °C).

Various acetoxy-2,4-cyclohexadienone prepared by the present method are listed in **Table: 1,** which summarizes the reaction temperature, % yields and mp of various products obtained from the oxidative acetylation of various substituted phenols.

TABLE: 1

Compounds	**Reaction temp.** (°C)	**Cyclohexadienone (% Yield)**	**Triacetate (% Yield)**	**mp** (°C)
23	60	**24** (59)	-	85
25	85	**26** (52)	-	171
27	70	**28** (60)	-	134
29	Ambient	**30** (52)	-	102
31	75-80	-	**32** (51)	139
31	Ambient	**33** (45)	-	183-184

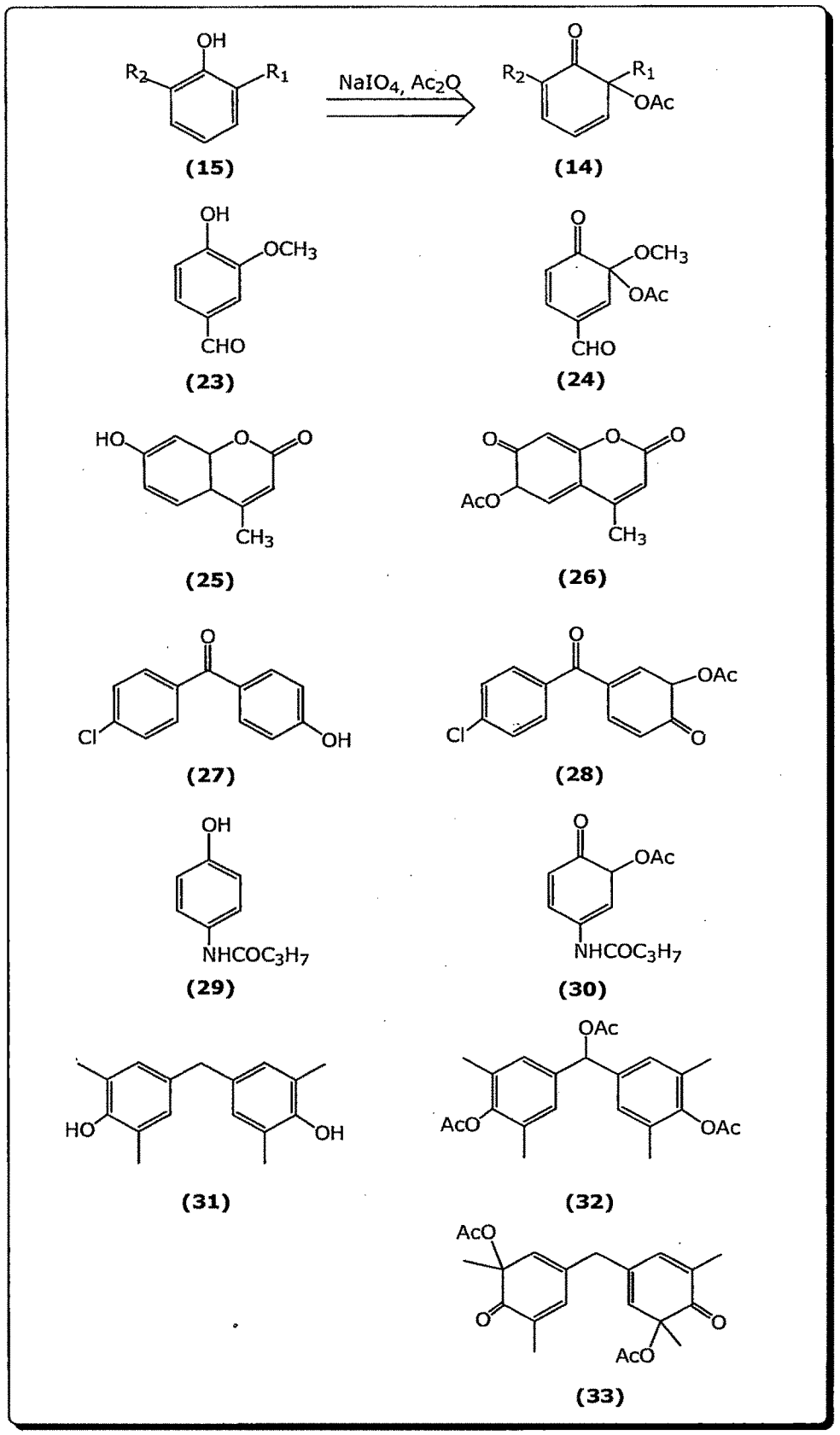

OH
R2
R1
NaIO4, Ac2O
O
R2
R1
OAc
(15)
(14)
OH
OCH3
CHO
O
OCH3
OAc
CHO
(23)
(24)
HO
O
O
CH3
O
O
O
AcO
CH3
(25)
(26)
O
Cl
OH
O
OAc
Cl
O
(27)
(28)
OH
NHCOC3H7
O
OAc
NHCOC3H7
(29)
(30)
HO
OH
OAc
AcO
OAc
(31)
(32)
AcO
O
O
AcO
(33)

Figure III.4

III.4 EXPERIMENTAL

Melting points were recorded in open capillary tubes and are uncorrected. Ultraviolet spectra were recorded on a Perkin-Elmer Lambda-19 Spectrometer. Infrared spectra were recorded on a Perkin-Elmer PC-16 FTIR Spectrophotometer. PMR (300 MHz) spectra and ^{13}CMR (50 MHz) were recorded either on a Bruker-300-FT-NMR using $CDCl_3$ as solvent containing tetramethylsilane as an internal standard. Mass spectra were recorded on a Shimadzu QP-5050-A mass spectrometer. Microanalyses were performed on a Perkin-Elmer 2400 series II Laser instrument. Column chromatography was performed using Acme's silica gel (60–120 mesh size) and the elution was done using light petroleum and ethyl acetate mixtures. The percent yields are reported based on the isolated material after column chromatography. Thin layer chromatography was performed using Acme's silica gel for TLC and spots were visualized in iodine vapor.

General procedure for the Oxidative Acetylation of substituted phenols:

To a stirred solution of phenol (1.00 mole) in acetic anhydride (15-20 mL) was added sodium metaperiodate (1.2 moles, excess) in portions over a period of 1 hour. Stirring was further continued for 5 hours either at room or at elevated temperatures. The reaction mixture was then poured into a saturated solution of sodium bicarbonate and stirred vigorously to neutralize the acetic acid. The aqueous layer was extracted with ethyl acetate (4 × 25 mL) and combined organic extracts were washed successively with saturated sodium bicarbonate (25 mL), water (25 mL) and brine solution (20 mL) followed by drying over anhydrous sodium sulphate. Removal of solvent under reduced pressure furnished a residue, which was chromatographed using mixtures of light petroleum and ethyl acetate to give corresponding acetoxycyclohexadienones.

3-Formyl-1-methoxy-6-oxocyclohexa-2,4-dienyl acetate (24): White crystalline solid (59 %), mp 85°C, ν_{max}: 3018, 1757, 1690, 1678, 1647, 1155 cm^{-1}, UV (λ_{max}): 320 nm. δ_H (300 MHz, $CDCl_3$): 9.91 (s, 1H C<u>H</u>O), 7.48 (s, 1H at C_2), 7.44 (d, J = 6 Hz, 1H at C_4), 7.21 (d, J = 6 Hz, 1H at C_5), 3.88 (s, 3H, -OC<u>H</u>$_3$), 2.32 (sharp s, 3H, -COC<u>H</u>$_3$). δ_c (50 MHz, $CDCl_3$): 20.36 (OCOC<u>H</u>$_3$), 55.87 (OC<u>H</u>$_3$), 110.57 (tetra subst., -O-<u>C</u>-O- type), 135, 144, 151, 168 (four olefinic C), 190.8, 191.2, 206.5 (three carbonyl C), MS m/z: 210 (M^+),

196, 168, 154, 104, 97, 89, 80, Elemental analysis: Found C; 57.21 %, H; 4.68 % requires C; 57.14 %, H; 4.76 % for $C_{10}H_{10}O_5$.

4-Methyl-2,7-dioxochroman-6-yl acetate (26): White crystalline solid (52 %), mp 171°C, ν_{max}: 3053, 2968, 1765, 1726, 1713 cm^{-1}, UV (λ_{max}): 280 nm, δ_H (300 MHz, $CDCl_3$): 7.59 (d, 1H at C_5), 7.10 (s, 1H at C_8), 6.25 (s, 1H, olefinic H at C_3), 2.42 (sharp s, 3H, -$COC\underline{H}_3$), 2.33 (sharp s, 3H, olefinic -$C\underline{H}_3$), 1.72 (broad s, 1H at C_6), δ_c (50 MHz, $CDCl_3$): 20.9 (-$OCOC\underline{H}_3$), 63.6 (olefinic -$\underline{C}H_3$), 96.4 (C_6), 110.4, 114.4, 118.0, 125.4, 132.2, 140.3 [six olefinic C (sp^2 type)], 154.1, 160.5, 168.8 (three carbonyl C), MS m/z: 234 (M^+), 217, 207, 192, 175, 165, 100, 77. Elemental analysis: Found C; 60.98 %, H; 4.19 % requires C; 61.53 %, H; 4.27 % for $C_{12}H_{10}O_5$.

3-(4-Chlorobenzoyl)-6-oxocyclohexa-2,4-dienyl acetate (28): White crystalline solid (60 %), mp 134°C, ν_{max}: 3051, 1757, 1694, 1683, 759 cm^{-1}, UV (λ_{max}): 300 nm, δ_H (300 MHz, $CDCl_3$): 7.79 (d, J = 8 Hz, aromatic ring p-substituted), 7.82 (d, J = 8 Hz, aromatic ring p-substituted), 7.45 (d, J = 11 Hz, 2H at C_4 & C_2), 7.49 (merged with signal of C_2-olefinic proton), 7.24 (d, J = 12 Hz,1H at C_5), 2.35 (sharp s, 3H, - $COC\underline{H}_3$), 1.63 (sharp s, 1H at C_6). δ_c (50 MHz, $CDCl_3$): 21.1 ($OCOCH_3$), 65.1(C_6), 101.9, 121.4, 121.6, 121.9 (four olefinic C), 128.9, 131.3, 131.8, 134.7, 135.8, 138.9 (six aromatic C), 154.1, 168.9, 194.3 (three carbonyl C), MS m/z: M^+ = 292.6, M+2 = 294.6 (of 1/3 intensity of M^+), M-140 (loss of $C_6H_4ClCO^+$) and M-60 (M-CH_3COOH). Elemental analysis: Found C; 61.88 %, H; 3.83 % requires C; 61.96 %, H; 3.78 % for $C_{15}H_{11}O_4Cl$.

3-Butyramido-6-oxocyclohexa-2,4-dienyl acetate (30): White crystalline solid (52 %), mp 102 °C, ν_{max}: 3310, 2945, 1763, 1661, 1532, 1366, 1221, 904, 835 cm^{-1}, UV (λ_{max}): 300 nm, δ_H (300 MHz, $CDCl_3$): 7.55 (d, 1H at C_2), 7.30 (s, 1H, N$\underline{H}$CO), 7.15 (d, 1H at C_4), 7.00 (d, 1H at C_5), 2.35 (t, merged with –$OCOCH_3$ signal, 2H, $NHCOC\underline{H}_2$-), 2.30 (s, 3H, –$OCOCH_3$), 1.75 (m, 2H, -$C\underline{H}_2$-CH_3), 1.60 (d, 1H at tetra substituted carbon), 1.00 (t, 3H, -$C\underline{H}_3$). δ_c (50 MHz, $CDCl_3$): 13.3, 18.4, 21.2, 39.3 (methyl and methylene C), 97.4 (tetra substituted C), 121.1, 122.0, 135.8, 146.6 (four olefinic C), MS m/z: 237 (M^+), 220, 178. Elemental analysis: Found C; 50.69 %, H; 6.28 %, N; 6.10 % requires C; 50.53 %, H; 6.33 %, N; 5.90 % for $C_{12}H_{15}NO_4$.

Bis(4-acetoxy-3,5-dimethylphenyl)methyl Acetate (32): White crystalline solid (51 %), mp 139 °C, ν_{max}: 3469, 3016, 2929, 1749, 1607, 1370, 1144 cm^{-1}, UV (λ_{max}): 250 nm, δ_H (300 MHz, $CDCl_3$): 7.02 (s, 4H, aromatic Hs), 6.75 (s, 1H, methane proton), 2.26 (sharp s, 6H, acetate methyl protons), 2.15 (s, 3H, –OCOC<u>H</u>$_3$ on the central tetra-substituted carbon), 2.14 (s, 12H, -C<u>H</u>$_3$ on aromatic ring). δ_c (75 MHz, $CDCl_3$): 16.6, 20.7, 21.6, 76.1, 127.5, 130.5, 137.6, 148.0, 168.9, 170.1. MS m/z: 398 (M^+), 339 (base peak, M-60, loss of acetic acid), 297 (loss of CH_3CO), 255 (loss of another CH_3CO). Elemental analysis: Found C; 68.93 %, H; 6.43 %; requires C; 69.34 %, H; 6.53 % for $C_{23}H_{26}O_6$.

Bis(3,5-dimethyl-3-acetoxy-4-oxocyclohexa-1,5-dienyl)methane (33)

LTA (2.66 gm, 0.006mol) was added to a solution of bis(3,5-dimethyl-4-hydroxyphenyl)methane (2) (0.5 gm, 0.002mol) in dry benzene (30mL) in portions with constant stirring. The reaction mixture was stirred for 1 h at room temperature after which it was diluted with ethyl acetate (150mL) and stirred further for 15 min. Removal of the residue by filtration and concentration of the filtrate furnished a pale yellow liquid, which was chromatographed over a column of silica gel. Elution of the column gave **(33)** as a light yellow crystalline solid (45%). Mp 183–184 °C, ν_{max} : 2994, 2919, 1734, 1669, 1437, 1371, 1253, 1225, 1060, 859, and 762 cm^{-1}, δ_H (300 MHz, $CDCl_3$); 1.37 (s, 6H, methyl protons), 1.92 (s, 6H, olefinic methyl protons), 2.06 (s, 6H, acetate methyl protons), 3.05 (s, 2H, methylene protons), 5.86 (s, 2H, olefinic H), 6.59 (s, 2H, olefinic H). δ_c (50 MHz, $CDCl_3$): 15.90, 21.07, 24.63, 40.51, 78.93, 131.26, 134.61, 137.03, 139.85, 169.91, 199.31. M/z: 372.0 (M^+), 313 (M-59) (loss of acetate ion, base peak), (M-119) (loss of two acetate ions). Elemental analysis found: C, 67.71%; H, 6.44%; requires C, 67.74%; H, 6.45% for $C_{21}H_{24}O_6$.

III.5 CONCLUSION

A single step procedure for the oxidative acylation of phenols having different types of reactive functional groups and structural variations like aldehyde, anilide, etc. is reported. Vanillin, 4-methyl-7-hydroxy coumarin, 4-hydroxy-4'-chlorobenzophenone, 4-hydroxy butyranilide etc, were treated with sodium metaperiodate in acetic anhydride at different temperatures and gave corresponding acetoxy-cyclohexadienone as single final product with moderate yield. This suggests selective oxidation and ortho acetylation of the phenol without affecting the remaining sensitive functional groups on the ring in a single step.

A simple one-pot method for the preparation of acetoxy-2,4-cyclohexadienones has been demonstrated. A novel triacetate or bis(4-acetoxy-3,5-dimethylphenyl)methyl acetate has also been prepared using the present method from tetramethyl bisphenol-F.

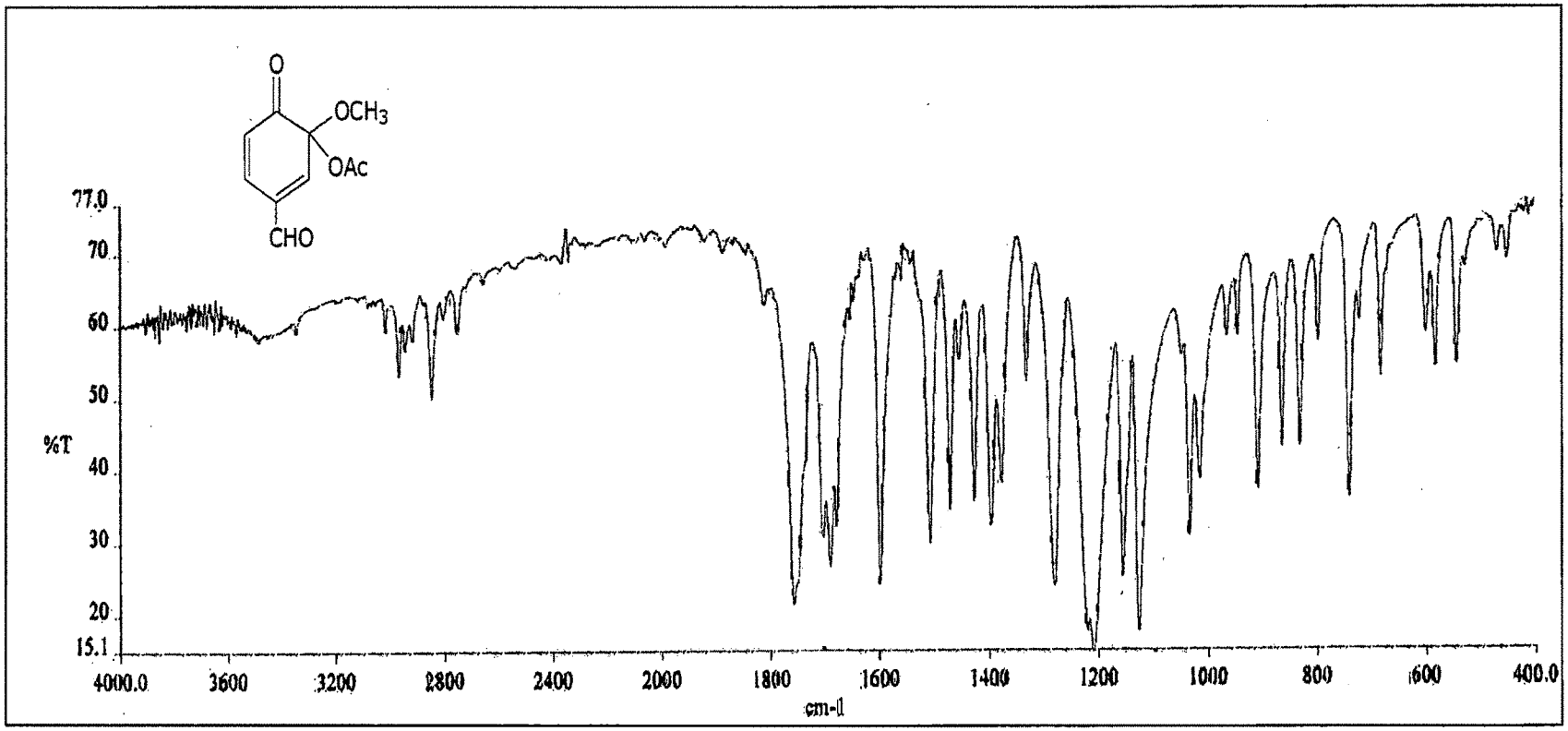


Figure III.5: FTIR Spectrum of the compound 24

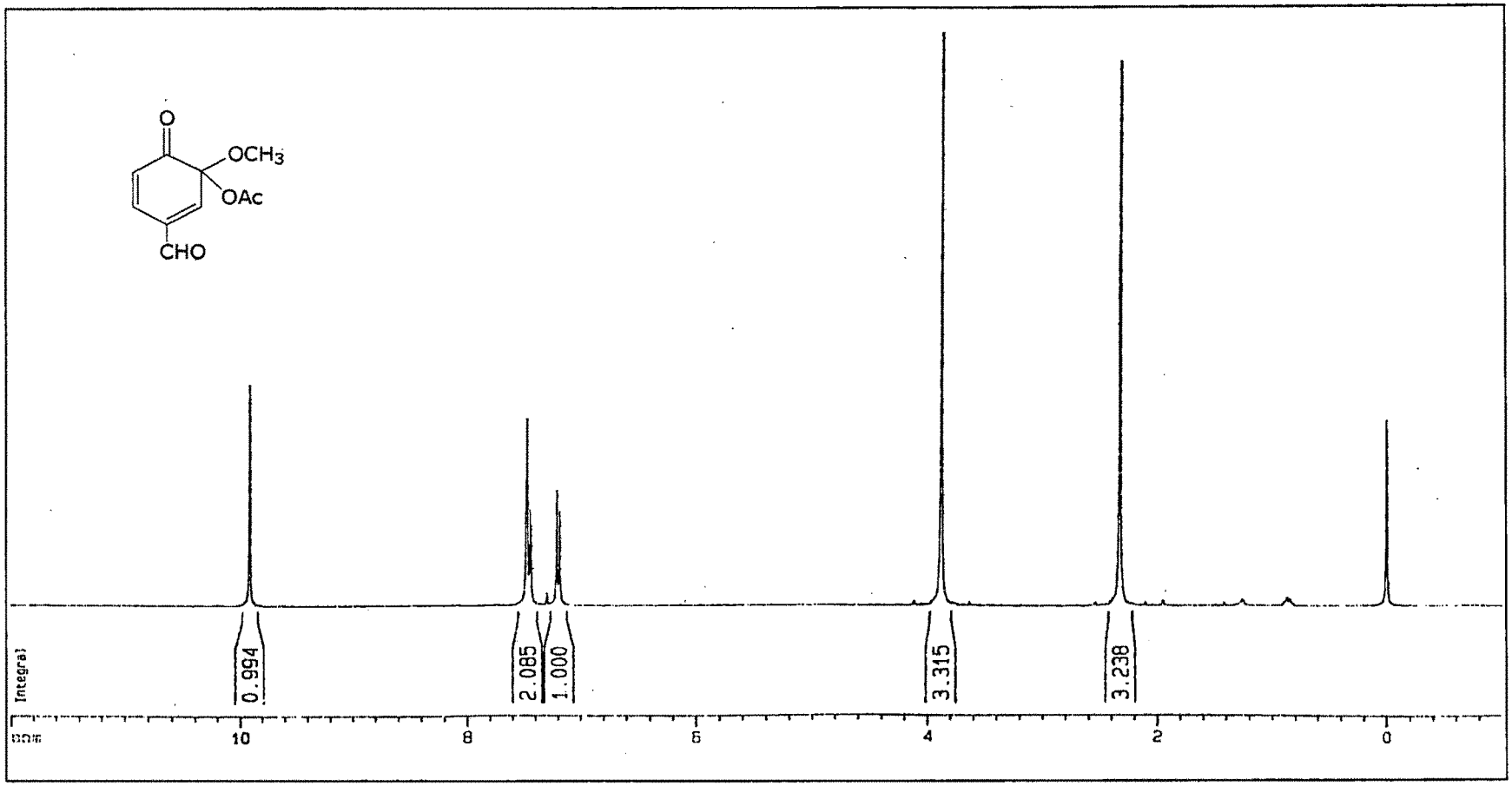


Figure III.6: PMR Spectrum of the compound 24

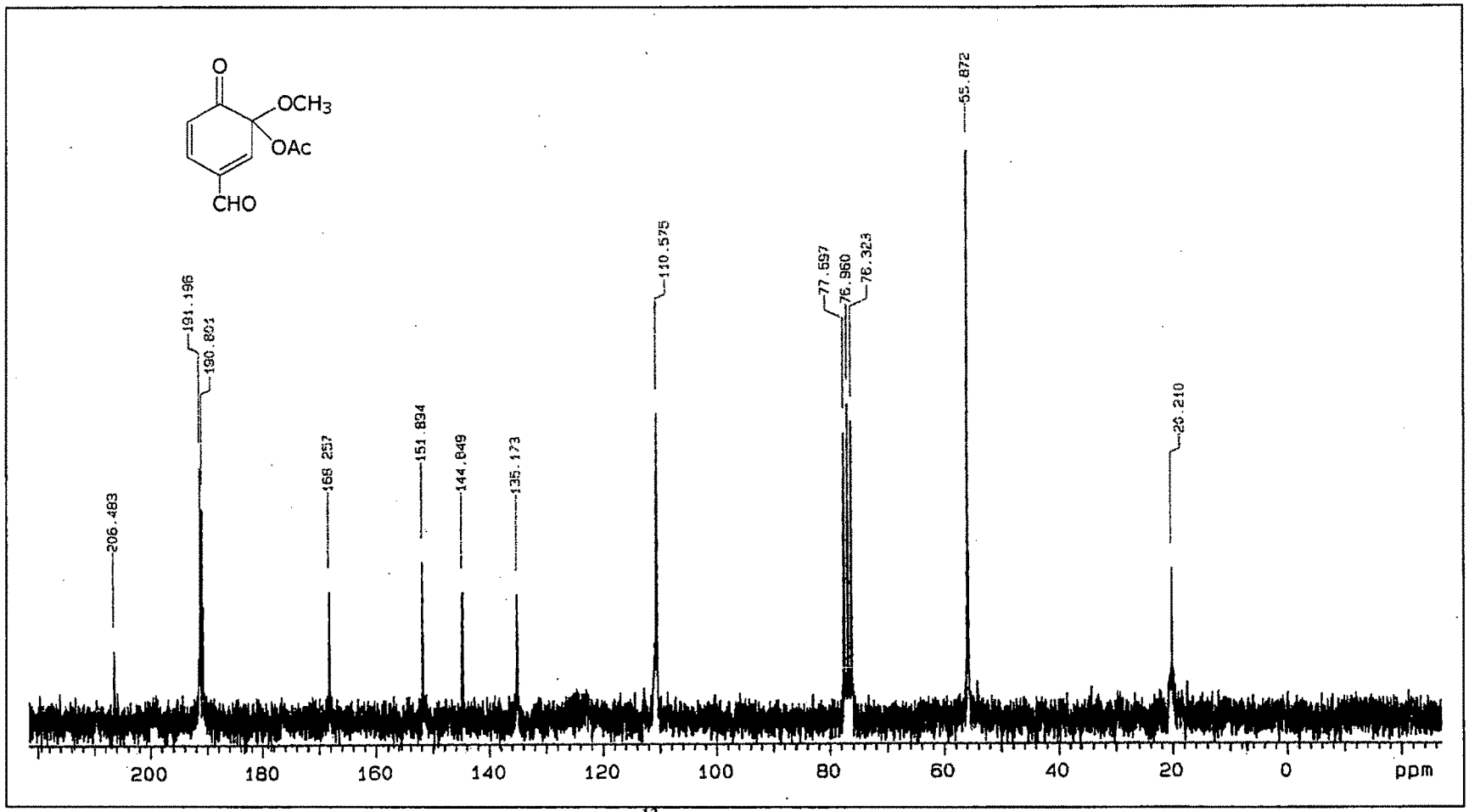


Figure III.7: ^{13}C NMR of the compound 24

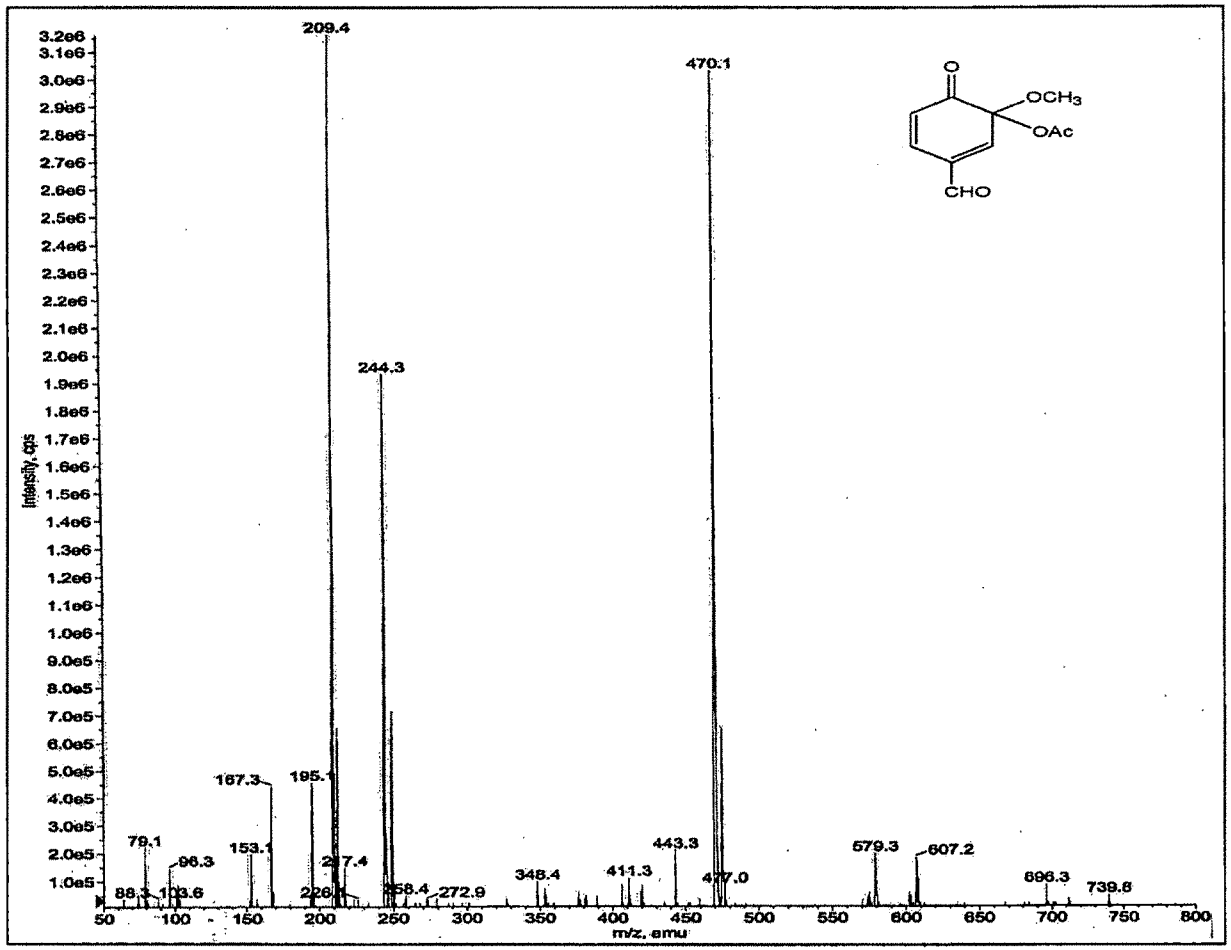


Figure III.8: Mass spectrum of the compound 24

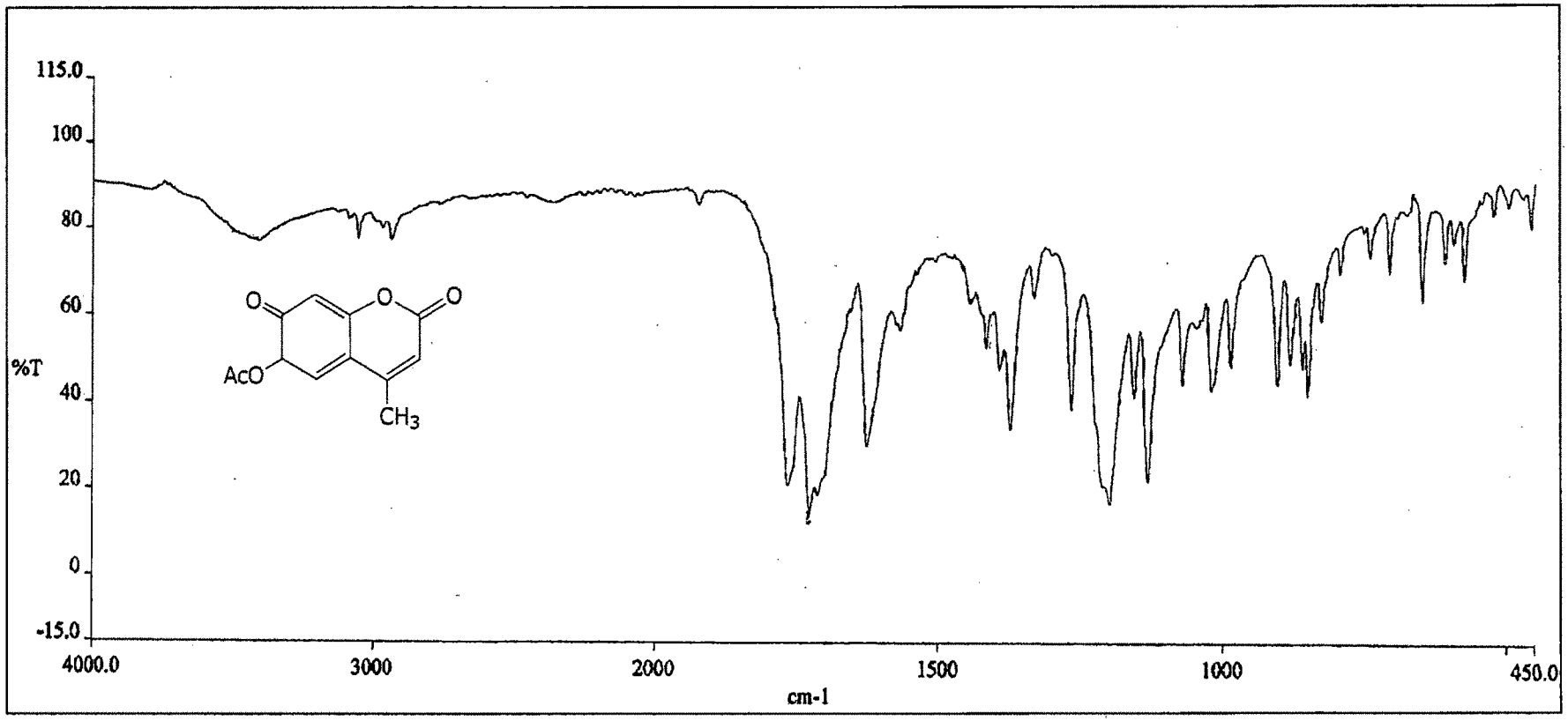


Figure III.9: FTIR Spectrum of the compound 26

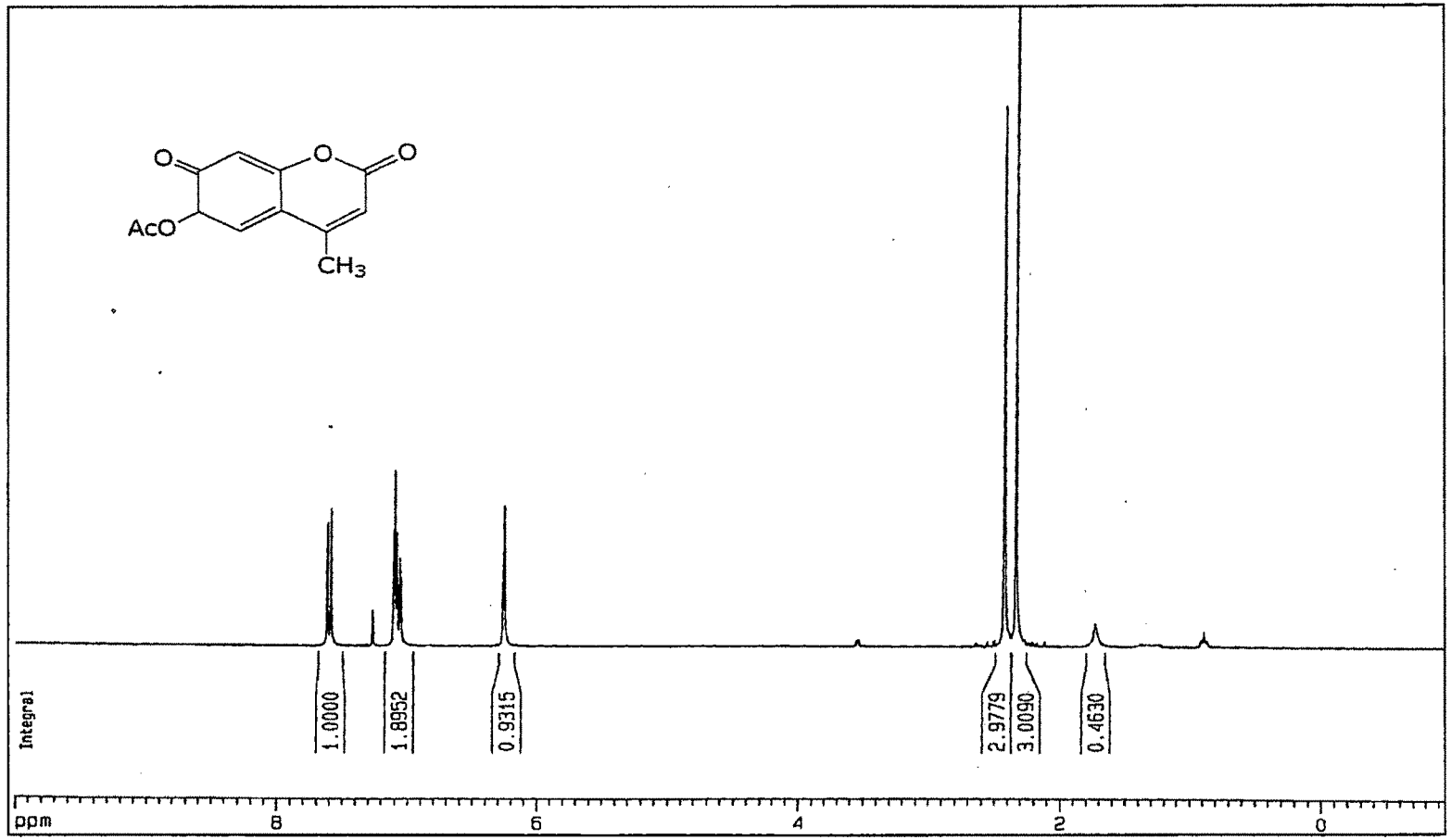


Figure III.10: PMR Spectrum of the compound 26

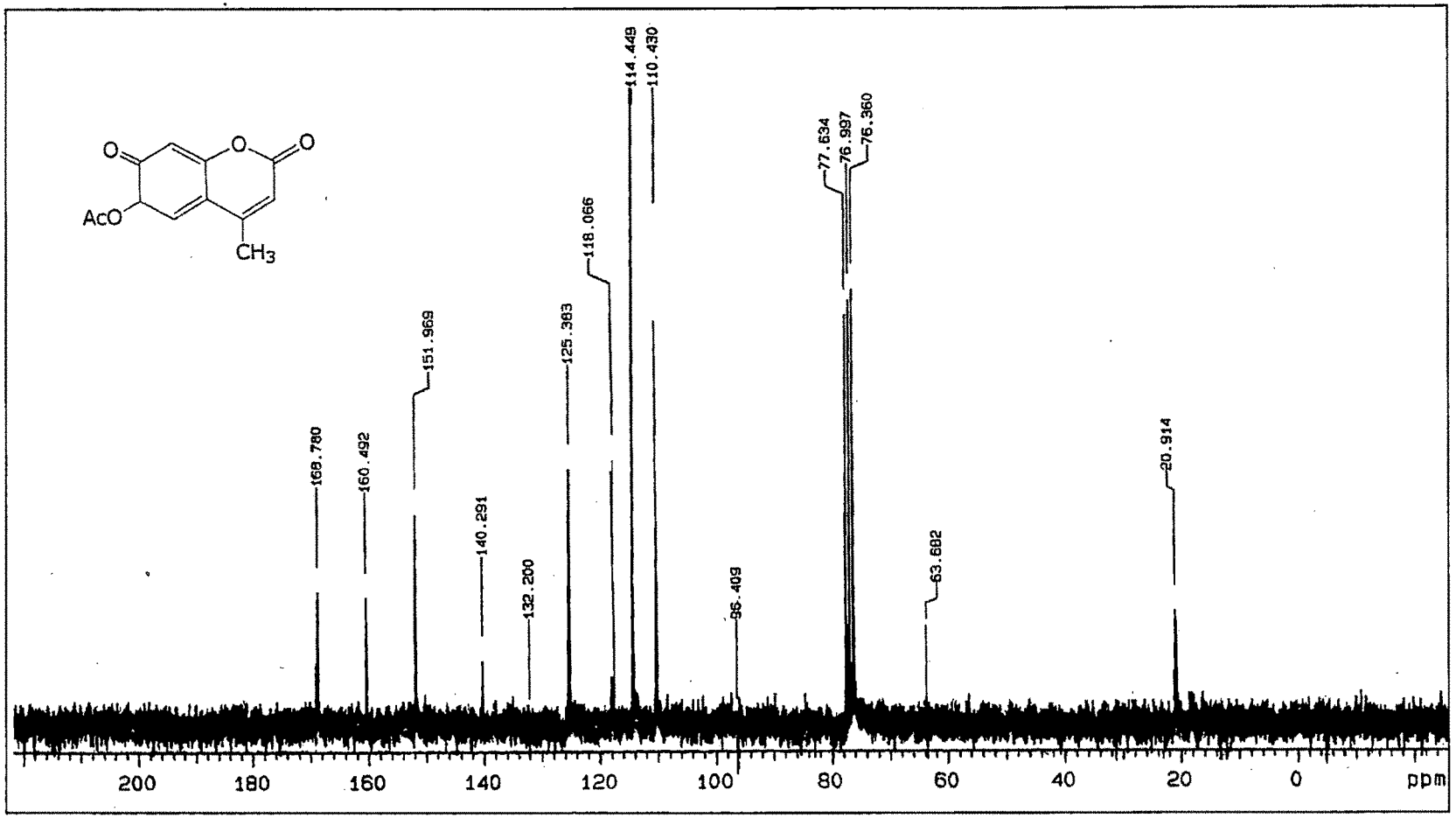


Figure III.11: ^{13}C NMR of the compound 26

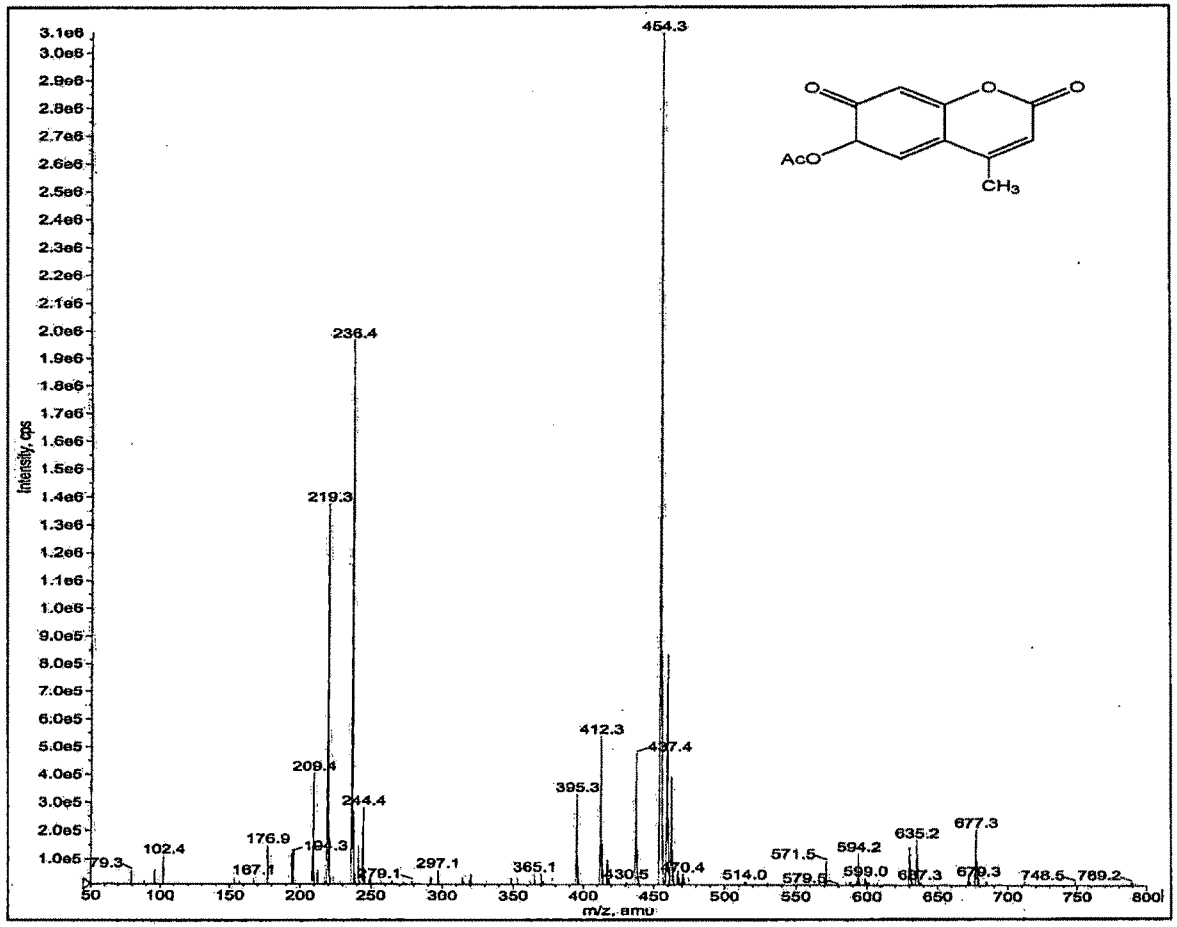


Figure III.12: Mass spectrum of the compound 26

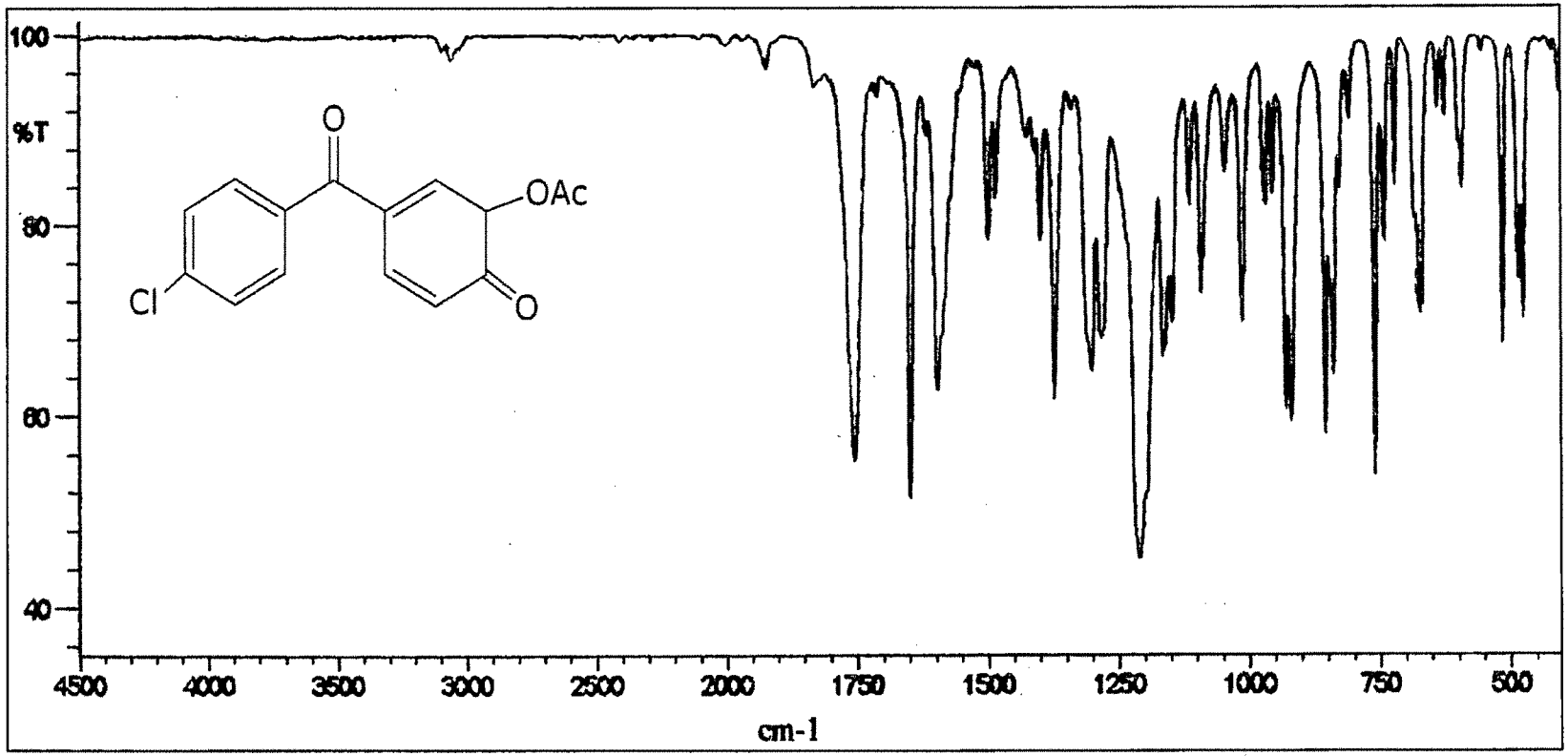


Figure III.13: FTIR Spectrum of the compound 28

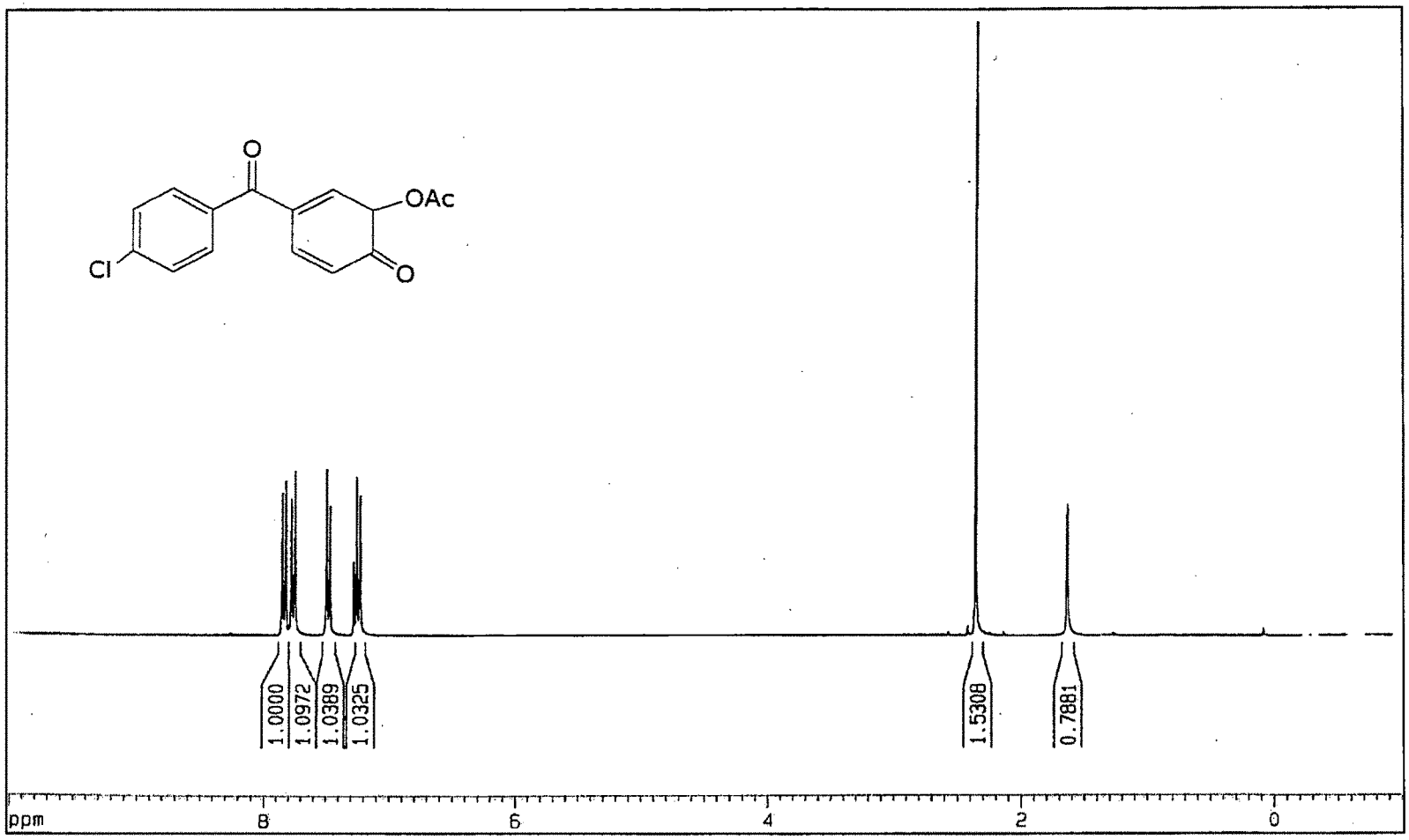


Figure III.14: PMR Spectrum of the compound 28

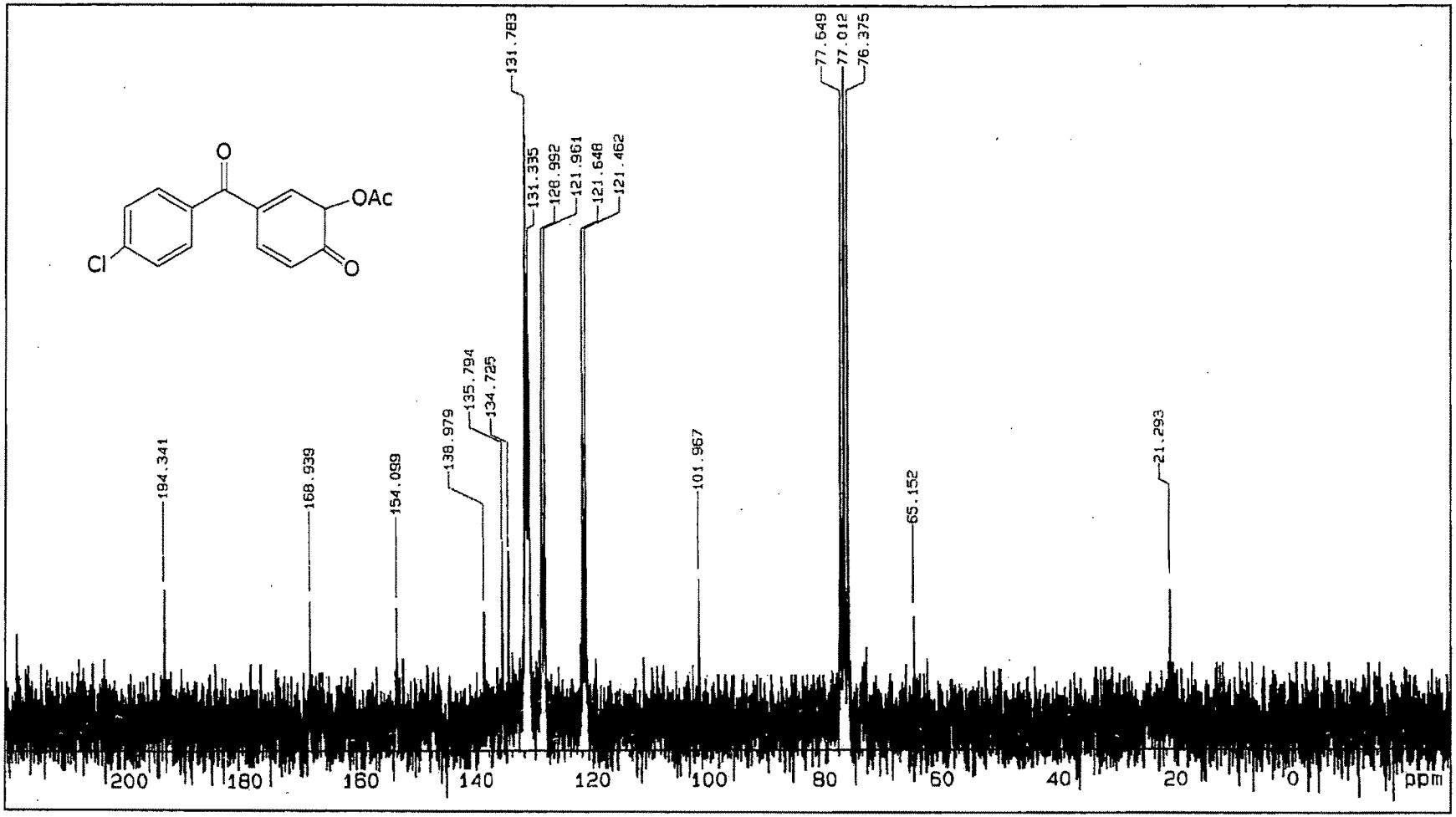


Figure III.15: ^{13}C NMR of the compound 28

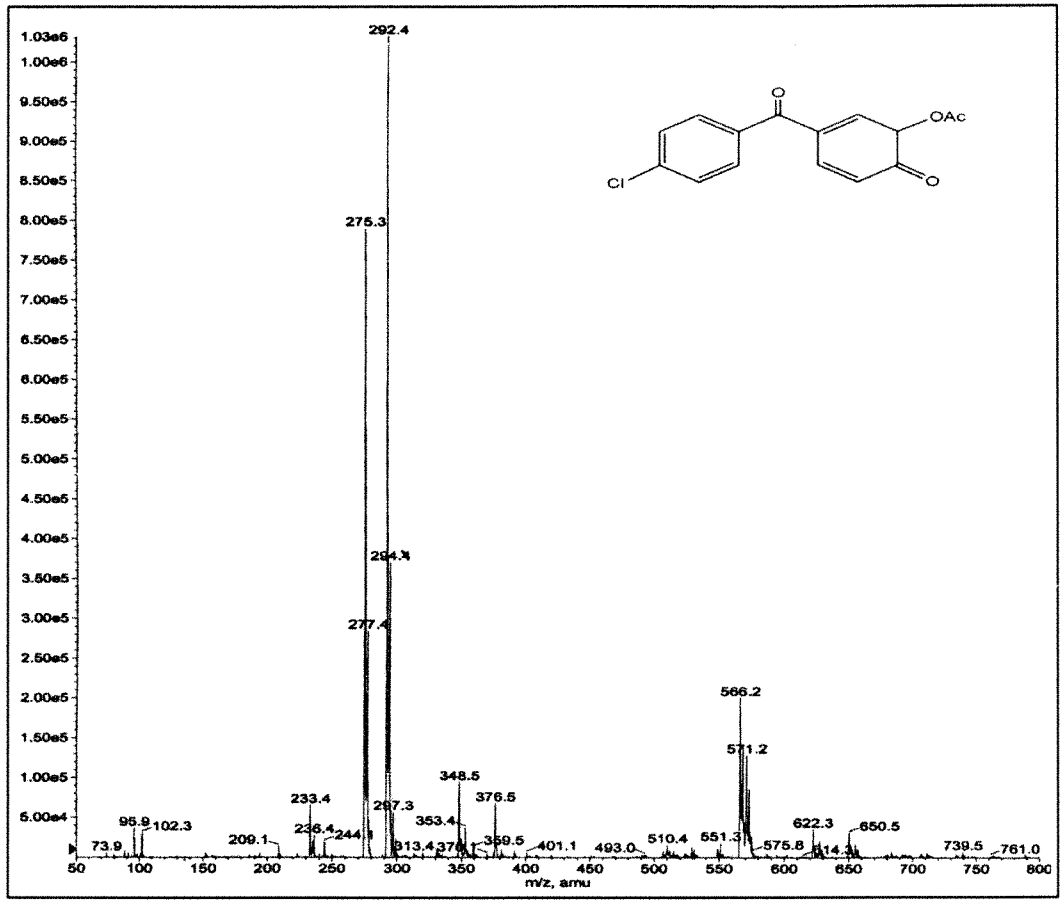


Figure III.16: Mass spectrum of the compound 28

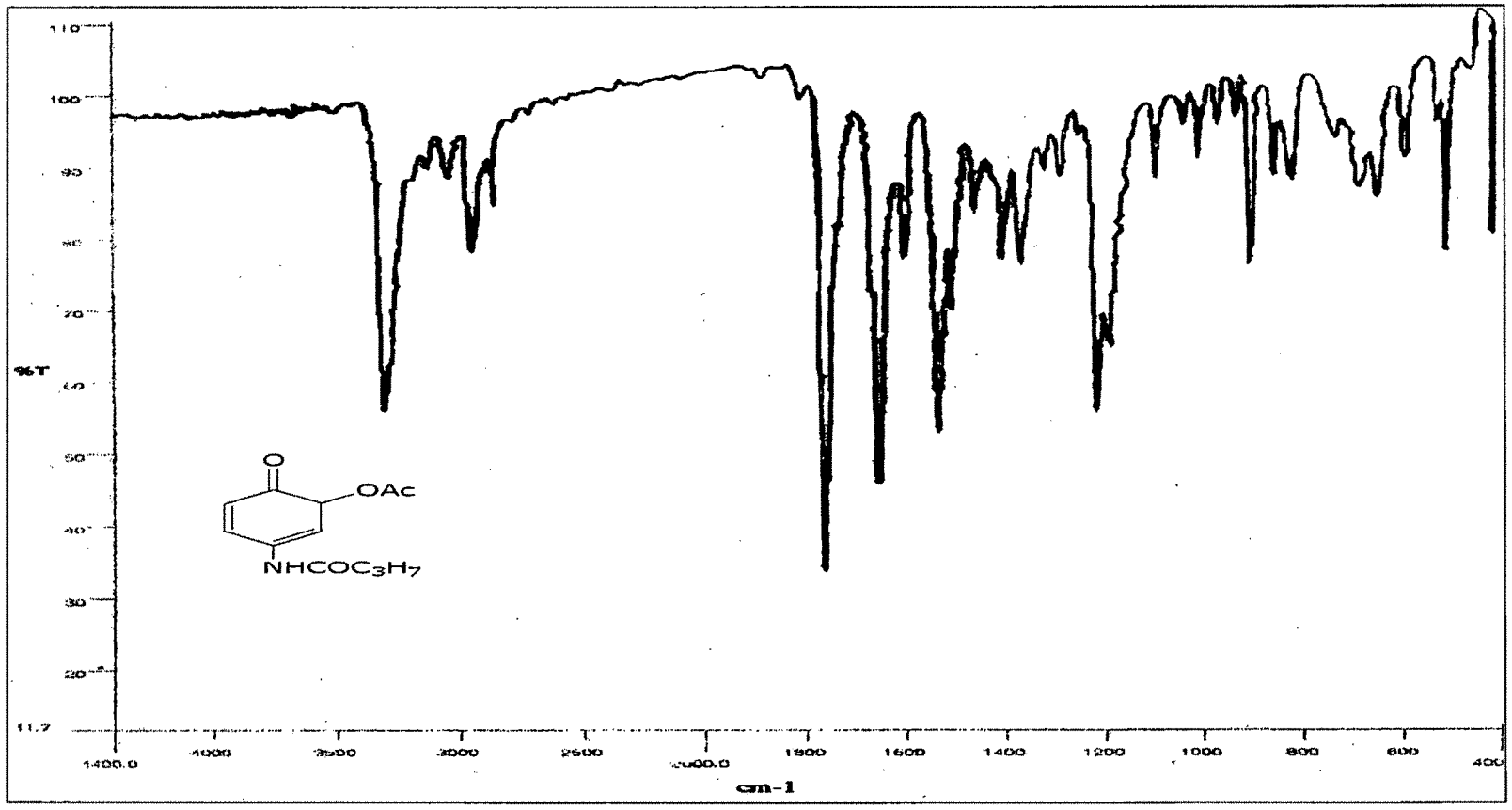


Figure III.17: FTIR Spectrum of the compound 30

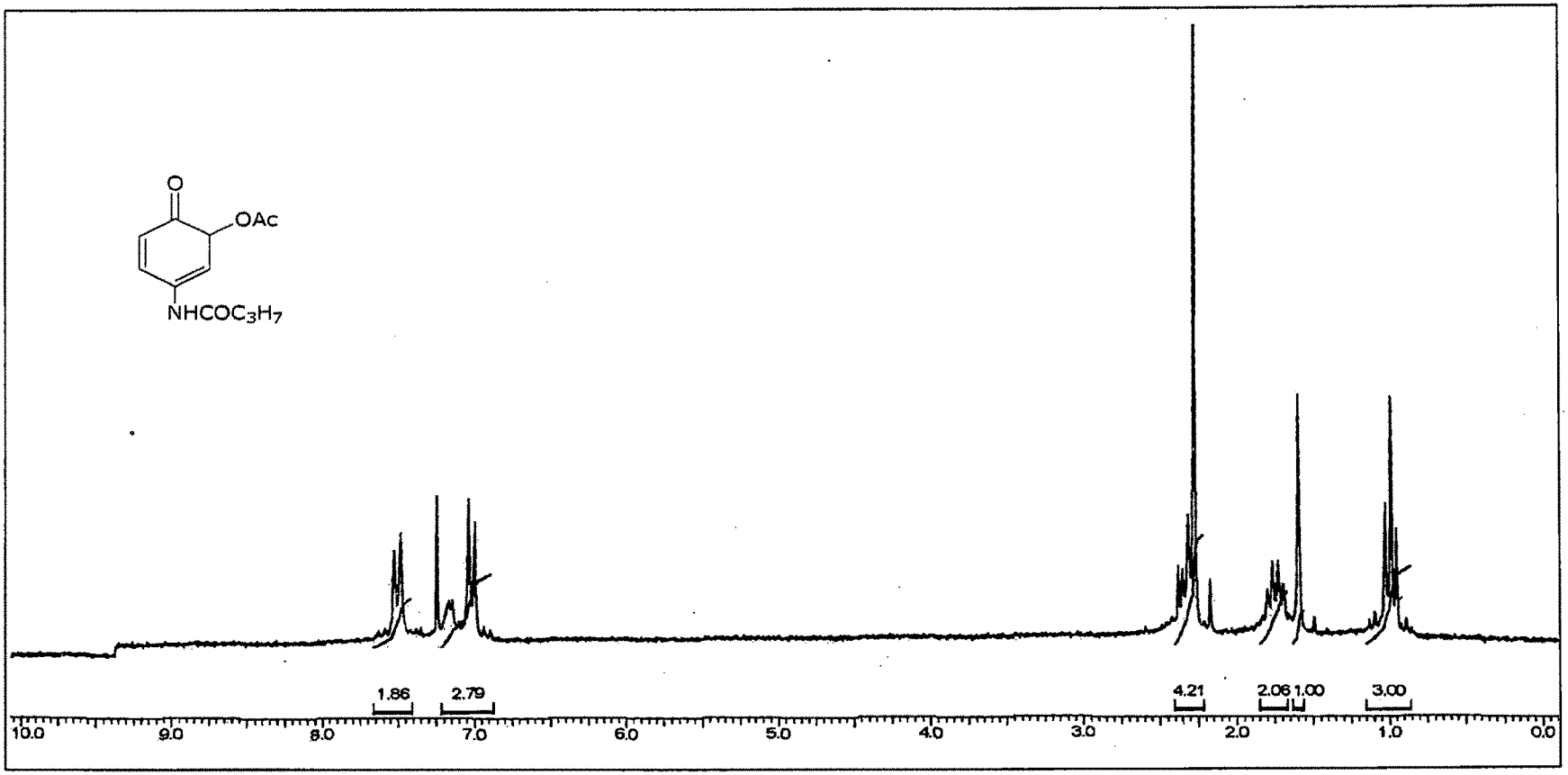


Figure III.18: PMR Spectrum of the compound 30

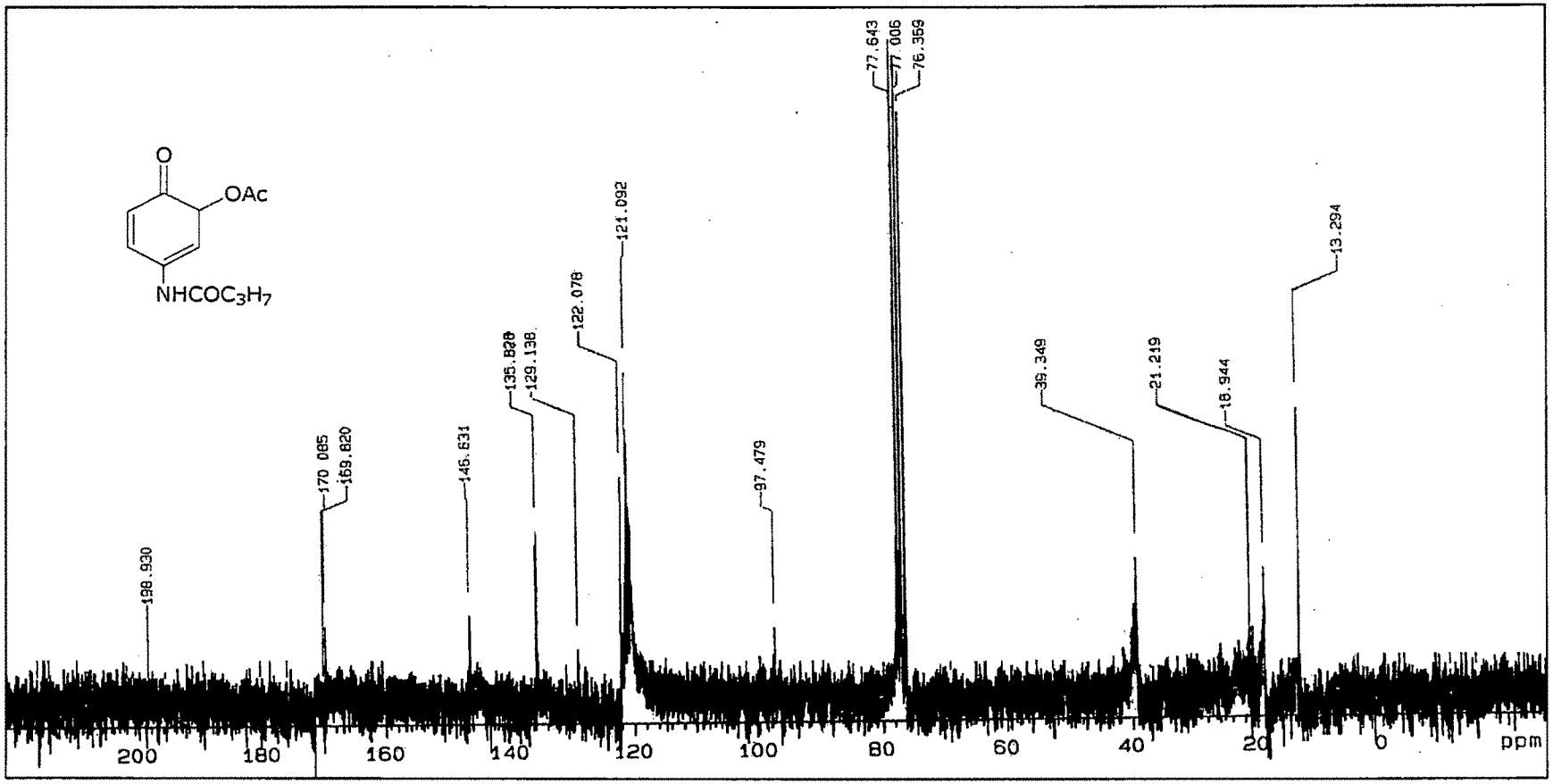


Figure III.19: ^{13}C NMR of the compound 30

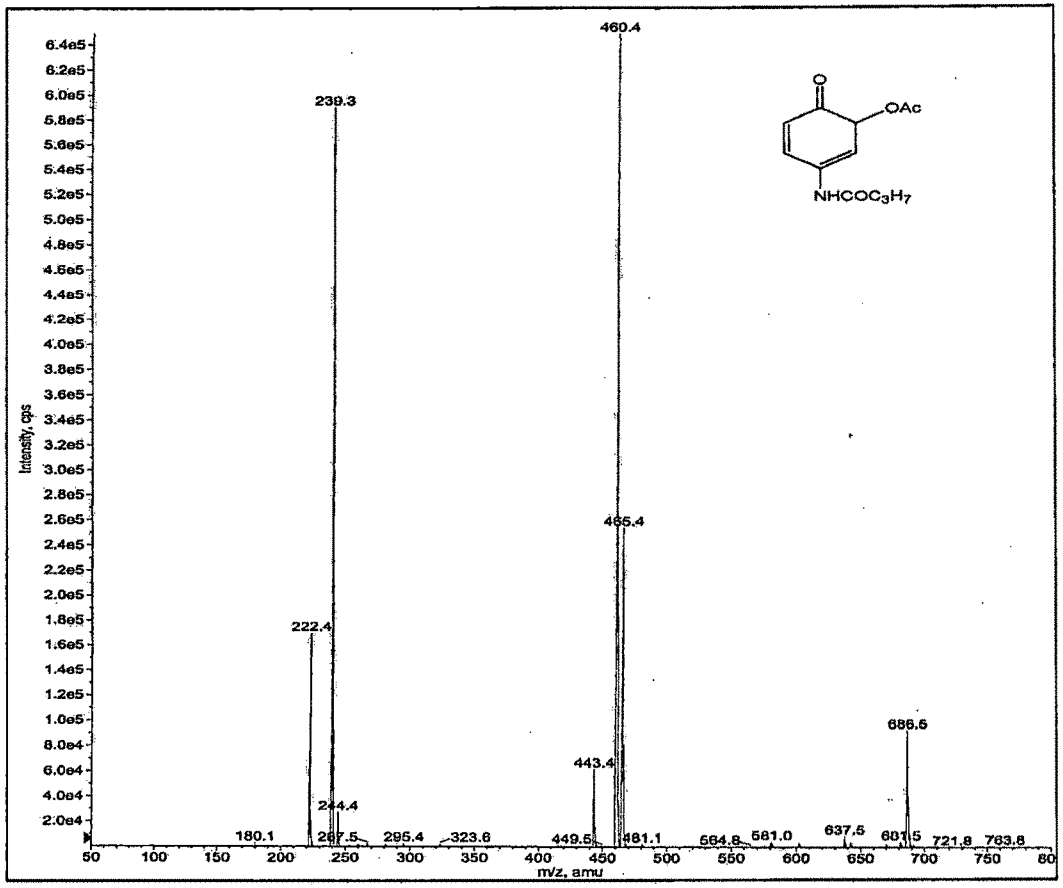


Figure III.20: Mass spectrum of the compound 30

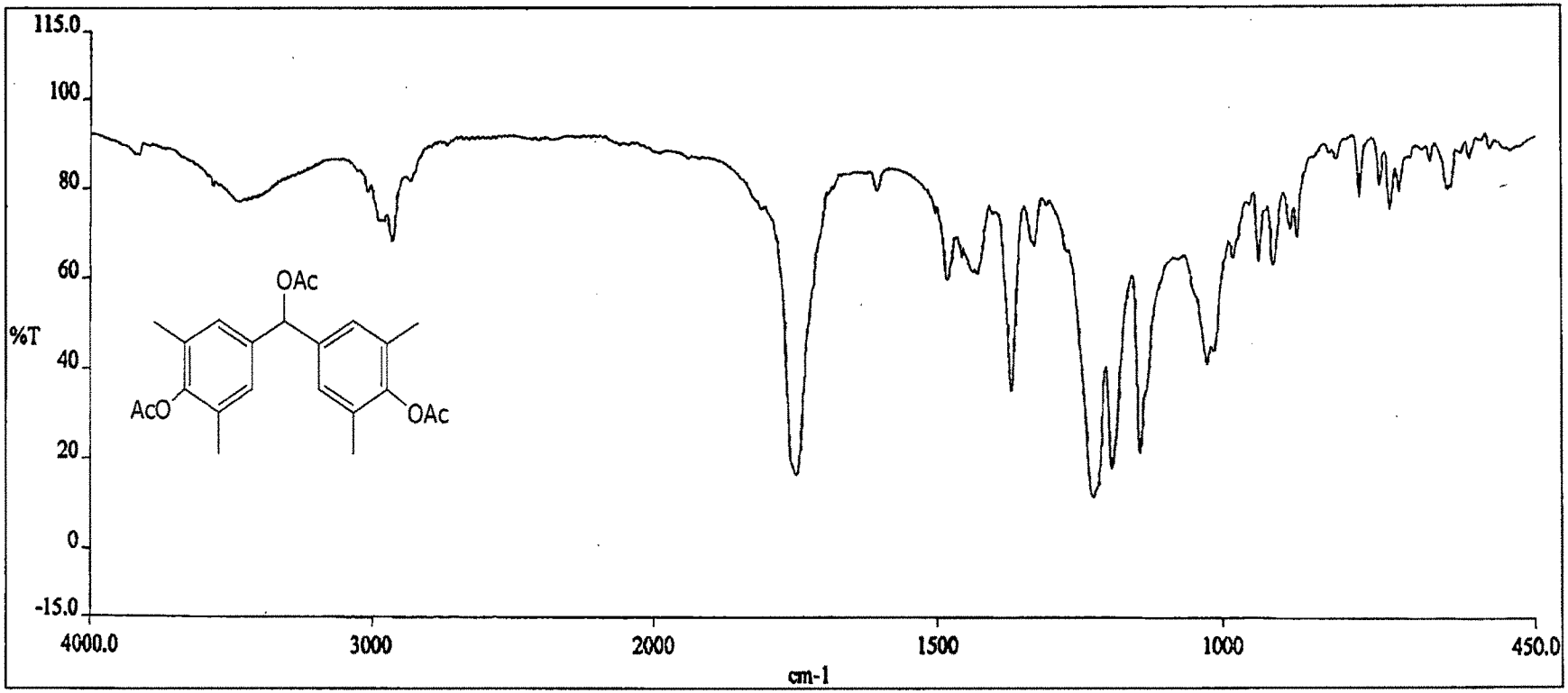


Figure III.21: FTIR Spectrum of the compound 32

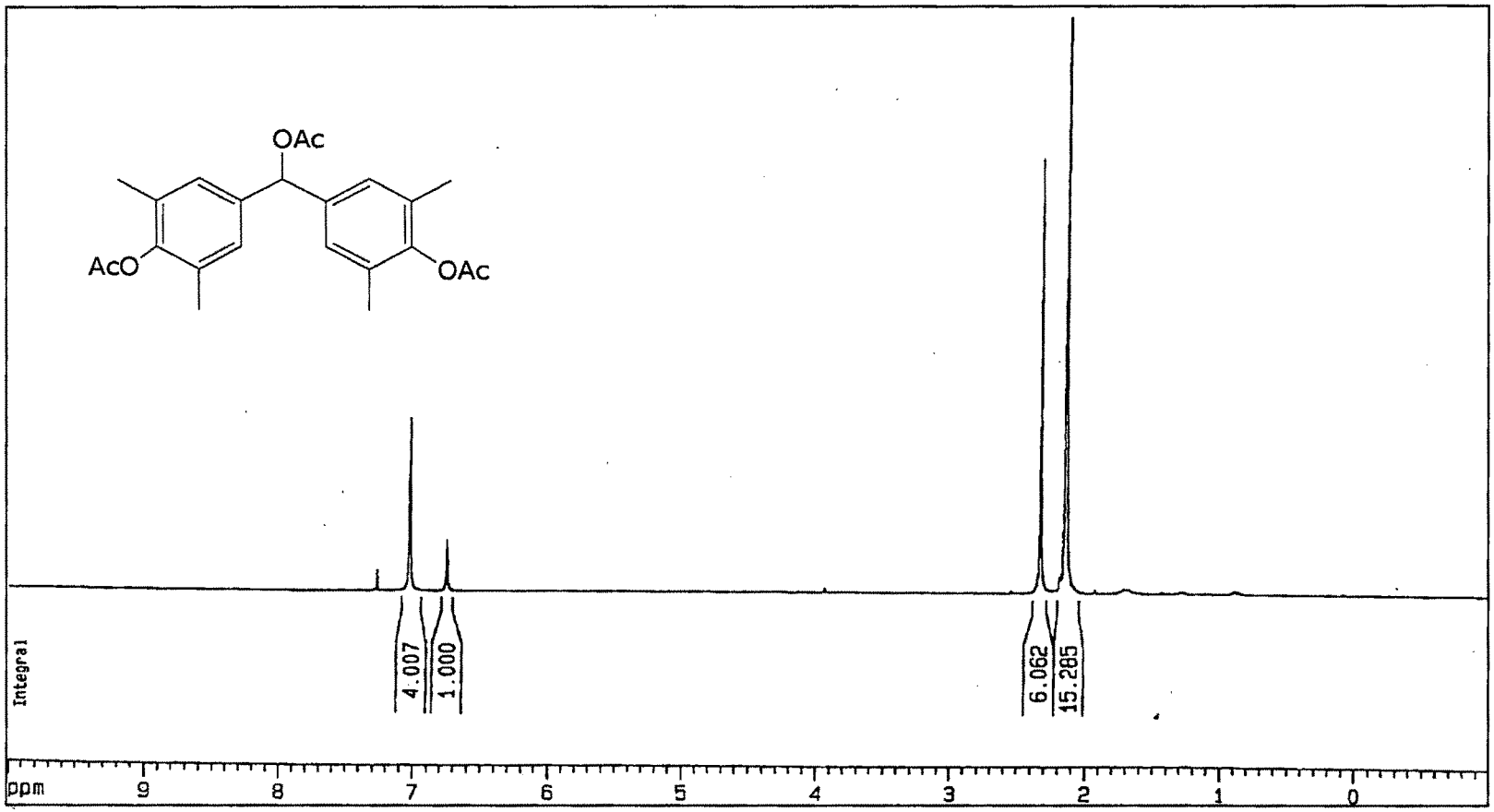


Figure III.22: PMR Spectrum of the compound 32

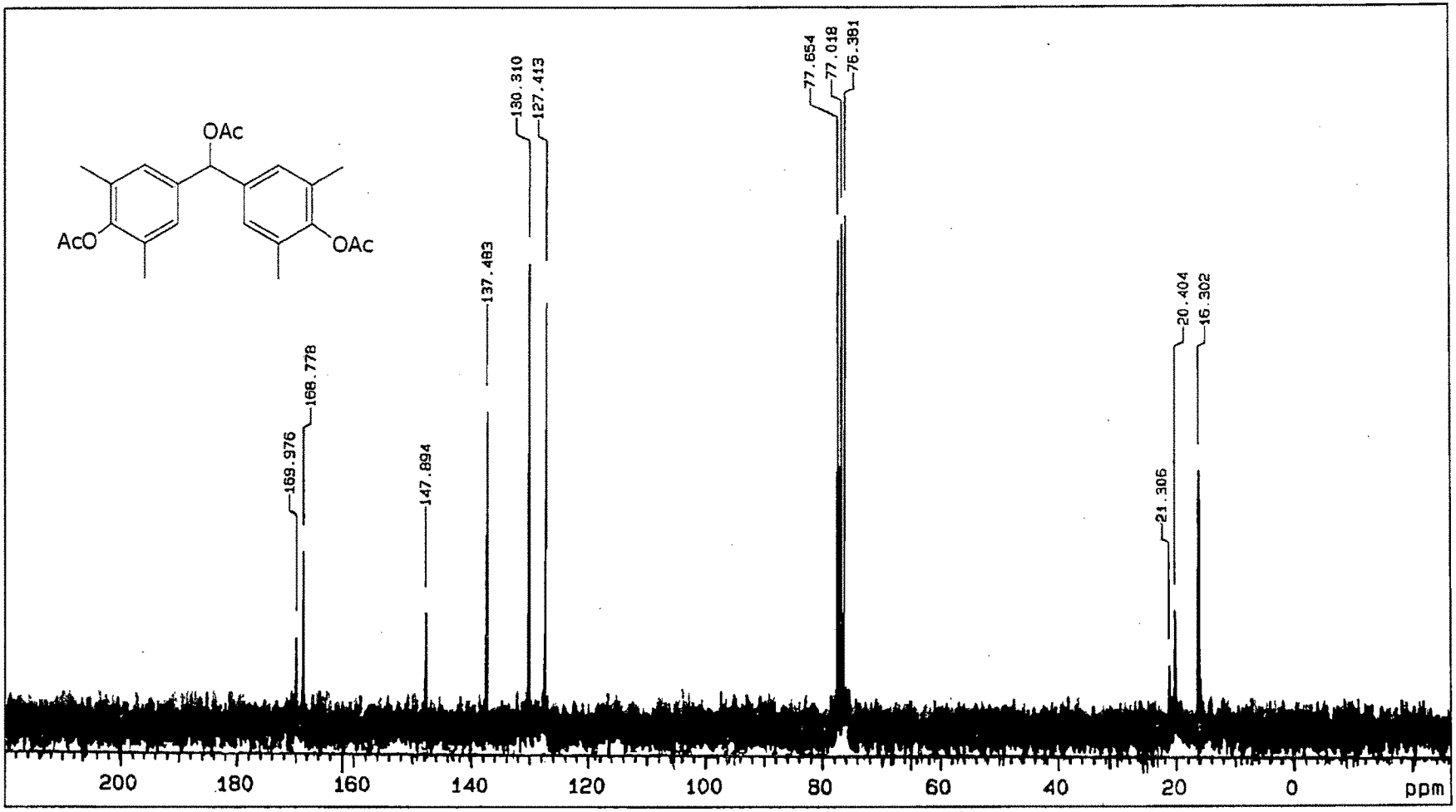


Figure III.23: ^{13}C NMR of the compound 32

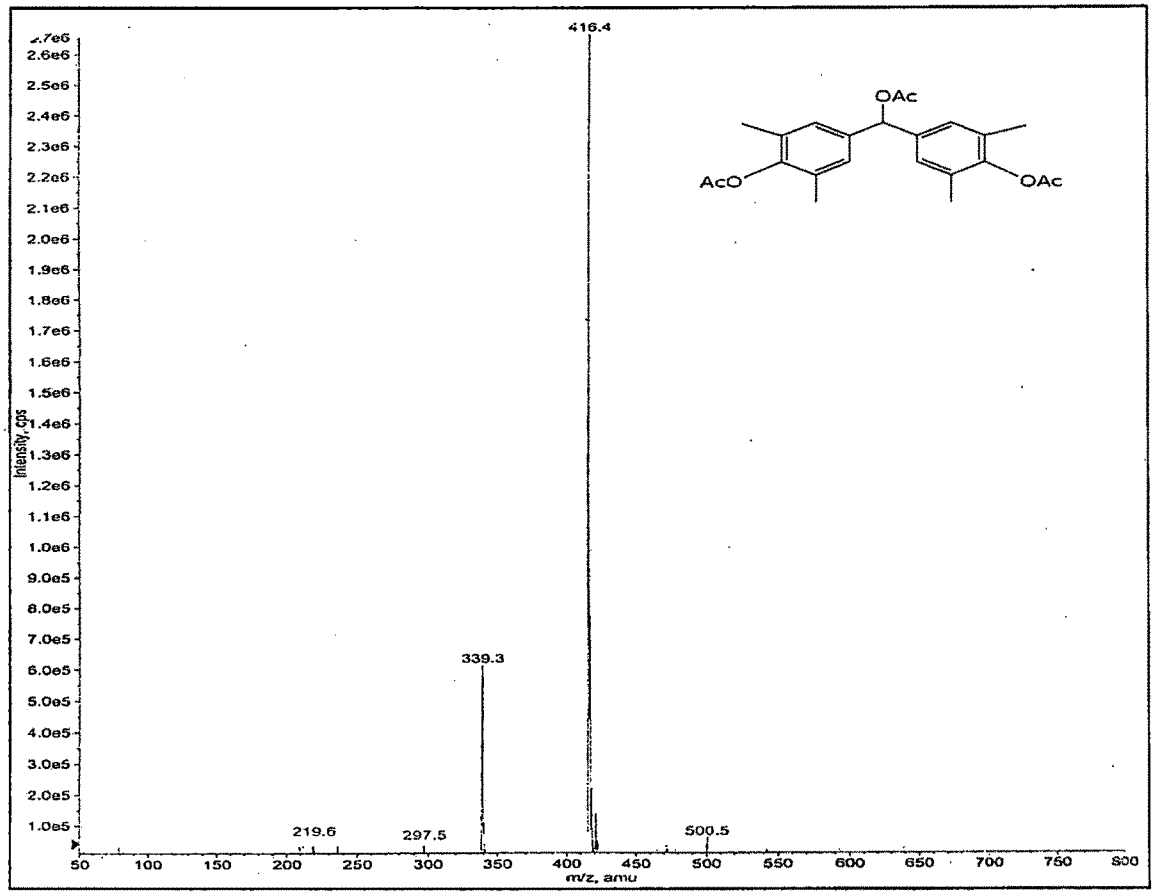


Figure III.24: Mass spectrum of the compound 32

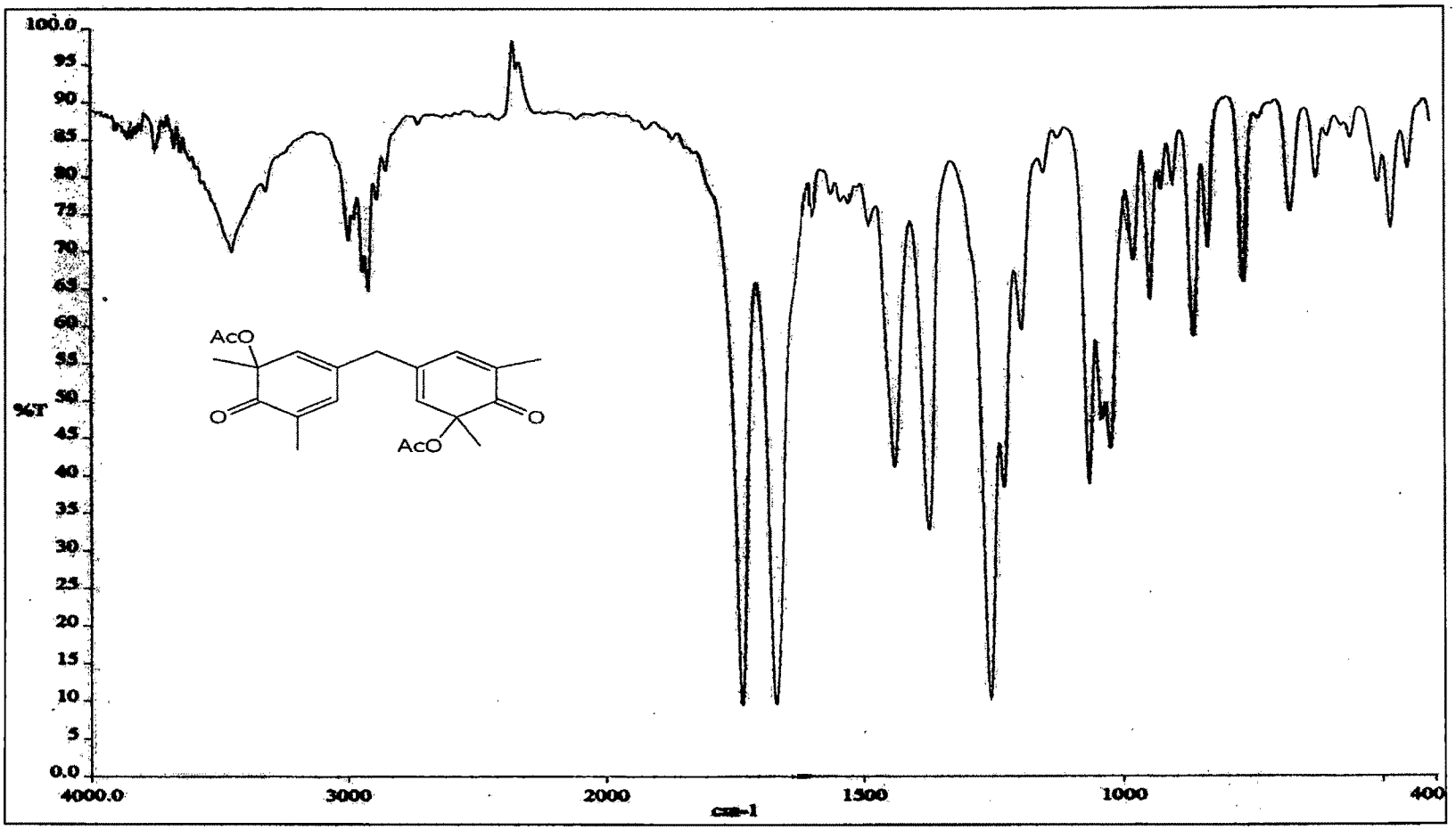


Figure III.25: FTIR Spectrum of the compound 33

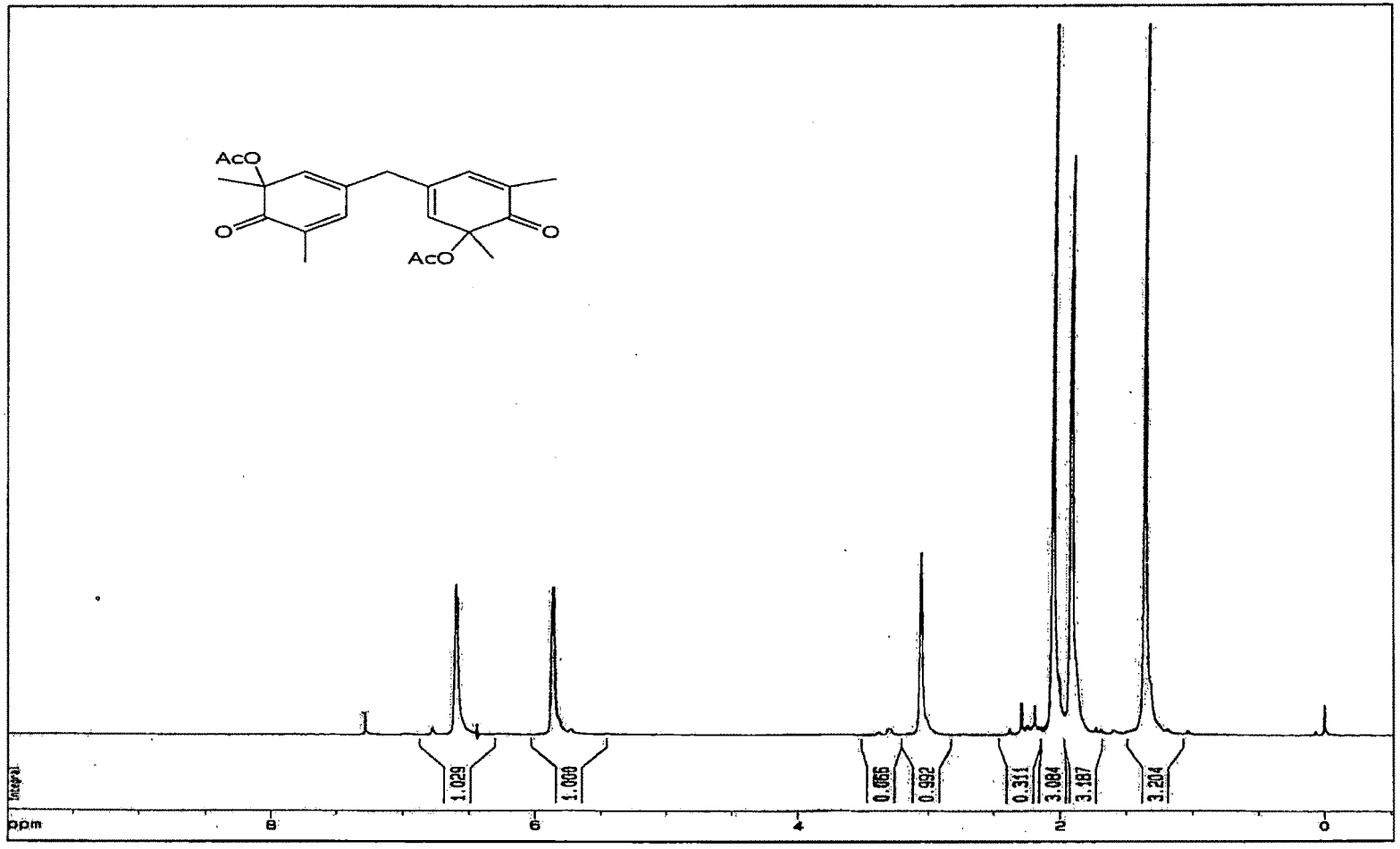


Figure III.26: PMR Spectrum of the compound 33

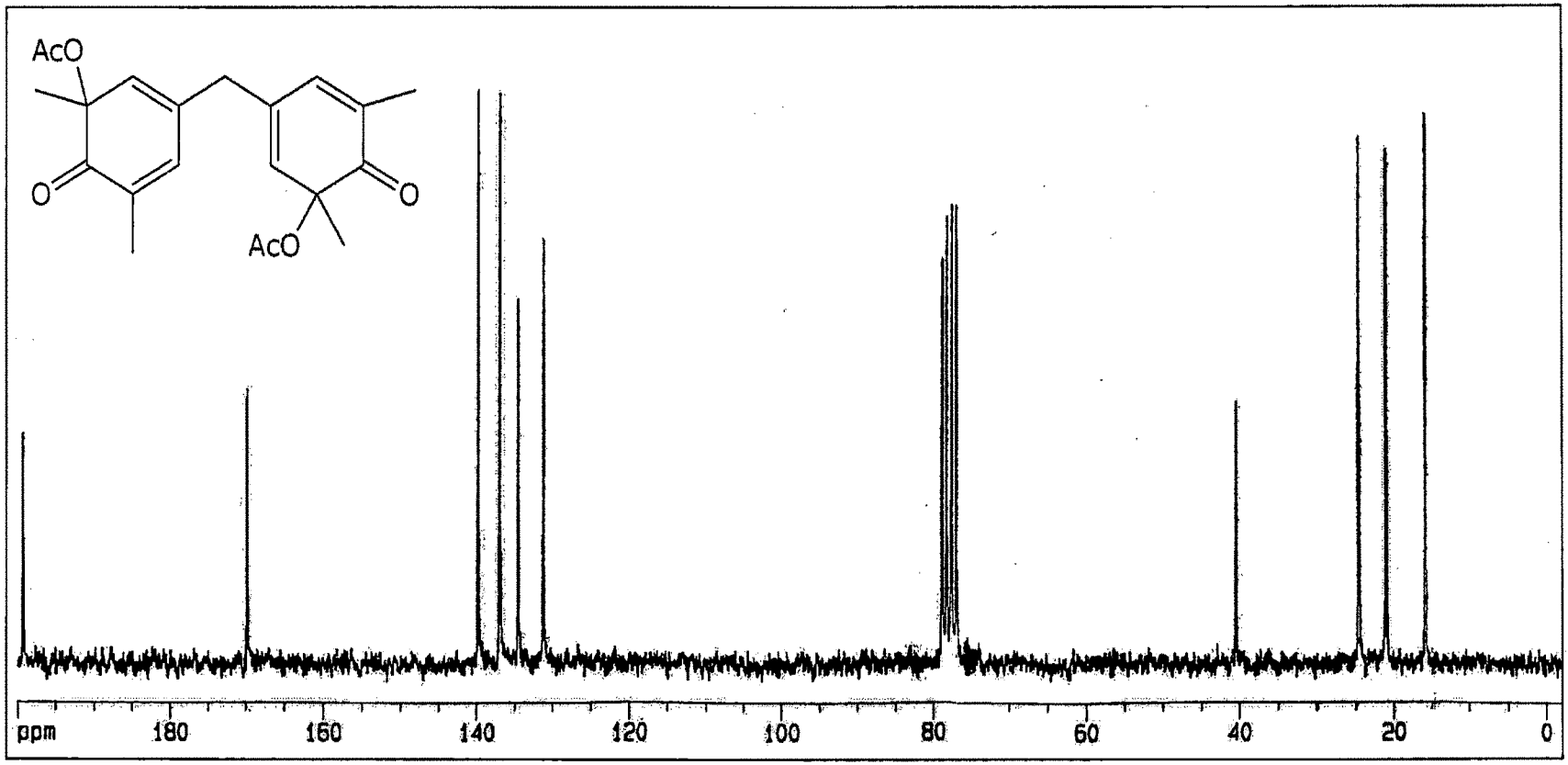


Figure III.27: ^{13}C NMR of the compound 33

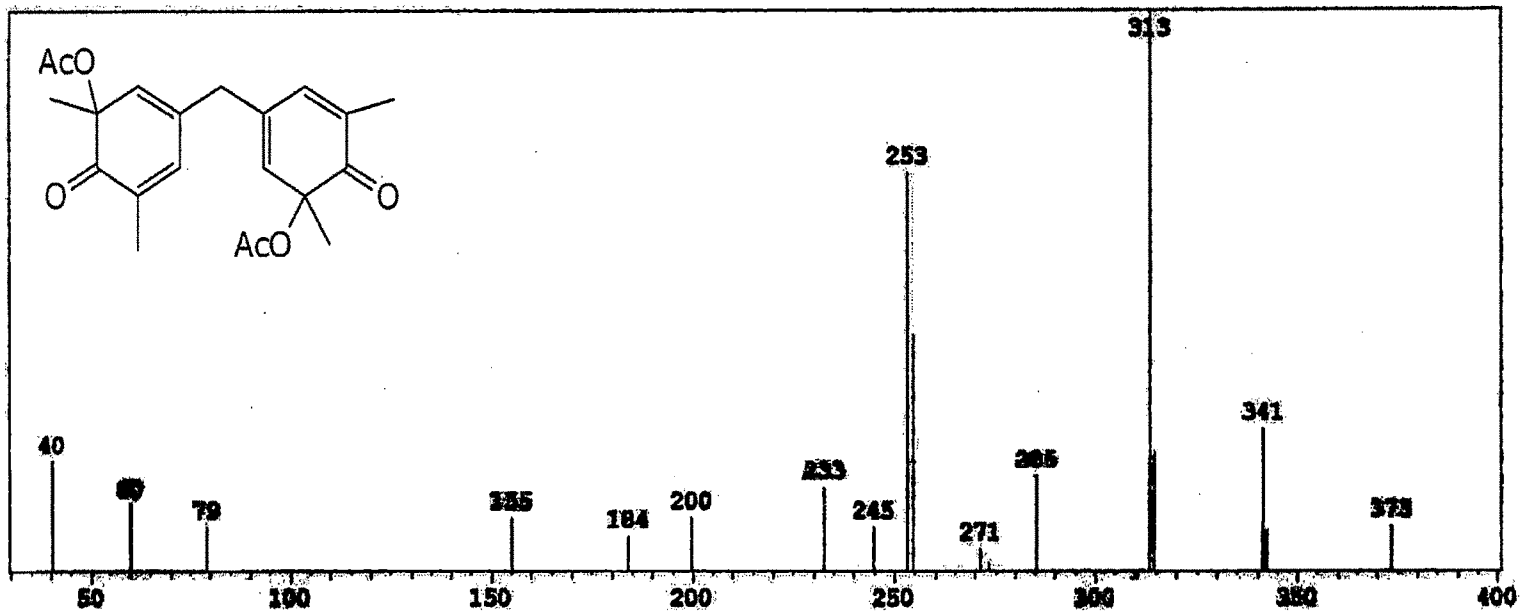


Figure III.28: Mass spectrum of the compound 33

III.6 REFERENCES

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