FRIEDEL-CRAFTS ALKYLATION OF INDOLES WITH ENONES: SYNTHESIS AND CHARACTERIZATION OF 3-SUBSTITUTED INDOLES

A DISSERTATION

Submitted in partial fulfillment of the
requirements for the award of the degree
of
MASTER OF TECHNOLOGY
in
ADVANCED CHEMICAL ANALYSIS

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CANDIDATE'S DECLARATION

I here by declare that the work which is being presented in the dissertation entitled, **"FRIEDEL-CRAFTS ALKYLATION OF INDOLES WITH ENONES: SYNTHESIS AND CHARACTERIZATION OF 3-SUBSTITUTED INDOLES"** in partial fulfilment of the requirement for the degree of **"MASTER OF THECHNOLOGY"** submitted in the Department of Chemistry, Indian Institute of Technology Roorkee. The work has been carried out during the period from July 2007 to June 2008 under the supervision of Dr. R. K. Peddinti, Department of Chemistry, Indian Institute of Technology Roorkee, Roorkee.

I have not submitted the material presented in this dissertation report for the award of any other degree or diploma of this or any other institute/university. In keeping with the general practice of reporting scientific observation, due acknowledgement has been made wherever the work described is based on the findings of other investigators.

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Deepika Kanwar

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ABSTRACT

Indole moiety is a key constituent of many biologically important natural and unnatural compounds. Among the derivatives of indoles, 3-substituted indoloyl ketones are important building blocks for the synthesis of several natural products. Consequently, alkylation of indoles has attracted tremendous attention for simplification or improvement of the existing methods. Synthesis of 3-substituted indoles from the reaction of different indoles with enones using copper(II) chloride as a novel catalyst is described. This methodology proved to be very efficient with several sets of indoles and enones at room temperature to afford the products in reasonable yields without noticeable side reactions. All the products are characterized completely based on IR, NMR and GC-MS spectral analysis.

ABBREVIATIONS

Abbreviation	Full form
CH_3CN	Acetonitrile
AR	Analytical reagent
$SbCl_3$	Antimony chloride
Ar	Aryl (substituted aromatic ring)
$CuCl_2$	Copper(II)chloride
$CDCl_3$	Deuteriated chloroform
Hrs	Hours
$IrCl_3$	Iridium(III) chloride
LR	Laboratory reagent
$MgCl_2$	Magnesium chloride
MHz	Megahertz
mg	Milligrams
mM	Millimoles
Ph	Phenyl
r.t.	Room temperature
NaCl	Sodium chloride
TMS	Tetramethylsilane
TLC	Thin layer chromatography

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INTRODUCTION

Introduction

Indole and its myriad derivatives continue to capture the attention of synthetic organic chemists, and a large number of original indole ring syntheses and applications of known methods to new problems in indole chemistry have been reported [1]. The development of synthetic methods leading to indole derivatives has attracted much attention in organic synthesis because of their biological activities. Various indoles are components of drugs and are commonly found in molecules of pharmaceutical interest in a variety of therapeutic areas. Generally, 3-substituted indoles exhibit numerous biological activities. Since the 3-position in indoles is the preferred site for electrophilic substitution, 3-alkyl or acyl indoles are versatile intermediates for the synthesis of a wide range of indole derivatives. In fact, the 3-substituted ketones are highly interesting building blocks for the synthesis of biologically active compounds as well as natural products [2].

1.1 Examples

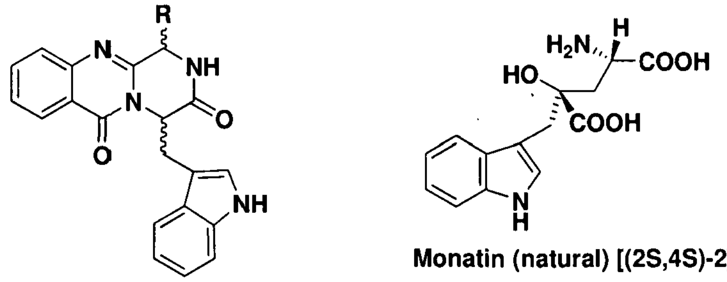
The use of indole derivatives can be divided into following categories:

1. Medicinal uses
2. Intermediates in the synthetic routes for biologically active compounds - The conjugate addition of indoles to α,β-unsaturated ketones constitutes a key reaction in the total synthesis of complex natural products
3. Ligands containing indole group

Below are a few examples showing different biological activities of indole derivatives.

a) Several fungal metabolites shown in Fig. 1 contain an indole ring along with a pyrazino[2,1*b*]quinazoline-3,6-dione moiety [3].

Glyantrypine, R = H
Fumiquinazoline F, R = CH_3 (1S,4R)
Fumiquinazoline G, R = CH_3 (1R,4R)
Fiscalin B, R = $CH(CH_3)_2$ (1S,4R)



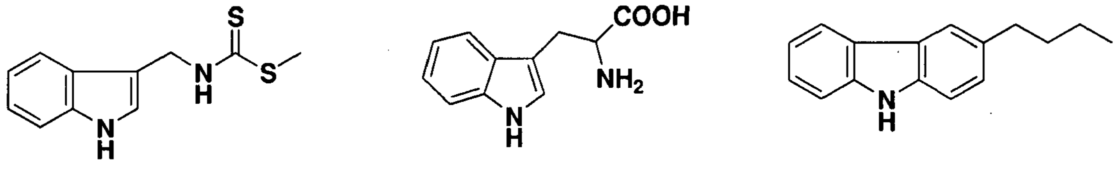
Monatin (natural) [(2S,4S)-2]

Figure 1.

b) Monatin is biologically important, naturally occurring, unusual amino acid monatin [(2*S*,4*S*)-2] , which is a high-intensity sweetener (Fig. 1) [4a].

c) Brassinin (Fig. 2) a natural product is a moderate inhibitor of indoleamine-2,3-dioxygenase (IDO), a new cancer immuno suppression target. It has also demonstrated anti fungal activity.

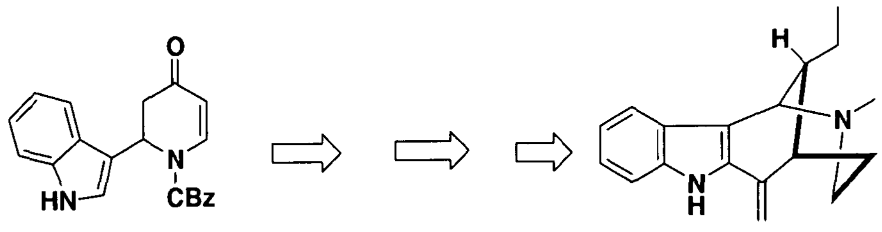
A structure activity shows that substitution of S-methyl group of brassinin with large aromatic groups provides inhibitors that are three times more potent in vitro than the most commonly used IDO inhibitor, 1-methyl tryptophan (Fig. 2). Inhibition of IDO has been also targeted for other therapies, most notably neurological disorders. A recent review summarized the range of compounds that have been tested as IDO inhibitors [4b]. Almost all IDO inhibitors retain the indole ring of the natural substrate. Currently, most potent IDO inhibitor is 3-butyl-β-carboline (Fig. 2) [5].



Brassinin **1-Methyltryptophan** **3- Butyl -β -carboline**

Figure 2.

d) A three substituted indole, 2-indolyldihydropyridone is a middle product in the synthesis route of epiuliene which is a member of strychnos indole alkaloids. These alkaloids show anti-plasmodial and cytotoxic action (Scheme 1) [6].



9

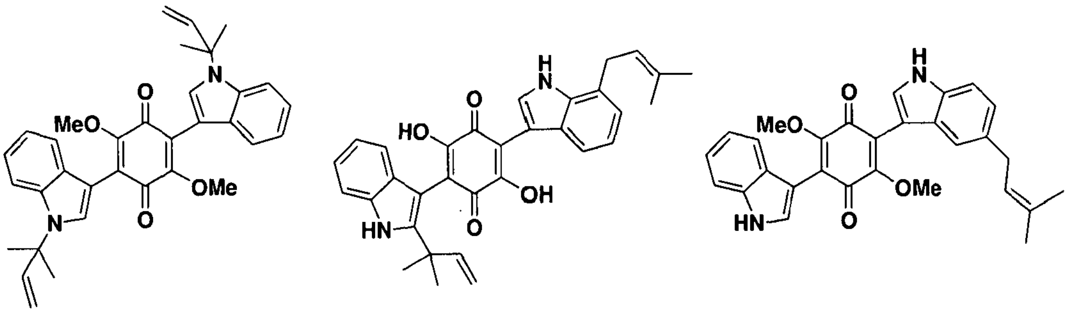
2-indolyl-dihydropyridone

10

(+/-)-20-Epiuleine

SCHEME 1

e) A large class of fungal natural products derived from *Aspergillus Pseudomassaria*, species is based upon a dihydoxy-bis-indolylquinone unit that is variously prenylated and sometimes o-methylated. Most often they are called *Asterri-quinones.* Bis-indolylquinones exhibits a range of medicinal activities like antitumor activity by asterriquinone A1, anti-diabetic activity by demethylasterri-quinone B1, antibacterial fungistatic and fungicidal properties by cochliodinol (Fig. 3) [7].



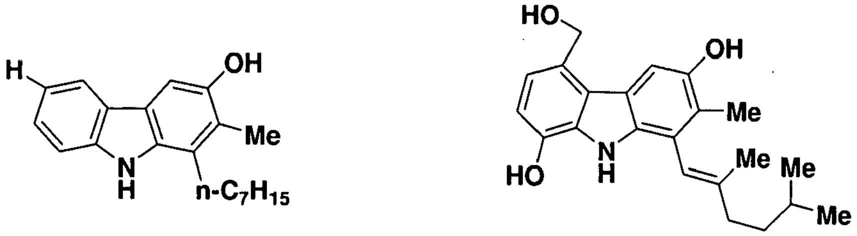
Asterriquinone A1
(shows anti tumor activity)

Demethylasterriquinone B1
(shows anti diabetic activity)

Cochliodinol
(exihibits anti bacterial, fungistatic and fungicidal properties)

Figure 3.

f) Some more examples of indole containing natural products with interesting biological activities like carazostatin and carbazomadurin A show antioxidant and neuroprotactive activities (Fig.4) [8]. Also cyclobrassinin is reported to possess anti cancer properties and we have an oxindole alkaloid horsfiline (Fig.4) [9].



Carazostatin

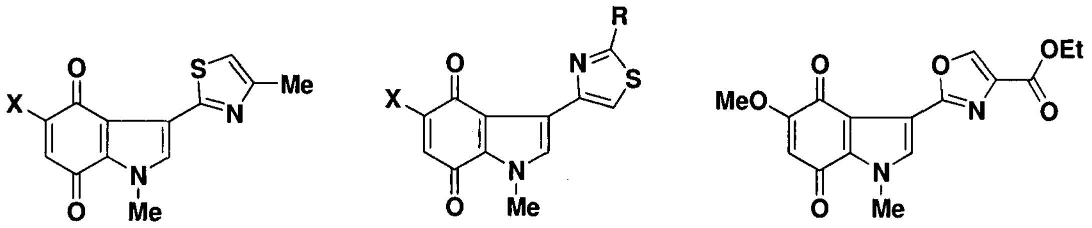
Carbazomadurin A

Cyclobrassinin
(possess anti-cancer properties)

Horsfiline
(oxindole alkaloid)

Figure 4.

g) The molecules depicted in Fig.5 are thiazolyl (and oxazolyl) indolequinones which are analogues of BE 10988, a reported potent inhibitor of topoisomerase II [10].



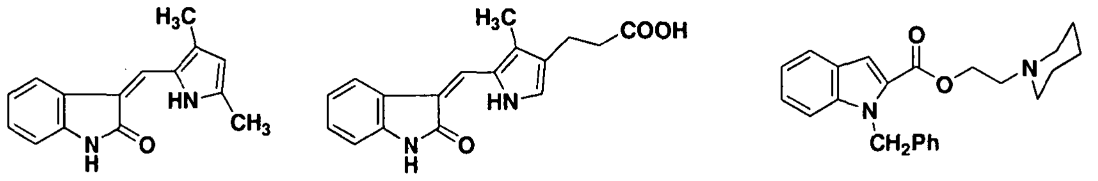
Thiazolylindolequinones
$X = OMe, NH_2$

Thiazolylindolequinones
$X = OMe, NH_2$
$R = CO_2Et, CONH_2$

Oxazolylindolequinone

Figure 5.

h) The molecules shown in Fig.6 were examined for their in vitro anti-tyrosine kinase activity and they exhibited anti-tyrosine kinase activity. Tyrokinase inhibitors (TKIs) are reported as potent and selective inhibitor against enzymes which have involved in tumor growths metastasis and angiogenesis [11].

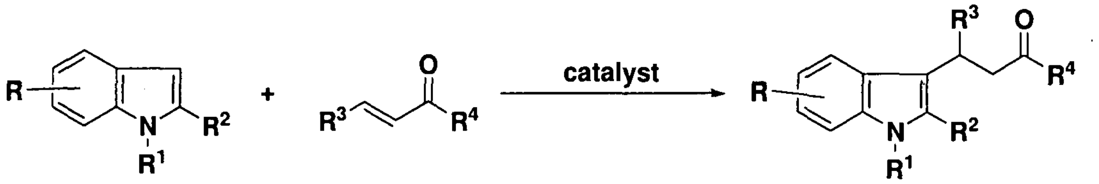


SU 5416 **SU 6668** **1-Benzylindole-2-piperidinoethylcarboxylate**

Figure 6.

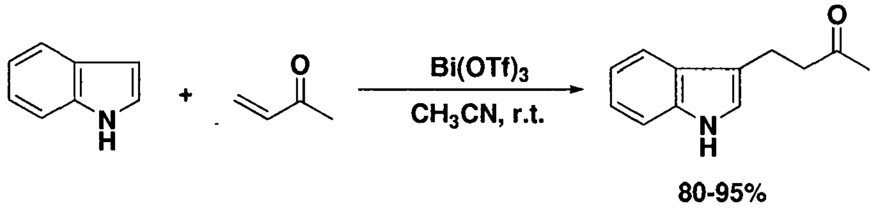
1.2 LITERATURE SURVEY

The simple and direct method for the synthesis of 3-alkyl indoles involves the conjugate addition of indoles to α,β-unsaturated carbonyl compounds in the presence of protic or Lewis acids (Scheme 2).



SCHEME 2

In the past decade, stoichiometric amounts of Lewis acids promoted Friedel-Crafts procedures have been replaced by milder and more environmentally friendly methods. A variety of transition metal salts, such as $Sc(OTf)_3$, $Zr(OTf)_3$, $Yb(OTf)_3$, $Cu(OTf)_2$, $Bi(OTf)_3$, $CeCl_3.7H_2O$–NaI, $ZrCl_4$, $FeCl_3{\cdot}6H_2O$, WCl_6, SmI_3, GaI_3, $RuCl_3$, $SnCl_2.2H_2O$, $InBr_3$, $InCl_3$, $CuBr_2$, $Bi(NO_3)_3$ and other Lewis acid catalysts, have also been applied in this reaction for the preparation of 3-substituted indoles, which are important substructures and building blocks for the synthesis of natural products and therapeutic agents. Also recently, $TiCl_4/Et_3N$, HCl, $BF_3.Et_2O$, H_3PO_4, $HClO_4$, I_2, aluminium dodecyl sulfate trihydrate, *p*-toluenesulfonic acid (TsOH), 2,6-pyridinedicarboxylic acid (PDA), fluorapatite doped zinc bromide, zinc bromide supported on hydroxyapatite (Zn-HAP) and Fe-modified clays were used as efficient catalysts in this transformation. However, the acid-catalyzed conjugate addition of indoles requires careful control of acidity to prevent side reactions such as dimerization or polymerization, whereas Lewis acid–catalyzed reactions involve toxic and expensive reagents coupled with long reaction times. Similarly, various α,β-unsaturated ketones such as cyclic enones, acyclic enones such as chalcones and naphthoquinone were reacted with indole, 2-methylindole and 5-methoxyindole using bismuth triflate as Lewis acid catalyst (Scheme 3), which is inexpensive and easy to prepare, to give the corresponding Michael adducts in excellent yields at ambient temperature with high selectivity [12].

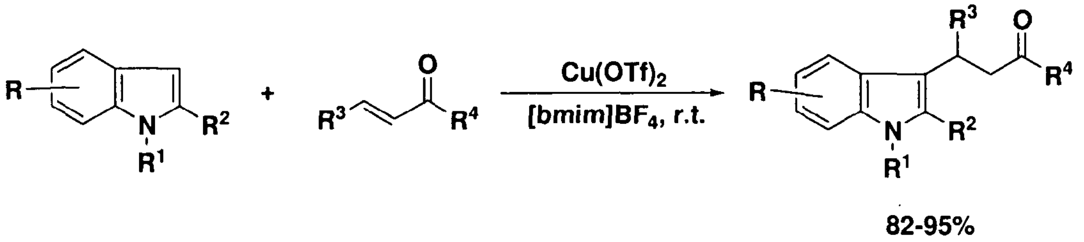


SCHEME 3

Numerous methods have been reported for the conjugate addition of indoles to electron-deficient olefins through the activation of enones or nitro alkenes by Lewis acids. Asymmetric versions of conjugate additions of indoles to α,β-unsaturated ketones have also been reported using chiral Lewis acid catalysts to produce enantiomerically enriched indole derivatives. Typically, conjugate addition reactions are performed under the influence of strong bases such as alkali metal alkoxides or hydroxides. The strong basic conditions often lead to a number of undesirable side reactions such as aldol cyclizations, ester solvolysis, base induced rearrangements such as retro-Claisen or retro-Michael reactions and polymerization reactions. Subsequently, Lewis acids have been found to catalyze conjugate addition reactions under mild conditions. However, most of the catalysts cannot be recovered and reused because they decompose under the quenching conditions.

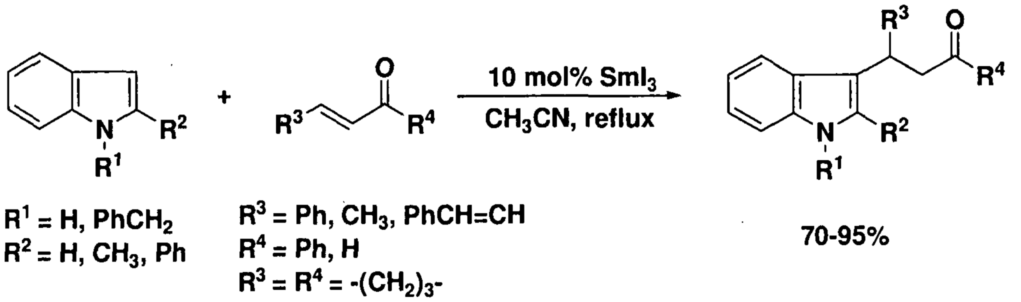
Indoles undergo smooth conjugate addition with α,β-unsaturated ketones in the presence of 10 mol% copper(II) triflate immobilized in air and moisture stable

[bmim]BF_4 ionic liquid under mild conditions to afford the corresponding conjugate addition products in good yield (Scheme 4). The recovery of $Cu(OTf)_2$ is facilitated by the ionic liquid and recovered catalyst can be reused also [13].



SCHEME 4

The SmI_3-catalyzed reaction of indoles with electron-deficient olefins (Scheme 5) generated the corresponding Michael adducts in high yields. The substitution on the indole nucleus occurred exclusively at the 3-position. The reactions were clean and the products were obtained in high yields without the formation of any side products such as N-alkylation product [14].



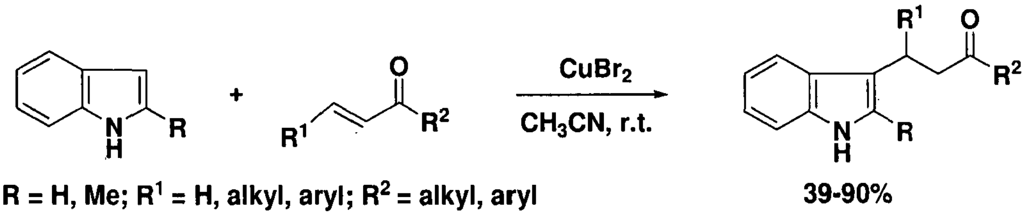
R^1 = H, $PhCH_2$
R^2 = H, CH_3, Ph

R^3 = Ph, CH_3, PhCH=CH
R^4 = Ph, H
$R^3 = R^4 = -(CH_2)_3-$

SCHEME 5

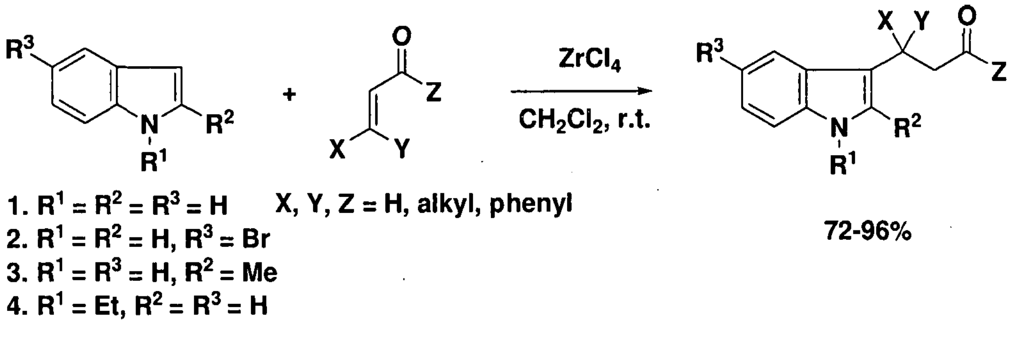
Also inexpensive and commercially available $SnCl_2.2H_2O$ has been shown to be an alternative to Lewis acidic ionic liquids by carrying out a variety of organic synthesis. The reaction medium is recyclable and the reaction time is comparable with the microwave reactions. Since $SnCl_2.2H_2O$ is a strong reductant, its treatment with oxidising agents, nitrates, peroxides, conc. nitric acid should be strictly avoided [15].

Next example is of $CuBr_2$ which is used as an efficient and mild Lewis acid catalyst for alkylation of indoles with α,β-unsaturated carbonyl compounds giving products in good yields (Scheme 6) [16].



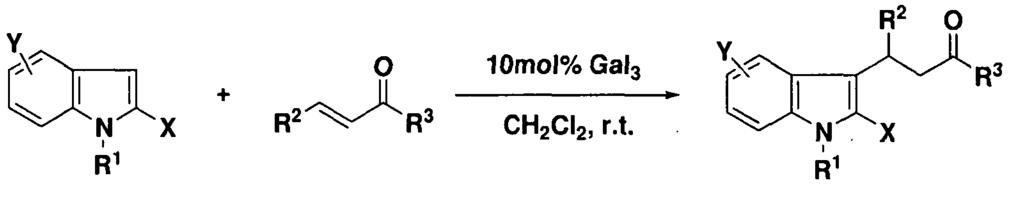
SCHEME 6

$ZrCl_4$ have emerged as a safe, economical, air and moisture tolerant alternative Lewis acid in various organic transformations. $ZrCl_4$ has been demonstrated to be a highly selective and efficient catalyst (Scheme 7) for the Friedel Crafts reaction of heterocyclic enamines to a variety of electron deficient olefins, providing the desired products in excellent yields. The presence of a substituent either on the indole nitrogen or the aromatic ring did not affect the Friedel-Crafts reaction as indoles with a wide variety of functionalities reacted with various cyclic and acyclic enones to provide the respective conjugate addition products in excellent yields [17].



SCHEME 7

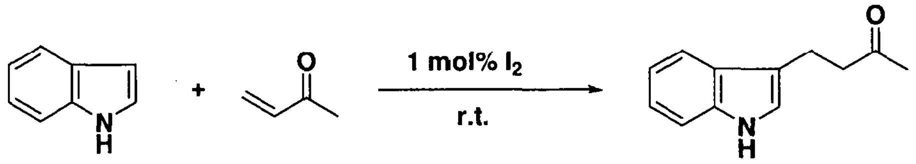
Reactions of indoles and α,β-unsaturated ketones could also be effectively catalyzed by using 10 mol% gallium triiodide (Scheme 8) to give the corresponding adducts in good to excellent yields. Gallium triiodide (GaI_3) can be easily prepared by the reaction of metal gallium with iodine [18].



X = H, Me; Y = H, 5-Br, 7-CH_3;
R^1 = H, CH_3; R^2 = H, alkyl, aryl; R^3 = alkyl, aryl

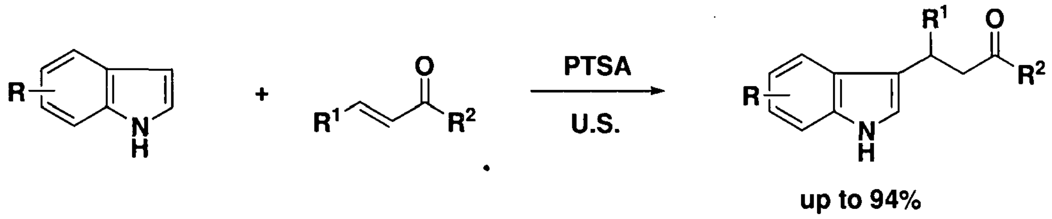
SCHEME 8

The method of iodine-catalyzed Friedel Crafts reaction of indoles with enones is very simple and efficient. The starting materials (indoles and ketones, 1:1, 1 mmol scale) are mixed with iodine (1 mol%) and the mixtures are stirred. The crude material is sufficiently pure (Scheme 9) [19].



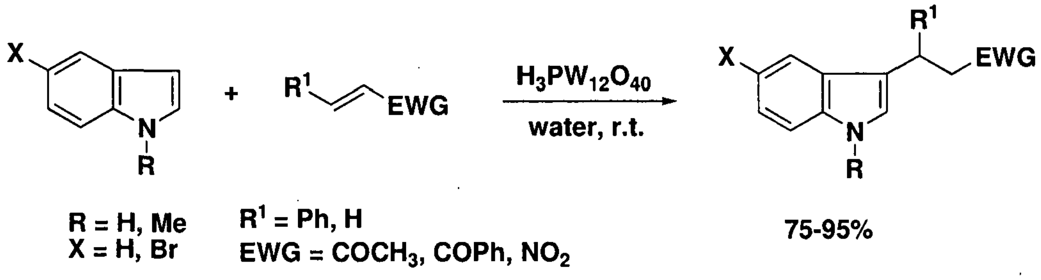
Scheme 9

A survey of literature shows that many organic reactions have recently been accelerated by ultrasonic irradiation. PTSA catalyzes the Friedel Crafts reaction of indole to α,β-unsaturated carbonyl ketones under ultrasonic irradiation (Scheme 10) to afford the corresponding product β-indolylketones in excellent yields (up to 94%) [20].



SCHEME 10

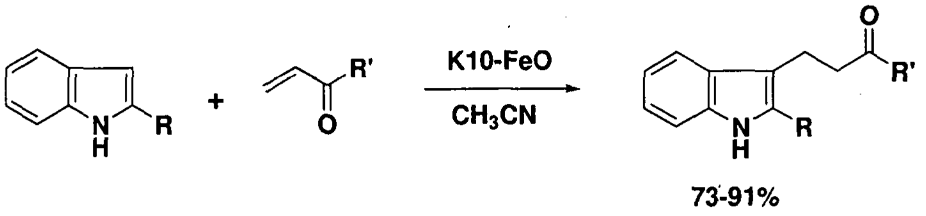
Following is an example of organocatalysed reaction. The special bifunctional Brønsted acid 2,6-pyridinedicarboxylic acid (PDA) could be used in the chemoselective acetalization of aldehydes for preparation of corresponding acetals in excellent yields, and the Michael-type Friedel-Crafts reactions of indoles with α,β-unsaturated enones were also promoted by the same catalyst efficiently. It is well known that 2,6-pyridinedicarboxylic acid is a relatively stable, easy to handle solid that is insensitive to small amounts of air and moisture. All examples reacted smoothly at room temperature for 24 h, and the isolated yields were good in almost all cases (63–85%). The yields were not sensitive to the substrates employed. Nearly all reactions are similarly in isolated yields, and the reaction is clean with no formation of side products like dimers or trimers, which are normally observed by the influence of strong acids [21]. Also $H_3PW_{12}O_{40}$ is a highly efficient catalyst for Friedel–Crafts alkylation of indole with electron-deficient olefins in water at room temperature (Scheme 11) with good to excellent yields. This procedure offers several advantages including the use of green and low-loading catalyst, green solvent, improved yields, cleaner reactions and simple experimental procedures, which make it a useful and attractive strategy in multicomponent reactions and combinational chemistry [22].



SCHEME 11

In recent years, the use of solid acidic catalysts, such as clays and zeolites, has received considerable attention in different areas of organic synthesis because of their environmental compatibility, reusability, greater selectivity, operational simplicity, nontoxicity, noncorrosiveness, low cost, and ease of isolation. In particular, clay catalysts make the reaction convenient, more economic, and environmentally benign. They act as both Brønsted and Lewis acids in their natural and ion-exchanged forms. We have recently reported the high activity of Fe-modified clays for the Friedel–Crafts sulfonylation of arenes with sulfonyl chloride, acylation of sulfonamides, the Friedel–Crafts benzylation of arenes with benzyl chlorides, the Beckmann rearrangement, and nitrile formation.

Conjugate addition of indoles with a variety of electron-deficient olefins in the presence of Fe-exchanged montmorillonite K10 affords the corresponding adducts in excellent yields with high selectivity (Scheme 12). The catalyst was also found to be recyclable [23].



SCHEME 12

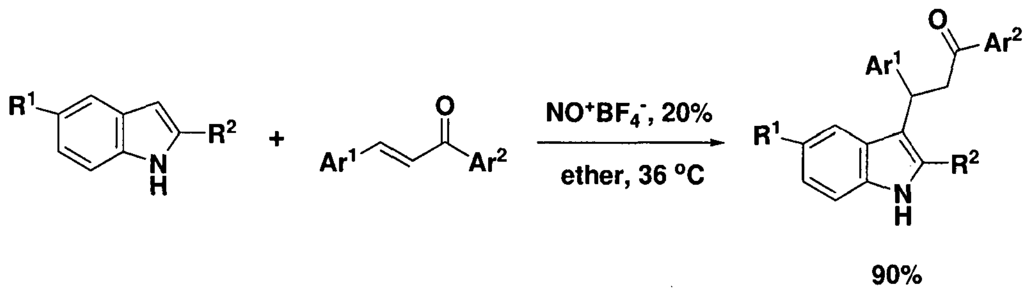
Fluorapatite doped zinc bromide was found to be a very efficient heterogeneous catalyst for the preparation of 3-substituted indoles from Friedel Crafts reaction of indoles to α,β-unsaturated ketones in good to excellent yields. The substitution on the indole nucleus occurred exclusively at the 3-position and *N*-alkylation products have not been observed. The efficiency of this catalyst is very general, simple, high yielding, and oxygen and moisture tolerant. Also, the mildness of the reaction conditions and low cost of reagents makes this methodology synthetically useful. The synthesis of fluorapatite [$Ca_{10}(PO_4)_6F_2$] is carried out by following co-precipitation method [24].

$$6(NH_4)_2HPO_4 + 10Ca(NO_3)_2 + 6NH_4OH + 2NH_4F$$

$$\downarrow$$

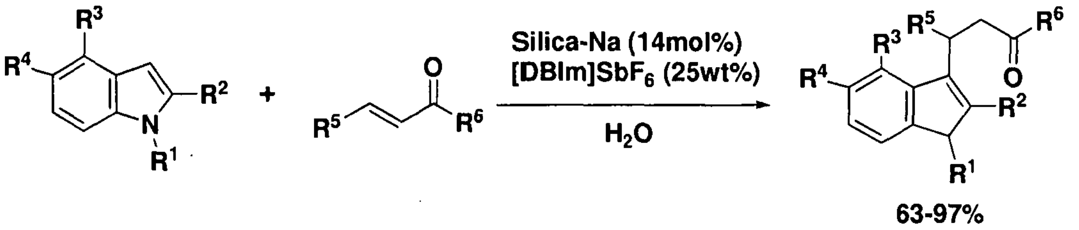
$$Ca_{10}(PO_4)_6F_2 + 20NH_4(NO_3) + 6H_2O$$

Also, zinc bromide supported on hydroxyapatite (Zn-HAP) in presence of acetonitrile as solvent was found to be a very efficient heterogeneous catalyst to promote the synthesis of 3-substituted indoles from Friedel-Crafts reaction of indoles to α,β-unsaturated ketones. The substitution on the indole nucleus occurred exclusively at the 3-position and *N*-alkylation products have not been observed. Moreover, the catalyst was readily recovered by simple filtration and could be reused with only minor decrease in its catalytic activity. Recently, hydroxyapatite (HAP) has attracted wide attention due to its use as macroligand for different catalytic active centers. Indeed, Kaneda and co-workers demonstrated the utility of HAP as a solid support for Ru, Pd and La species to perform many organic transformations [25]. Moreover, a new family of heterogeneous catalysts has been developed based on apatite structures that can be used directly or after activation by several methodologies to promote organic reactions. Thus, these materials have been used successfully in Knoevenagel reaction, Friedel–Crafts alkylation, the synthesis of chalcones, and Friedel Crafts reaction. An efficient Friedel Crafts reaction of indoles to unsaturated enones was achieved in the presence of a catalytic amount of nitrosonium tetrafluoroborate in ethyl ether providing the desired products in excellent yields (Scheme 13) [26].



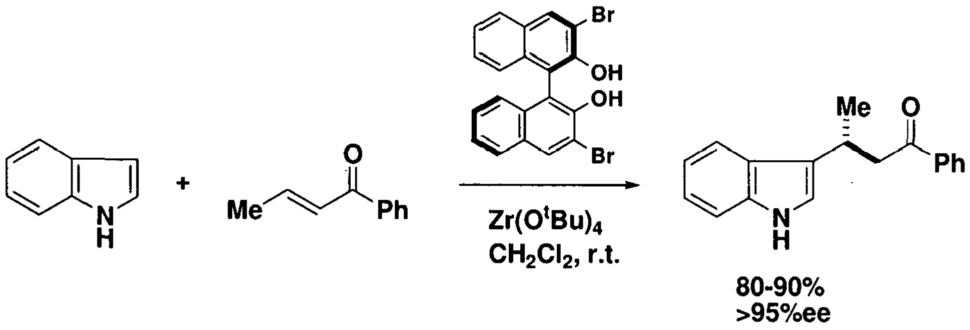
SCHEME 13

Recently a neutral catalytic system for Friedel-Crafts reactions of indoles has been developed by combining silica-supported benzenesulfonic acid sodium salt with hydrophobic ionic liquid in water (Scheme 14). An efficient hydrophobic environment could be created on the surface of the silica-sodium material under the conditions. The system can be readily recycled without appreciable loss of reactivity. Simplicity of operation as well as the neutral, mild, and environmentally benign nature of the reaction could enable expansion to a wide variety of acid-labile substrates, even to a larger scale reaction. Various indole derivatives and α,β-unsaturated carbonyl compounds including some acid-labile substrates were successfully applied to this system with water as the sole solvent to afford the desired adducts in high yields [27].



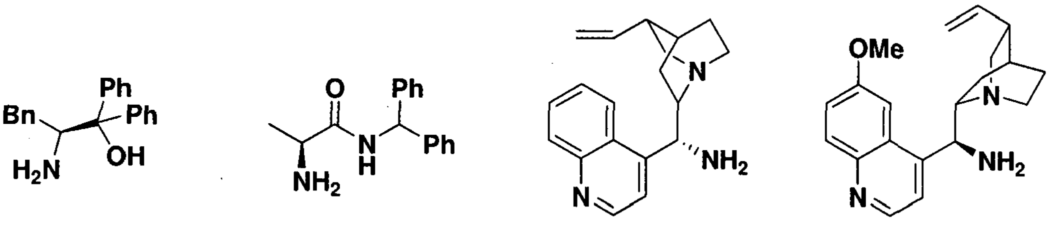
SCHEME 14

To date most of the successful examples of such processes are limited to the use of bidentate chelating carbonyl substrates, including α,β-unsaturated ketoesters, acyl phosphonates, alkylidene malonates, α-hydroxy enones, 2-acyl imidazoles, and other acylheterocycle compounds and nitroalkenes. Complexes of BINOL-based ligands with $Zr(O^tBu)_4$ catalyze the Friedel Crafts alkylation reaction of indoles with nonchelating α-substituted α,β-enones at room temperature affording the expected products with good yields and ee's above 95% (Scheme 15). Additional advantages are the use of ligands that are commercially available in both enantiomeric forms, and a simple experimental procedure at room temperature [28].



SCHEME 15

The C3-selective enantioselective Michael-type Friedel–Crafts alkylations of indoles with nonchelating α,β-unsaturated alkyl ketones, catalyzed by a chiral primary amine derived from natural cinchonine, were investigated. The reactions, in the presence of 30 mol% catalyst shown in Fig.7, were smoothly conducted at 0 to –20 ºC. Moderate to good ee's (47–89%) have been achieved [29].



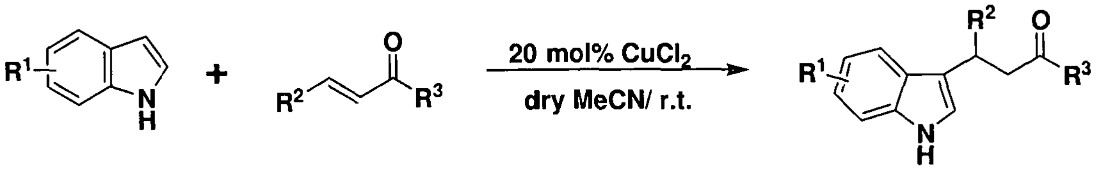
Structures of the chiral primary amine catalysts

Figure 7.

1.3 AIM AND SCOPE OF THE PRESENT WORK

Indole is a very special heterocyclic ring. Many natural products and biologically active compounds are found to contain 3-substituted indole as their basic structure making these molecules pharmaceutically useful and important. Also, alkylation reaction of indoles to α,β-unsaturated ketones constitutes a key reaction in the total synthesis of complex natural products. Typically, such reactions are performed under the influence of strong bases such as alkali metal alkoxides or hydroxides.

The strong basic conditions often lead to a number of undesirable side reactions such as aldol cyclization, ester solvolysis, base induced rearrangements such as retro-Claisen or retro-Michael reactions and polymerization reactions. Subsequently, Lewis acids have been found to catalysed Friedel Crafts alkylation reaction in mild condition. Previously also many Lewis acids have been used for the substitution reactions of indoles. The aim of this project is to synthesize 3-substituted indoles using $CuCl_2$ as a mild and cheap catalyst. The 3-alkylation of various indoles with unsaturated ketones such as chalcones, methylvinylketone and cyclohexenone has been studied which is presented by Scheme 16. To the best of our knowledge, alkylation of indoles in the presence of copper(II) chloride has not been reported in literature.



SCHEME 16

EXPERIMENTAL SECTION

2.1 Chemicals and Suppliers

S. No.	CHEMICAL	SUPPLIER	GRADE
1.	Acetonitrile	Rankem	AR
2.	5-Bromoindole	Aldrich	HPLC
3.	But-3-en-2-one	Aldrich	-
4.	6-Chloroindole	Aldrich	-
5.	3-(4-Chlorophenyl)-1-phenylprop-2-en-1-one	¶	-
6.	Copper(II)chloride	Rankem	LR
7.	Cyclohex-2-enone	Aldrich	-
8.	4-(3,4-Dimethoxyphenyl)but-3-en-2-one	¶	-
9.	1,3-Diphenylprop-2-en-1-one	¶	-
10.	Ethyl acetate	Rankem	LR
11.	Hexane	Rankem	LR
12.	Indole	SRL	AR
13.	5-Methoxyindole	Aldrich	-
14.	1-Methylindole	Aldrich	-
15.	2-Methylindole	Aldrich	-
16.	5-Methylindole	Aldrich	-
17.	Silica gel (column) 100-200 mesh	Rankem	LR
18.	Silica gel G (TLC)	Merck	-

¶ Synthesized (see Appendix I)

2.2 Make and Model of the Instruments

IR spectra were recorded on a NEXUS FT-IR (THERMONICOLET). Solid samples were recorded as KBr wafers and liquid samples as film between NaCl plates. ^1H spectra were recorded at Bruker 500 MHz and ^{13}C NMR spectra were recorded at 125 MHz in $CDCl_3$, and chemical shifts are reported in δ (ppm) using TMS reference as the internal reference. All the electronspray ionization mass spectra were recorded by Waters-HAB213 LC-MS spectrometer.

2.3 General

All the solvents used for the reactions were dried and distilled using suitable drying agents before use. All the reactions were carried out under dry conditions. $CuCl_2$ was dehydrated at 120 ºC in oven for three hours before using as catalyst (as per merck index). All the reactions were monitored by TLC on glass plates (7 x 2 cm) coated with silica gel G. The spots were visualized by short exposure to iodine vapour. The products were purified by silica gel column chromatography with ethyl acetate and hexanes as eluent.

2.4 Procedures

General procedure for synthesis of various 3-substituted indoles:

To a mixture of indole (1-2 mM) and α,β-unsaturated ketone (1-2 mM) in the solvent (2-4 mL) was added anhydrous $CuCl_2$ (20 mol%) at room temperature. The reaction was monitored by TLC at regular intervals. After the reaction was complete, the reaction mixture was extracted with ethyl acetate and washed with water. The organic layer was dried over anhydrous sodium sulphate. The solvent was evaporated and the residue thus obtained was purified by column chromatography on silica gel using a mixture of ethyl acetate and hexanes as eluent.

2.4.1 Synthesis of 3-(3-indolyl)-1,3-diphenylpropan-1-one (1):

The product **1** was obtained from the reaction of indole (232 mg, 2 mM) with 1,3-diphenylprop-2-en-1-one (416 mg, 2 mM) in the presence of $CuCl_2$ (54 mg, 0.4 mM, 20 mol%) in dry acetonitrile.

Reaction time: 40 hrs

Yield: 91%

M.P.: 131-132°C
[lit value: 130-132 °C] [30a]

IR (KBr) ν_{max}: 3407, 3117, 3052, 3019, 1740, 1675, 1593, 1450, 739, 698 cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ 7.99 (bs, 1H), 7.93 (d, *J* = 8.0 Hz, 2H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.44-7.41 (m, 3H), 7.36-7.30 (m, 3H), 7.27-7.22 (m, 2H), 7.15 (q, *J* = 8.0 Hz, 2H), 7.03-7.00 (m, 2H), 5.07 (t, *J* = 7.0 Hz, 1H), 3.82 (dd, *J* = 7.0, 16.5 Hz, 1H), 3.72 (dd, *J* = 7.5, 16.5 Hz, 1H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 198.5, 144.1, 137.0,136.5, 132.9, 128.4, 128.3, 128.0, 127.7, 126.5, 126.1, 122.0, 121.3, 119.4, 119.2, 119.1, 111.0, 45.1, 38.2

MS (relative intensity): m/z 348.1364 (M+Na), 326.1548 (M+H).

2.4.2 Synthesis of 3-(5-bromo-3-indolyl)-1,3-diphenylpropan-1-one (2):

The product **2** was obtained as solid from the reaction of 5-bromoindole (390 mg, 2 mM) with 1,3-diphenylprop-2-en-1-one (418 mg, 2 mM) in the presence of $CuCl_2$ (54 mg, 0.4 mM, 20 mol%) in dry acetonitrile.

Reaction time:	18hrs
Yield:	71%
M.P.:	159-160°C
IR (KBr) ν_{max}:	3338, 3113, 3052, 3019, 2884, 1953, 1724, 1675, 1597, 1446, 1295, 980, 882, 792, 747, 698 cm^{-1}.
^1H NMR ($CDCl_3$, 500 MHz):	δ 8.04 (d, *J* = 8.5 Hz, 1H), 8.00 (bs, 1H), 7.93 (d, *J* = 8.5 Hz, 2H), 7.61-7.52 (m, 3H), 7.5-7.41 (m, 4H), 7.22-7.18 (m, 3H), 7.02 (s, 1H), 5.00 (t, *J* = 7 Hz, 1H), 3.77 (dd, *J* = 7.5, 17 Hz, 1H), 3.70 (dd, *J* = 7.5, 17 Hz, 1H).
^{13}C NMR ($CDCl_3$, 125 MHz):	δ 198.3, 143.8, 136.9, 135.2, 133.1, 128.7, 128.6, 128.4, 128.1, 127.7, 126.5, 125.0, 122.6, 122.0, 118.9, 112.7, 112.5, 45.2, 37.9.
MS (relative intensity): m/z	426.0461 (M+Na), 404.0658 (M+H)

2.4.3 Synthesis of 3-(5-methoxy-3-indolyl)-1,3-diphenylpropan-1-one (3):

The product **3** was obtained as solid from the reaction of 5-methoxyindole (290 mg, 2 mM) with 1,3-diphenylprop-2-en-1-one (414 mg, 2 mM) in the presence of $CuCl_2$ (54 mg, 0.4 mM, 20 mol%) in dry acetonitrile.

Reaction time: 30hrs

Yield: 58%

M.P.: 144-145°C

IR (KBr) ν_{max}: 3367, 3117, 3064, 2991, 2929, 2893, 2827, 1957, 1675, 1622, 1585, 1209, 1025, 923, 800, 747, 694cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.93 (d, *J* = 7.5 Hz, 2H), 7.83 (bs, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.45-7.41 (m, 3H), 7.35 (d, *J* = 7 Hz, 2H), 7.27 (s, 1H), 7.21-7.15 (m, 2H), 6.98 (s, 1H), 6.84 (s, 1H), 6.81-6.79 (m, 1H), 5.02 (t, *J* = 7.5 Hz, 1H), 3.79 (dd, *J* = 7, 16.5 Hz, 1H), 3.75-3.69 (m, 4H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 198.4, 153.6, 144.0, 137.0, 132.8, 128.7, 128.4, 128.3, 128.1, 127.9, 127.7, 126.9, 122.0, 118.9, 112.1, 111.6, 101.3, 55.6, 45.0, 38.0.

MS (relative intensity): m/z 378.1470 (M+Na), 356.1651 (M+H).

2.4.4 Synthesis of 3-(5-methyl-3-indolyl)-1,3-diphenylpropan-1-one (4):

The product **4** was obtained as solid from the reaction of 5-methylindole (130 mg, 1 mM) with 1,3-diphenylprop-2-en-1-one (204 mg, 1 mM) in the presence of $CuCl_2$ (27 mg, 0.2 mM, 20 mol%) in dry acetonitrile.

Reaction time: 29hrs

Yield: 47%

M.P.: 170-171°C
[lit value: 167-168 °C] [20]

IR (KBr) ν_{max}: 3440, 3126, 3060, 3023, 2913, 1957, 1887, 1724, 1679, 1589, 1487, 1442, 1266, 1099, 1025, 800, 747, 690 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.93 (d, *J* = 7 Hz, 2H), 7.87 (s, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 8 Hz, 2H), 7.35 (d, *J* = 7.5 Hz, 2H), 7.27-7.22 (m, 3H), 7.21-7.19 (d, *J* = 8.5 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 6.97 (d, *J* = 7.5 Hz, 1H), 6.93 (s, 1H), 5.04 (t, *J* = 7 Hz, 1H), 3.79 (dd, *J* = 7.5, 17 Hz, 1H), 3.72 (dd, *J* = 7.5, 16.5 Hz, 1H), 2.36 (s, 3H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 198.4, 144.1, 137.0, 134.7, 132.8, 128.5, 128.4, 128.3, 127.9, 127.6, 126.7, 126.1, 125.6, 123.6, 121.4, 118.9, 110.6, 45.1, 37.9, 30.8.

MS (relative intensity): m/z 362.1520 (M+Na), 340.1701 (M+H).

2.4.5 Synthesis of 3-(2-methyl-3-indolyl)-1,3-diphenylpropan-1-one (5):

The product **5** was obtained as brown oil from the reaction of 2-methylindole (262 mg, 2 mM) with 1,3-diphenylprop-2-en-1-one (412 mg, 2 mM) in the presence of $CuCl_2$ (54 mg, 0.4 mM, 20 mol%) in dry acetonitrile.

Reaction time: 40hrs

Yield: 44%

IR (KBr) ν_{max}: 3375, 3056, 2917, 2856, 1957, 1896, 1679, 1601, 1446, 1319, 1209, 747, 690 cm^{-1}.

^{1}H NMR (CDCl$_3$, 500 MHz): δ 7.94 (d, *J* = 8 Hz, 2H), 7.87 (bs, 1H); 7.54 (t, *J* = 7.5 Hz, 1H), 7.48-7.41 (m, 5H), 7.35 (d, *J* = 8 Hz, 2H), 7.24-7.20 (m, 3H), 6.95 (s, 1H), 5.04(t, *J* = 7.0 Hz, 1H), 3.80 (dd, *J* = 6.5, 17 Hz, 1H), 3.73 (dd, *J* = 7.5, 17 Hz, 1H), 2.37 (s, 3H).

^{13}C NMR (CDCl$_3$, 125 MHz): δ 198.9, 144.0, 137.0, 135.3, 132.7, 131.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.4, 125.7, 120.5, 119.0, 110.2, 43.3, 36.5.

MS (relative intensity): m/z 340.1704 (M+H), 338.1547 (M+H-2).

2.4.6 Synthesis of 3-(1-methyl-3-indolyl)-1,3-diphenylpropan-1-one (6):

The product **6** was obtained from the reaction of 1-methylindole (0.25 ml, 2 mM) with 1,3-diphenylprop-2-en-1-one (413 mg, 2 mM) in the presence of CuCl$_2$ (54 mg, 0.4 mM, 20 mol%) in dry acetonitrile.

Reaction time: 36hrs

Yield: 82%

M.P.: 125-126ºC
[lit value: 127-129 °C] [30a]

IR (KBr) ν_{max}: 3060, 3019, 2925, 2848, 1973, 1940, 1903, 1728, 1671, 1597, 1364, 1246, 923, 739, 694 cm^{-1}.

^{1}H NMR (CDCl$_3$, 500 MHz): δ 7.99 (d, *J* = 8 Hz, 1H), 7.94-7.90 (m, 2H), 7.56-7.50 (m, 2H), 7.35-7.32 (m, 2H), 7.18-7.13 (m, 3H), 7.02-6.95 (m, 3H), 6.92-6.81 (m, 1H), 6.81 (s, 1H), 5.04 (t, *J* = 7.5 Hz, 1H), 3.83-3.78 (m, 1H), 3.77-3.70 (s, 4H).

^{13}C NMR (CDCl$_3$, 125 MHz): δ 198.5, 144.4, 137.3, 137.1, 133.0, 128.5, 128.4, 128.1, 127.8, 126.9, 126.2, 121.6, 119.6, 118.8, 117.8, 109.2, 99.9, 45.3, 38.1, 32.7, 30.9.

MS (relative intensity): m/z 362.1527 (M+Na), 340.1700 (M+H).

2.4.7 Synthesis of 3-(6-chloro-3-indolyl)-1,3-diphenylpropan-1-one (7):

The product **7** was obtained from the reaction of 6-chloroindole (151 mg, 1 mM) with 1,3-diphenylprop-2-en-1-one (206 mg, 1 mM) in the presence of CuCl$_2$ (27 mg, 0.2 mM, 20 mol%) in dry acetonitrile.

Reaction time: 24hrs

Yield: 64%

M.P.: 157-158°C

IR (KBr) ν_{max}: 3420, 3134, 3080, 3052, 3023, 2880, 1728, 1671, 1446, 1397, 1258, 907, 751, 698 cm^{-1}.

^{1}H NMR (CDCl$_3$, 500 MHz): δ 7.98 (bs, 1H), 7.93 (d, *J* = 7 Hz, 2H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 8 Hz, 2H), 7.33-7.29 (m, 4H), 7.28-7.25 (m, 2H), 7.19-7.16 (m, 1H), 7.00 (s, 1H), 6.96 (d, *J* = 8 Hz, 1H), 5.02 (t, *J* = 7 Hz, 1H), 3.79 (dd, *J* = 7.5, 16.5 Hz, 1H), 3.69 (dd, *J* = 7, 16.5 Hz, 1H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 198.2, 143.8, 136.8, 136.7, 132.9, 128.4, 128.3, 127.9, 127.6, 126.3, 125.1, 121.7, 120.3, 120.0, 119.3, 110.9, 99.9, 44.9, 37.9.

MS (relative intensity): m/z 360.1005 (M+H).

2.4.8 Synthesis of 3-(3-indolyl)-3-(4-chlorophenyl)-1-phenylpropan-1-one (8):

The product **8** was obtained from the reaction of indole (226 mg, 2 mM) with 3-(4-chlorophenyl)-1-phenylprop-2-en-1-one (483 mg, 2 mM) in the presence of $CuCl_2$ (54 mg, 0.4 mM, 20 mol%) in dry acetonitrile.

Reaction time:	38hrs
Yield:	62%
M.P.:	134-135°C
IR (KBr) ν_{max}:	3391, 3130, 3052, 2974, 2917, 2884, 1736, 1679, 1593, 1483, 1095, 813, 739, 686 cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ 8.00 (bs, 1H), 7.93 (d, $J = 8.0$ Hz, 2H), 7.55 (t, $J = 7$ Hz, 1H), 7.46-7.39 (m, 3H), 7.34 (d, $J = 8.5$ Hz, 1H), 7.29-7.20 (m, 4H), 7.16 (t, $J = 7.5$ Hz, 1H), 7.03 (t, $J = 8$ Hz, 1H), 7.00 (s, 1H), 5.04 (t, $J = 7.5$ Hz, 1H), 3.80 (dd, $J = 6.5$, 17 Hz, 1H), 3.70 (dd, $J = 8$, 17 Hz, 1H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 198.2, 142.7, 136.9, 136.5, 133.2, 129.6, 129.2, 128.6, 128.5, 128.1, 126.4, 122.3, 121.3, 119.5, 119.4, 118.9, 111.2, 44.9, 37.5.

MS (relative intensity): m/z 382.0973 (M+Na), 360.1159 (M+H).

2.4.9 Synthesis of 3-(5-bromo-3-Indolyl)-3-(4-chlorophenyl)-1-phenylpropan-1-one (9):

The product **9** was obtained from the reaction of 5-bromoindole (392 mg, 2 mM) with 3-(4-chlorophenyl)-1-phenylprop-2-en-1-one (483 mg, 2 mM) in the presence of $CuCl_2$ (54 mg, 0.4 mM, 20 mol%) in dry acetonitrile.

Reaction time: 38hrs

Yield: 66%

M.P.: 147-148°C

IR (KBr) ν_{max}: 3407, 3064, 2954, 2913, 2852, 1896, 1687, 1487, 1446, 1099, 976, 878, 800, 694, 592 cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ 8.17 (bs, 1H), 7.95 (d, *J* = 7.5 Hz, 2H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.53 (s, 1H), 7.47 (t, *J* = 8 Hz, 2H), 7.28-7.22 (m, 4H), 7.20-7.19 (m, 2H), 7.00 (s, 1H), 4.99 (t, *J* = 7.5 Hz, 1H), 3.77 (dd, *J* = 6.5, 17 Hz, 1H), 3.69 (dd, *J* = 7.5, 17 Hz, 1H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 198.0, 142.2, 136.6, 135.1, 133.2, 132.0, 128.9, 128.6, 128.5, 128.0, 127.9, 125.0, 122.4, 121.6, 118.2, 112.7, 112.6, 44.8, 37.2.

MS (relative intensity): m/z 460.0081 (M+Na), 438.0264 (M+H).

2.4.10 Synthesis of 3-(5-methoxy-3-indolyl)-3-(4-chlorophenyl)-1-phenylpropan-1-one (10):

The product **10** was obtained from the reaction of 5-methoxyindole (132 mg, 1 mM) with 3-(4-chlorophenyl)-1-phenylprop-2-en-1-one (253 mg, 1 mM) in the presence of $CuCl_2$ (27 mg, 0.2 mM, 20 mol%) in dry acetonitrile.

Reaction time:	28hrs
Yield:	52%
M.P.:	139-140ºC
IR (KBr) ν_{max}:	3403, 3003, 2929, 2840, 1900, 1838, 1667, 1626, 1577, 1483, 1348, 1213, 1082, 1017, 747, 686 cm^{-1}.
^1H NMR ($CDCl_3$, 500 MHz):	δ 7.93 (d, *J* = 8 Hz, 2H), 7.90 (bs, 1H), 7.56 (t, *J* = 7.0 Hz, 1H), 7.45 (t, *J* = 8 Hz, 2H), 7.29-7.27 (m, 2H), 7.24-7.21 (m, 3H), 6.97 (s, 1H), 6.83-6.80 (m, 2H), 4.99 (t, *J* = 7 Hz, 1H), 3.81-3.74 (m, 4H), 3.69 (dd, *J* = 8, 17 Hz, 1H).
^{13}C NMR ($CDCl_3$, 125 MHz):	δ 195.9, 151.4, 140.2, 134.5, 130.7, 129.5, 129.3, 126.8, 126.2, 126.1, 125.9, 125.6, 119.7, 116.1, 109.8, 109.4, 98.9, 53.4, 42.4, 35.1
MS (relative intensity): m/z	412.1082 (M+Na), 390.1146 (M+H).

2.4.11 Synthesis of 3-(1-methyl-3-indolyl)-3-(4-chlorophenyl)-1-phenylpropan-1-one (11):

The product **11** was obtained from the reaction of 1-methylindole (0.13 ml, 1 mM) with 3-(4-chlorophenyl)-1-phenylprop-2-en-1-one (274 mg, 1 mM) in the presence of

$CuCl_2$ (27 mg, 0.2 mM, 20 mol%) in dry acetonitrile.

Reaction time: 25 hrs

Yield: 60%

M.P.: 153-154°C

IR (KBr) v_{max}: 3052, 2921, 1896, 1736, 1675, 1589, 1483, 1242, 1086, 1013, 821, 735, 682 cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ 7.92 (d, *J* = 8 Hz, 2H), 7.54 (t, *J* = 7.0 Hz, 1H), 7.46-7.37 (m, 3H), 7.29-7.26 (m, 3H), 7.22-7.16 (m, 3H), 7.01 (t, *J* = 8 Hz, 1H), 6.81 (s, 1H), 5.02 (t, *J* = 7.0 Hz, 1H), 3.78 (dd, *J* = 6, 17 Hz, 1H), 3.72-3.67 (m, 4H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 198.0, 142.8, 137.2, 136.8, 133.0,131,7, 129.1, 128.5, 128.4, 127.9, 126.6, 126.0, 121.7, 119.3, 118.8, 117.2, 109.1, 44.9, 37.3, 32.6.

MS (relative intensity): m/z 396.1137 (M+Na), 374.1313 (M+H).

2.4.12 Synthesis of 4-(3-indolyl)-4-(2-methoxyphenyl)-butan-2-one (12):

The product **12** was obtained as rust-brown viscous liquid from the reaction of indole (116 mg, 1 mM) with 4-(2-methoxyphenyl)but-3-en-2-one (179 mg, 2 mM) in the presence of $CuCl_2$ (27 mg, 0.2 mM, 20 mol%) in dry acetonitrile.

Reaction time: 40 hrs

Yield: 59%

IR (KBr) ν_{max}: 3412, 3052, 2995, 2921, 2840, 2043, 1896, 1703, 1593, 1487, 1454, 1348, 1238, 1017, 804, 743 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.03 (bs, 1H), 7.43 (d, *J* = 8 Hz, 1H), 7.33 (d, *J* = 8 Hz, 1H), 7.20-7.11 (m, 2H), 7.08-6.99 (m, 3H), 6.89 (d, *J* = 8 Hz, 1H), 6.79 (t, *J* = 7.5 Hz, 1H), 5.27 (t, *J* = 8.0 Hz, 1H), 3.91 (s, 3H), 3.13-3.11 (m, 2H), 2.12 (s, 3H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 207.4, 155.5, 135.4, 131.1, 127.3, 126.3, 125.8, 121.0, 120.9, 119.6, 118.4, 118.2, 117.0, 110.0, 109.5, 54.4, 48.6, 30.6, 28.3.

MS (relative intensity): m/z 294.1494 (M+H).

2.4.13 Synthesis of 4-(3-indolyl)butan-2-one (13):

The product **13** was obtained from the reaction of indole (222 mg, 2 mM) with but-3-en-2-one (0.2 ml, 2 mM) in the presence of $CuCl_2$ (54 mg, 0.4 mM, 20 mol%) in dry acetonitrile.

Reaction time: 0.5 hrs

Yield: 72%

M.P.: 69-70°C

IR (KBr) ν_{max}: 3318, 3048, 2962, 2913, 2843, 1695, 1614, 1564, 1348, 1262, 1164, 1095, 784, 735, 657 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.97 (bs, 1H), 7.59 (d, *J* = 8 Hz, 1H), 7.35 (d, *J* = 8 Hz, 1H), 7.19 (t, *J* = 8 Hz, 1H), 7.12 (t, *J* = 8 Hz, 1H), 6.98 (s, 1H), 3.05 (t, J = 8 Hz, 2H), 2.84 (t, J = 8 Hz, 2H), 2.14 (s, 3H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 208.6, 136.2, 127.0, 121.9, 121.3, 119.2, 118.5, 115.1, 111.0, 43.9, 29.9, 19.2.

MS (relative intensity): m/z 210.0897 (M+Na), 188.1079 (M+H).

2.4.14 Synthesis of 4-(1-methyl-3-indolyl)butan-2-one (14):

The product **14** was obtained as orange viscous liquid from the reaction of 1-methylindole (0. 25ml, 2 mM) with but-3-en-2-one (0.2 ml, 2 mM) in the presence of $CuCl_2$ (54 mg, 0.4 mM, 20 mol%) in dry acetonitrile.

Reaction time: 0.5 hrs

Yield: 75%

IR (KBr) ν_{max}: 3052, 2925, 2819, 1708, 1618, 1475, 1417, 1319, 1152, 1066, 735 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.58 (d, J = 8 Hz, 1H), 7.29 (d, J = 8 Hz, 1H), 7.22 (t, J = 7 Hz, 1H), 7.11 (t, J = 7.5 Hz, 1H), 6.84 (s, 1H), 3.73 (s, 3H), 3.04 (t, J = 7.5 Hz, 2H), 2.83 (t, J = 7.5 Hz, 2H), 2.14 (s, 3H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 208.6, 136.8, 127.4, 126.2, 121.4, 118.6, 118.5, 113.5, 109.0, 44.2, 32.4, 29.9, 19.1.

MS (relative intensity): m/z 224.1052 (M+Na), 202.1236 (M+H).

2.4.15 Synthesis of 4-(5-bromo-3-indolyl)butan-2-one (15):

The product **15** was obtained from the reaction of 5-bromoindole (324 mg, 2 mM) with but-3-en-2-one (0.2 ml, 2 mM) in the presence of $CuCl_2$ (54 mg, 0.4 mM, 20 mol%) in dry acetonitrile.

Reaction time:	0.5 hrs
Yield:	79%
M.P.:	74-75 ^{0}C
IR (KBr) ν_{max}:	3326, 2905, 2846, 1704, 1458, 1295, 1164, 878, 784.1, 645, 592 cm^{-1}.
^{1}H NMR ($CDCl_3$, 500 MHz):	δ 8.16 (bs, 1H), 7.69 (s, 1H), 7.27-7.22 (m, 1H), 7.21-7.17 (m, 1H), 6.96 (s, 1H), 2.97 (t, J = 7.5 Hz, 2H), 2.80 (t, J = 7.0 Hz, 2H), 2.13 (s, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz):	δ 208.3, 134.7, 128.8, 124.7, 122.7, 121.1, 114.8, 112.5, 112.4, 43.7, 29.9, 18.9.

2.4.16 Synthesis of 3-(3-indolyl)cyclohexan-1-one (16):

The product **16** was obtained as light green oil from the reaction of indole (219 mg, 2 mM) with cyclohex-2-en-1-one (0.2 ml, 2 mM) in the presence of $CuCl_2$ (54 mg, 0.4 mM, 20 mol%) in dry acetonitrile.

Reaction time:	1 hr
Yield:	62%

IR (KBr) ν_{max}: 3416, 2921, 2856, 1699, 1642, 1446, 1332, 1262, 878, 776, 739 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.01 (bs, 1H), 7.63 (d, *J* = 8 Hz, 1H), 7.37 (d, *J* = 8 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.12 (t, *J* = 8 Hz, 1H), 6.99 (s, 1H), 3.48-3.37 (m, 1H), 2.84-2.77 (m, 1H), 2.67-2.60 (m, 1H), 2.50-2.32 (m, 3H), 2.10-1.93 (m, 3H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 210.8, 135.4, 125.1, 121.2, 119.3, 118.6, 118.3, 118.0, 110.2, 47.0, 40.5, 34.9, 30.7, 23.8.

2.4.17 Synthesis of 3-(5-bromo-3-indolyl)cyclohexan-1-one (17):

The product **17** was obtained as dark red viscous liquid from the reaction of 5-bromoindole (384 mg, 2 mM) with cyclohex-2-en-1-one (0.2 ml, 2 mM) in the presence of $CuCl_2$ (54 mg, 0.4 mM, 20 mol%) in dry acetonitrile.

Reaction time: 1 hr

Yield: 70%

IR (KBr) ν_{max}: 3399, 2921, 2856, 1703, 1581, 1450, 1099, 1041, 874, 792, 584 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.10 (bs, 1H), 7.73 (s, 1H), 7.30-7.26 (m, 1H), 7.25-7.20 (m, 1H), 6.98 (s, 1H), 3.42-3.35 (m, 1H), 2.81-2.73 (m, 1H), 2.65-2.57 (m, 1H), 2.51-2.33 (m, 3H), 2.09-1.79 (m, 3H).

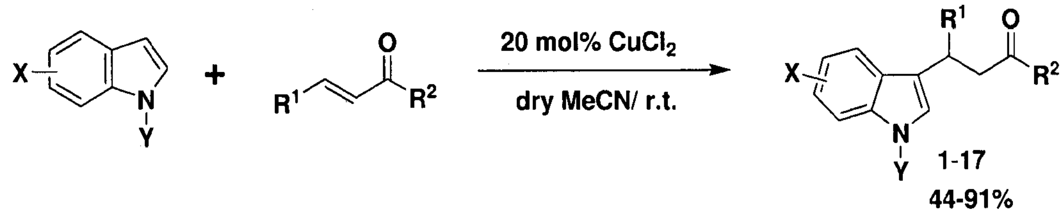
^{13}C NMR ($CDCl_3$, 125 MHz): δ 211.6, 134.9, 127.7, 124.9, 121.5, 121.4, 119.1, 112.6, 112.5, 47.7, 41.4, 35.6, 31.5, 24.6.

RESULTS AND DISCUSSION

Table 1. Optimization of catalyst and reaction conditions

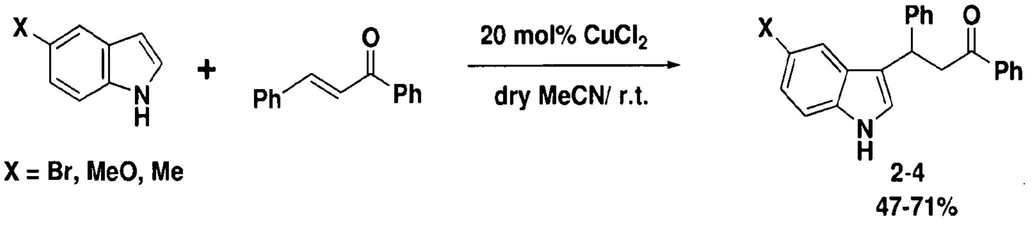
S.No.	Catalyst	Concentration (mol%)	Reaction Time	Solvent	Yield of **1**
1.	-	-	48 hrs	CH_2Cl_2	20%
2.	$SbCl_3$	20	48 hrs	CH_2Cl_2	59%
3.	$MgCl_2$	20	48 hrs	CH_2Cl_2	65%
4.	$IrCl_3$	20	48 hrs	CH_2Cl_2	49%
5.	$CuCl_2$	20	48 hrs	CH_2Cl_2	75%
6.	$CuCl_2$	20	48 hrs	CH_3CN	91%
7.	$CuCl_2$	20	24 hrs	CH_3CN	54%
8.	$CuCl_2$	5	48 hrs	CH_3CN	52%
9.	$CuCl_2$	10	48 hrs	CH_3CN	60%
10.	$CuCl_2$	30	48 hrs	CH_3CN	94%

The procedure worked well with various substituted indoles and α,β-unsaturated ketones (Scheme 18).

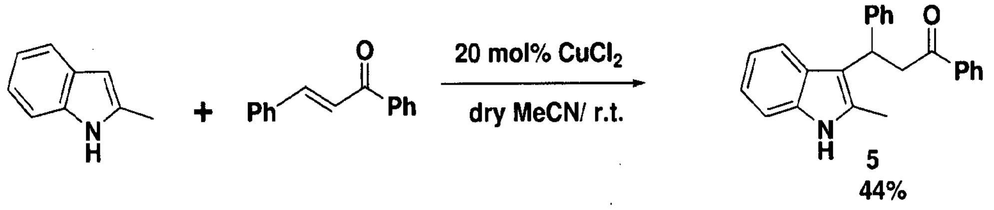


SCHEME 18

To start with we examined the reaction of indole (2 mM) with 1,3-diphenylprop-2-enone (2 mM) to produce corresponding 3-substituted indole **1** in 91% yield. This encouraged us to examine the reactions of different substituted indoles like 5-bromoindole, 5-methoxyindole, 5-methylindole, 2-methylindole, 1-methylindole and 6-chloroindole with 1,3-diphenylprop-2-enone in the presence of catalytic amount of $CuCl_2$ to furnish 3-alkylated indoles **2**-**7** in good yields (Schemes 19-22).



SCHEME 19



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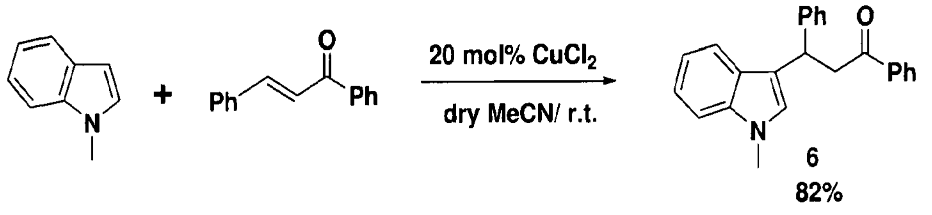
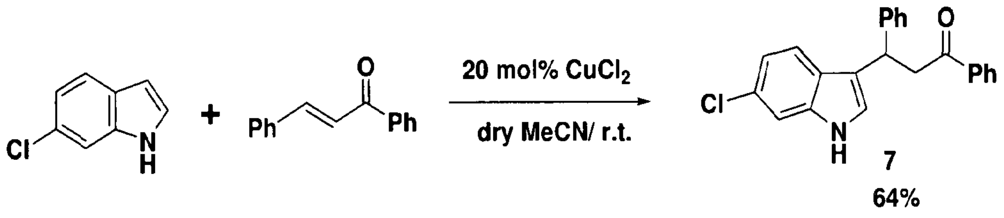
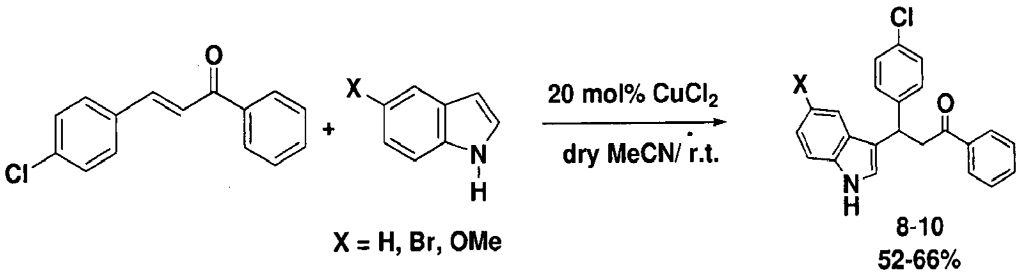


SCHEME 21

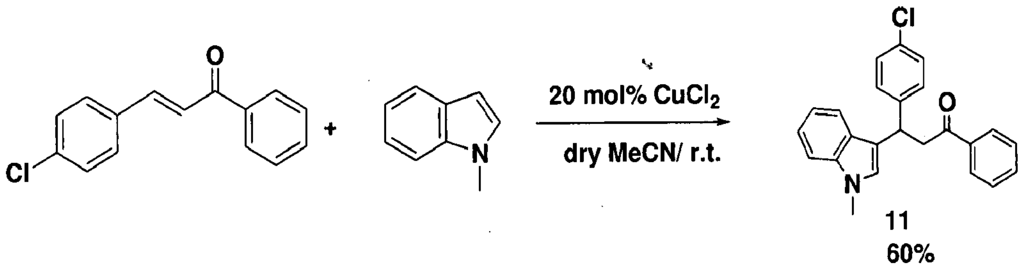


SCHEME 22

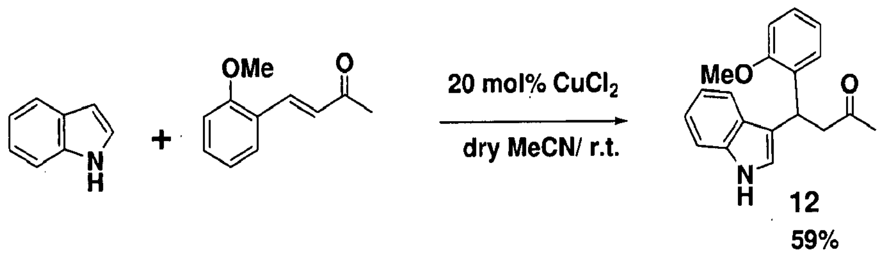
2-Methylindole afforded the corresponding indole derivative **5** in lowest yield *i.e.*, 44% which might be due to steric hindrance caused by methyl at C-2 position. Yet the reaction proceeded to give significantly pure product and no side product is formed. During our studies on Friedel-Crafts type alkylation of indoles, another enone from chalcone family *i.e.*, 3-(4-chlorophenyl)-1-phenylprop-2-ene-1-one was used with different indoles *viz.* indole, 5-bromoindole, 5-methoxyindole, 1-methylindole to furnish the corresponding 3-substituted indoles **8-10** in moderate yields of 52-66% (Scheme 23). *N*-Methylindole furnished the corresponding Friedel-Crafts type product in acceptable yield (Scheme 24). Also the alkylation of indole with 4-(2-methoxyphenyl)but-3-en-2-one provided the indole derivative **12** in 59% (Scheme 25).



SCHEME 23

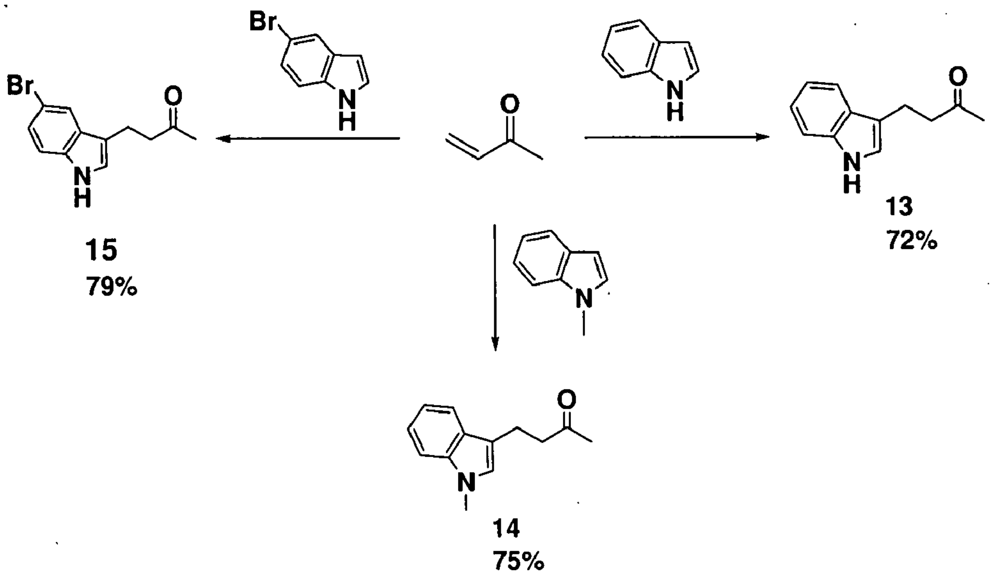


SCHEME 24

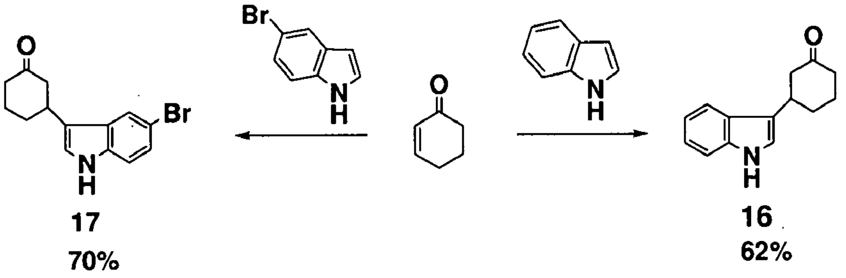


SCHEME 25

To broaden the scope of study, we also investigated reactions of indoles with methyl vinyl ketone and cyclohexenone. These α,β-unsaturated ketones being more reactive than chalcones, the reactions reached completion in 0.5 and 1 hours, respectively, with good yields (Schemes 26 & 27).



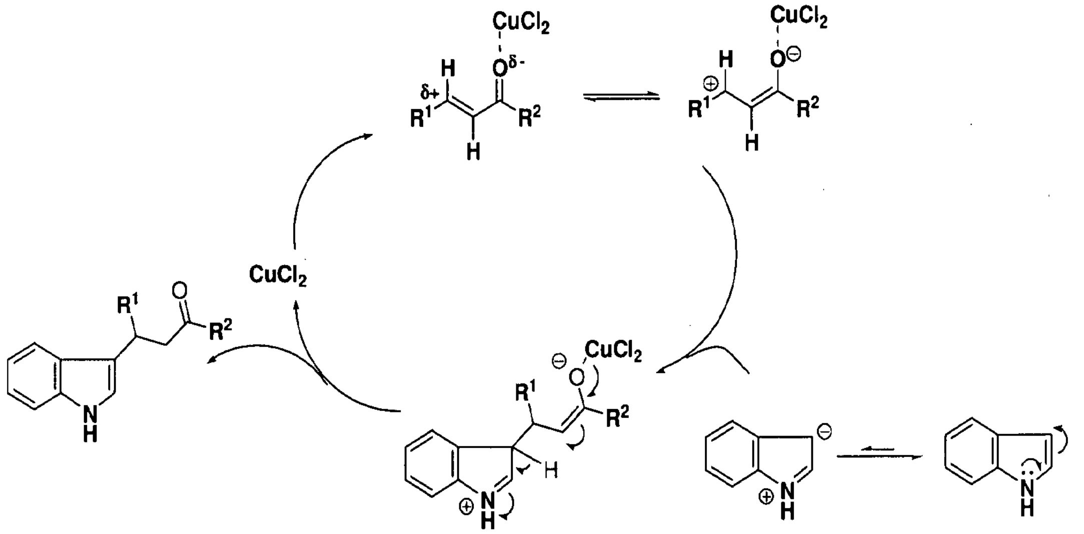
SCHEME 26



SCHEME 27

Mechanism:

The role of $CuCl_2$ in catalyzing the alkylation may be through proposed mechanism as shown in Scheme 28. $CuCl_2$ because being a Lewis acid got attached to the oxygen of carbonyl group of α,β-unsaturated ketones forming a $\delta+$ charge on β carbon which facilitate the nucleophilic attack of indoles at position-3. Subsequent generation of $CuCl_2$ facilitates its participation in the catalytic cycle.



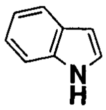
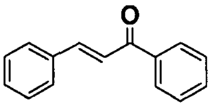
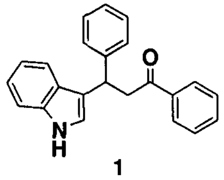
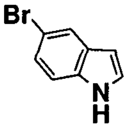
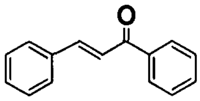
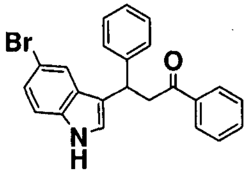
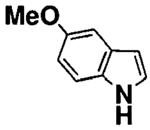
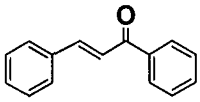
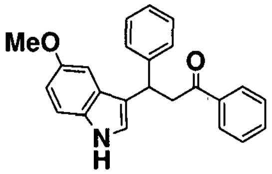
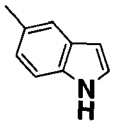
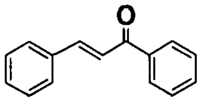
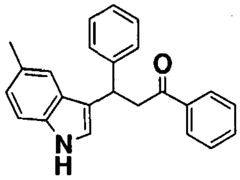
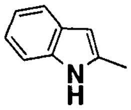
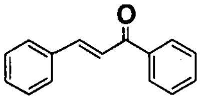
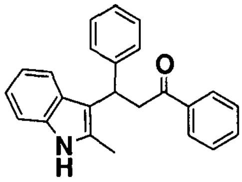
SCHEME 28

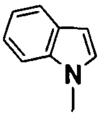
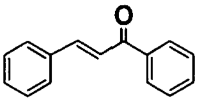
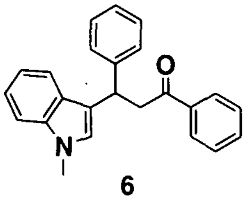
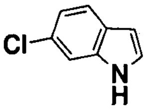
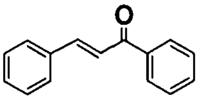
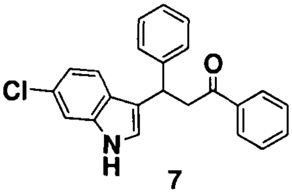
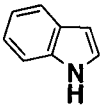
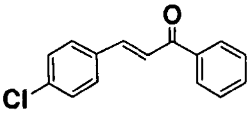
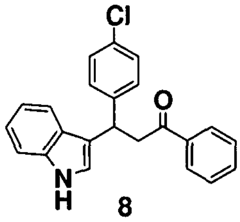
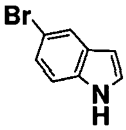
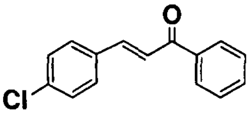
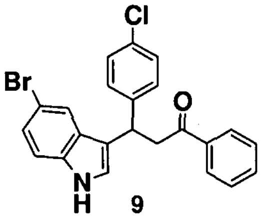
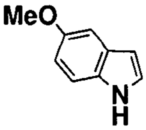
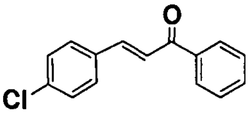
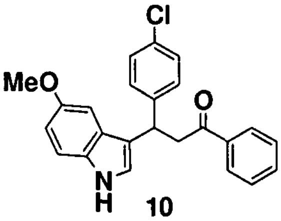
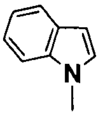
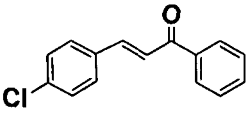
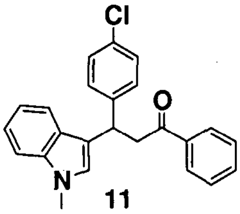
Characterization

The structures of 3-substitued indoles were assigned on the basis of their IR, ^{1}H NMR (500 MHz), ^{13}C NMR (125 MHz) and ESI-MS (electronspray ionization mass spectroscopy) spectral analysis. The product 3-(3-indolyl)-1,3-diphenylpropan-1-one (**1**) gives a singlet peak at 7.99 confirming the presence of N-H proton. Same apply for all examples except those with *N*-methylated indole *i.e.*, **6**, **11** and **14**. The downfield broad singlet, characteristic of compounds with N-H bond, is not present in ^{1}H NMR spectra of these molecules. Deuterium exchange was done on example **8** and **10** and the spectra show the exchange of proton by deuterium as the peak for N-H got exchanged (Fig 66 and 67 of spectra section). ^{13}C NMR spectra also show peak at 198, 145 which are characteristic of carbon attached to electronegative atoms and here for carbonyl carbon and carbon attached to nitrogen atom. Other peaks are for aromatic carbons and two alkyl carbons. IR spectra of all examples except **6**, **11** and **14** show peaks characteristic of N-H bond (3300-3400 cm^{-1}), carbonyl group (~1700 cm^{-1}) and peaks at aromatic region while spectra of **6**, **11** and **14** show peaks for carbonyl group and aromatic bonds only. Due to different substitution on indole and benzyl rings, IR spectra of all molecules show absorption bands in the range of 800-600 cm^{-1}.

The structures of all these examples (**1-17**) were confirmed by comparing chemical shifts of some particular protons from their ^{1}H NMR as shown in table 3-5. Furthermore, fragmentation of two products **1** and **13** is shown in Schemes 29 and 30. All the products show same pattern of fragmentation and their fragments have been tabulated in table 6. NMR and MS spectral data corroborate with the reported data for the known compounds in literature [30].

Table 2: Alkylation of indoles with α,β-unsaturated ketones

S.No.	Indole	α,β-unsaturated ketone	Reaction time	Product	Yield (%)
1.			40 hr	 **1**	91
2.			18 hr	 **2**	71
3.			30 hr	 **3**	58
4.			29 hr	 **4**	47
5.			40 hr	 **5**	44

6.			36 hr	 **6**	82
7.			24 hr	 **7**	64
8.			38 hr	 **8**	62
9.			38 hr	 **9**	66
10.			28 hr	 **10**	52
11.			25 hr	 **11**	60

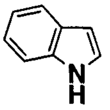
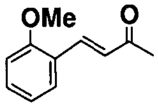
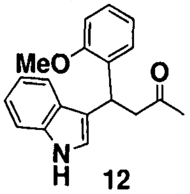
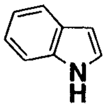
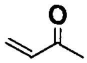
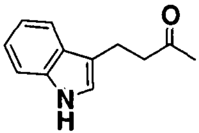
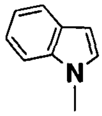
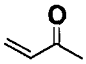
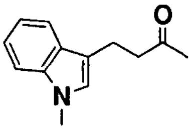
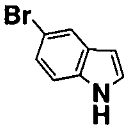
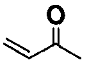
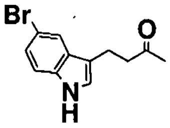
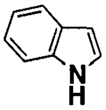
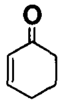
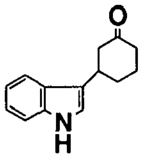
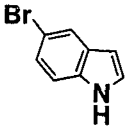
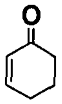
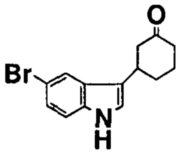
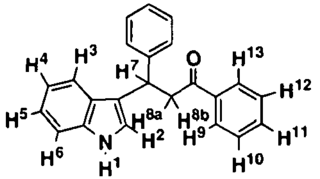
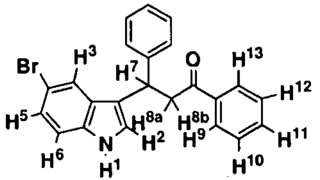
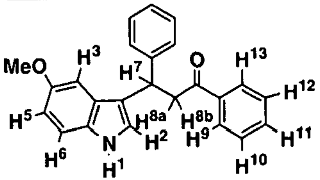
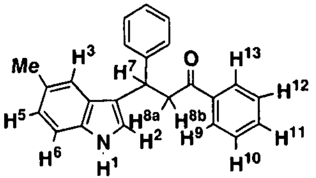
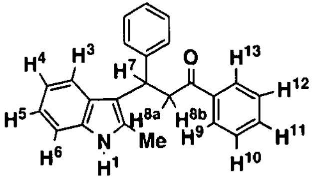
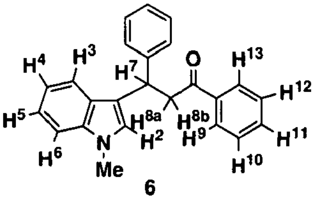
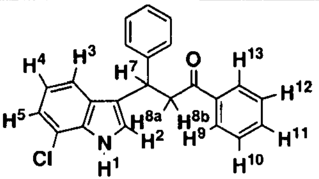
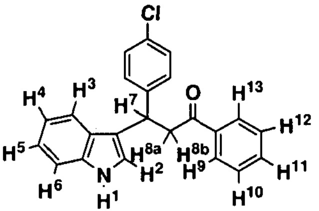
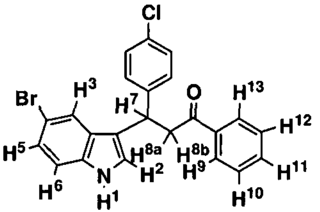
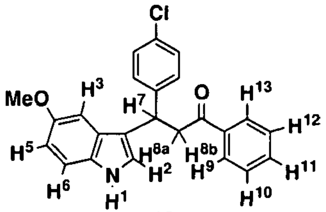
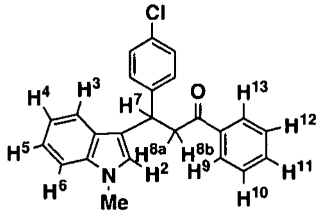
12.			40 hr	 **12**	59
13.			0.5 hr	 **13**	72
14.			0.5 hr	 **14**	75
15.			0.5 hr	 **15**	79
16.			1 hr	 **16**	62
17.			1 hr	 **17**	70

Table 3. Selected chemical shifts (in ppm) from ^{1}H NMR (500 MHz) spectra of products 1-12

Compound	H^1	H^2	H^7	H^{8a}	H^{8b}	H^9, H^{13}	H^{10}, H^{12}	H^{11}	Me, OMe, N-Me
 1	7.99	7.03-7.00	5.07	3.72	3.82	7.93	7.44-7.41	7.53	-
 2	8.00	7.02	5.00	3.77	3.70	7.93	7.50-7.41		-
 3	7.83	6.98	5.02	3.79	3.75-3.69	7.93	7.45-7.41	7.54	3.72
 4	7.87	6.93	5.04	3.79	3.72	7.93	7.42	7.53	2.36
 5	7.87	-	5.04	3.80	3.73	7.94	7.48-7.41	7.54	2.37

 **6**	-	6.76	4.98	3.83-3.78	3.77-3.70	7.94-7.90	7.35-7.32	7.56-7.50	3.71
 **7**	7.98	7.00	5.02	3.79	3.69	7.93	7.44	7.55	-
 **8**	8.00	7.00	5.04	3.80	3.70	7.93	7.46-7.39	7.55	-
 **9**	8.17	7.00	4.99	3.77	3.69	7.95	7.47	7.58	-
 **10**	7.90	6.97	4.99	3.81-3.74	3.69	7.93	7.45	7.56	3.74
 **11**	-	6.81	5.02	3.78	3.72-3.64	7.92	7.46-7.37	7.54	3.72

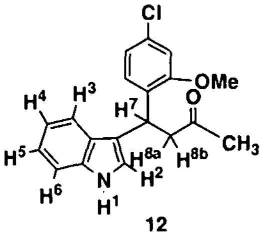
 12	8.03	6.79	5.27	3.13-3.11	7.43-7.33	7.08-6.99	Me: 2.12 OMe: 3.91

Table 4. Selected chemical shifts (in ppm) from ^{1}H NMR (500 MHz) spectra of products 13-15.

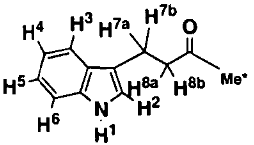
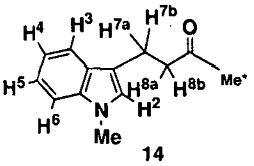
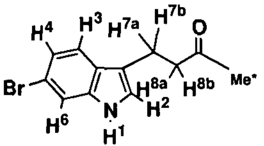
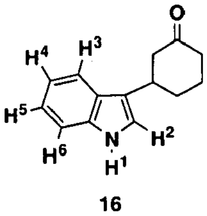
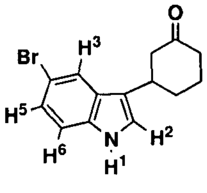
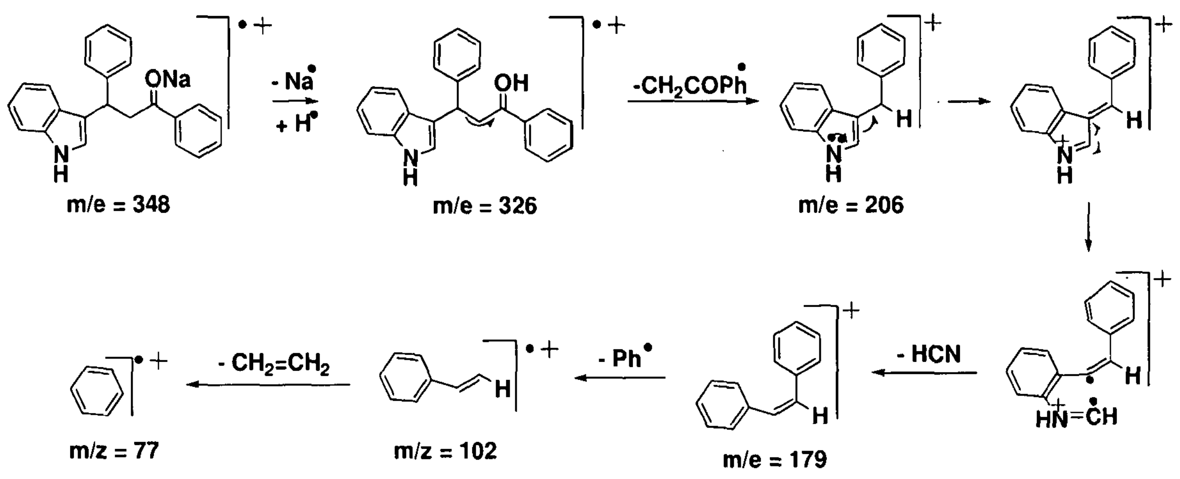
Compound	H^1	H^2	H^3	H^4	H^5	H^6	H^{7a}, H^{7b}	H^{8a}, H^{8b}	Me*	Me, OMe, N-Me
 13	7.97	6.98	7.35	7.12	7.19	7.59	3.05	2.84	2.14	-
 14	-	6.84	7.29	7.11	7.22	7.58	3.04	2.83	2.14	3.73
 15	8.16	6.96	7.27-7.22	7.21-7.17	-	7.69	2.97	2.80	2.13	-

Table 5. Selected chemical shifts (in ppm) from ^1H NMR (500 MHz) spectra of products 16-17

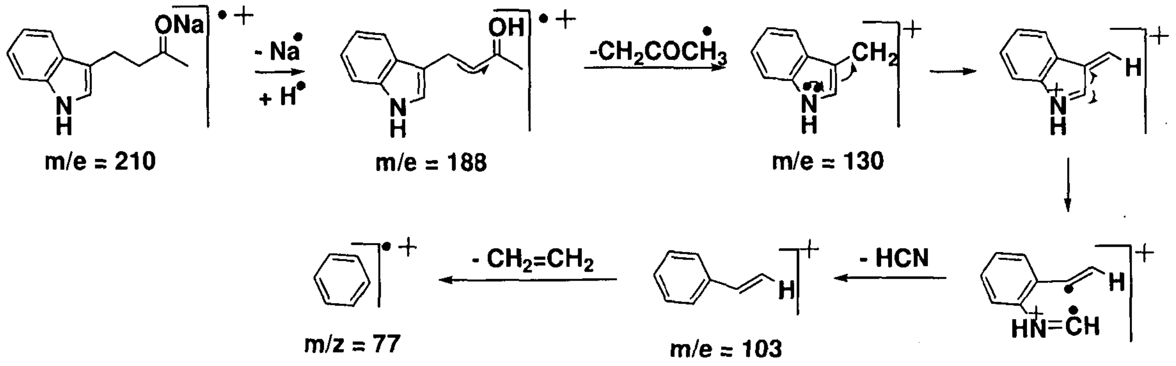
Compound	H1	H2	H3	H4	H5	H6
 16	8.01	6.99	7.37	7.12	7.21	7.63
 17	8.10	6.98	7.30-7.26	-	7.25-7.20	7.73

Proposed fragmentation of product **1** and **13** :



SCHEME 29

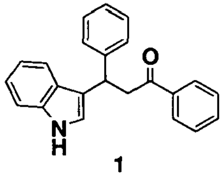
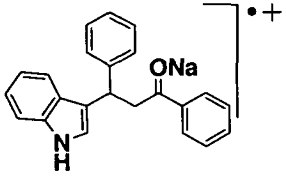
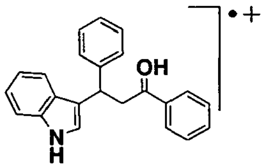
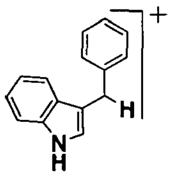
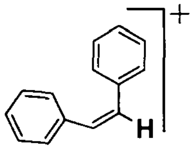
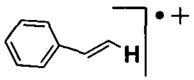
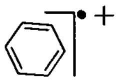
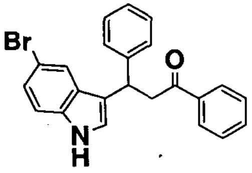
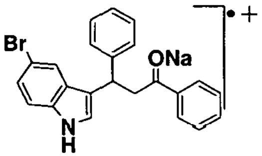
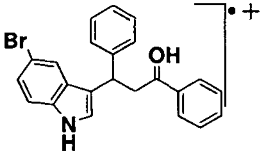
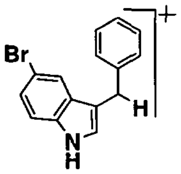
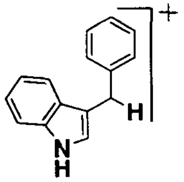
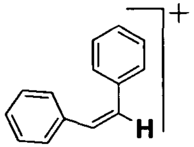
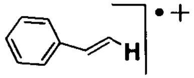
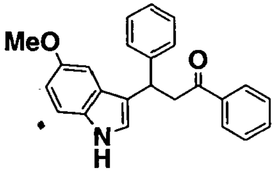
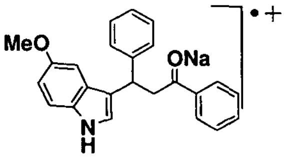
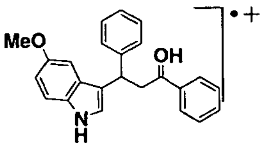
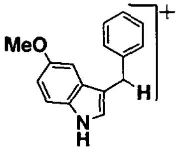
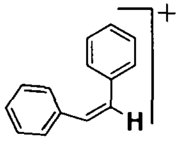
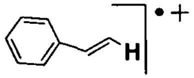
Scheme 29 shows the fragmentation of product **1** and Scheme 30 shows that of **13**. **1-12** and **13-14** shows common fragmentation pattern which have m/z values according to the substituent present. Their different fragments are shown in table 6.

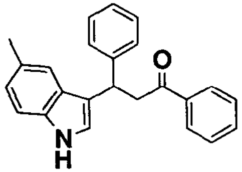
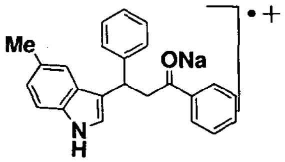
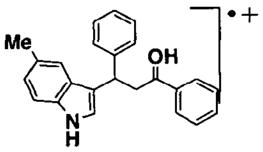
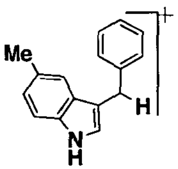
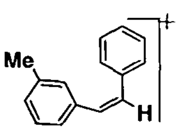
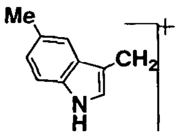
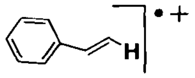
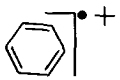
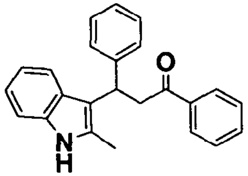
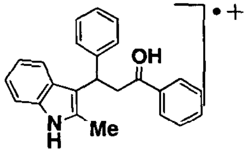
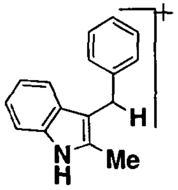
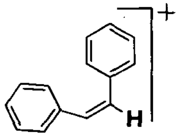
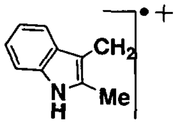
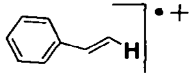
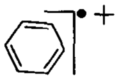
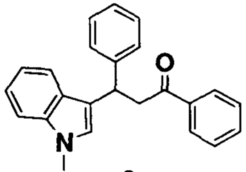
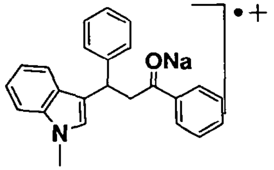
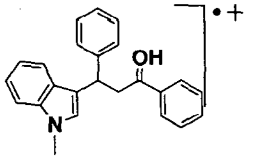
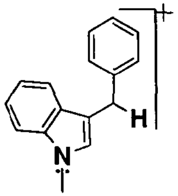
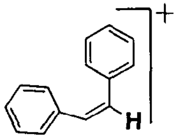
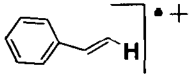
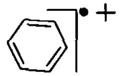
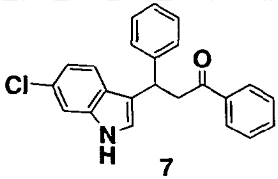
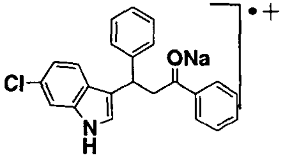
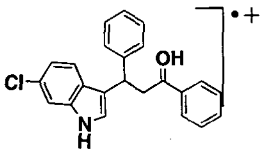
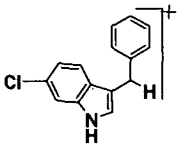
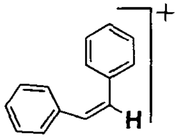
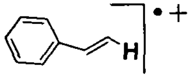
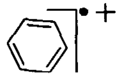


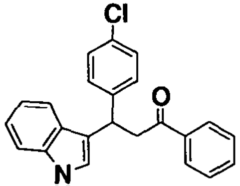
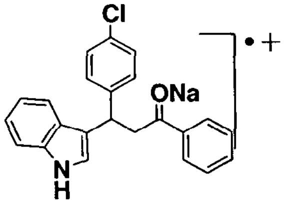
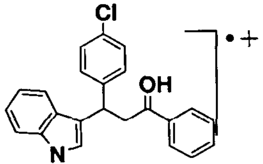
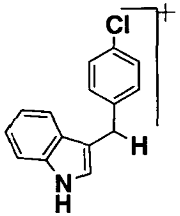
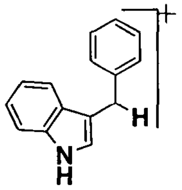
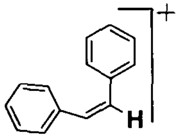
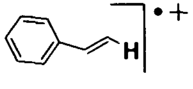
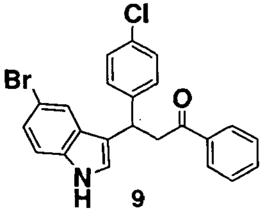
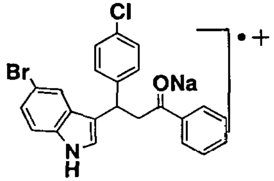
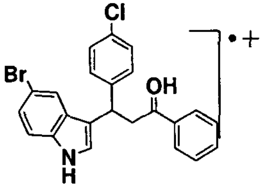
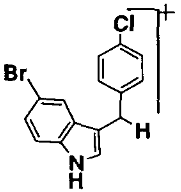
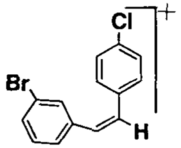
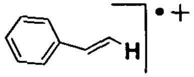
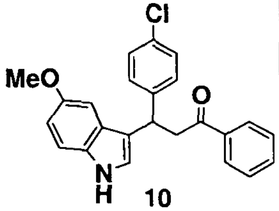
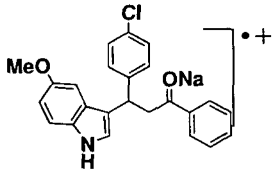
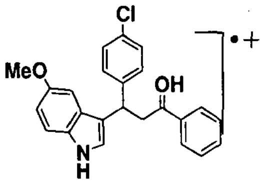
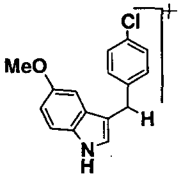
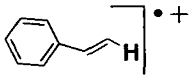
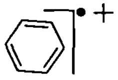
SCHEME 30

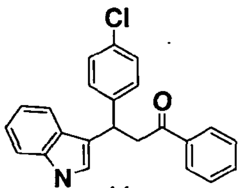
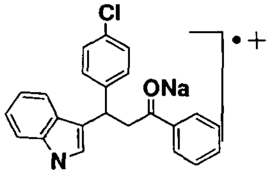
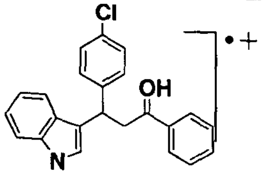
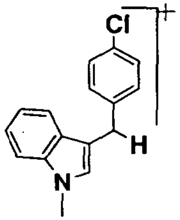
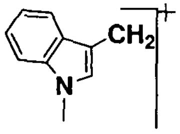
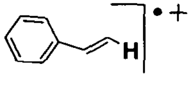
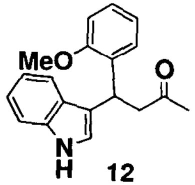
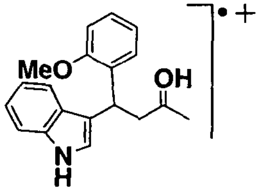
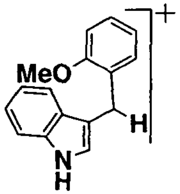
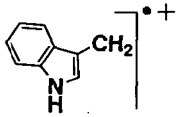
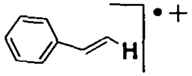
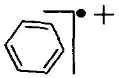
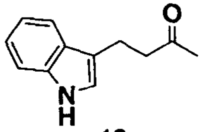
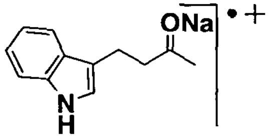
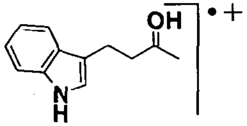
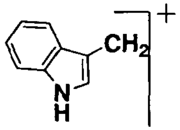
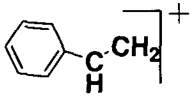
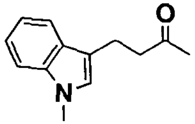
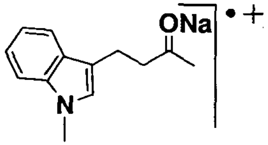
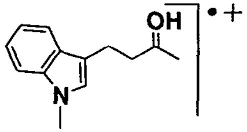
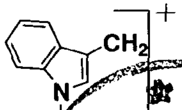
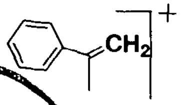
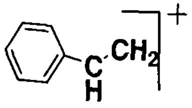
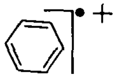
The mass spectra of bromo compounds **2** and **10** contains two molecular ion peaks (M and M+2) in almost equal intensity indicating presence of bromine atom in these molecules. Similarly, ESI mass spectra of chloro compounds **7**, **8**, **9**, **10**, **11** contains two molecular ion peaks (M and M+2) in 1:3 intensity ratio, which is characteristic of the presence of chlorine atom in molecules.

Table 6. Selected fragments from ESI-MS spectra of compounds 1-14.

Products	A	B	C	D	E	F	G
 1	 m/e = 348	 m/e = 326	 m/e = 206	 m/e = 179	 m/z = 102	 m/z = 77	-
 2	 m/e = 426	 m/e = 404	 m/e = 284	 m/e = 206	 m/e = 179	 m/z = 102	 m/z = 77
 3	 m/e = 378	 m/e = 356	 m/e = 237	 m/e = 179	 m/z = 102	 m/z = 77	-

 4	 m/e = 362	 m/e = 340	 m/e = 220	 m/e = 193	 m/e = 144	 m/z = 102	 m/z = 77
 5	-	 m/e = 340	 m/e = 220	 m/e = 179	 m/e = 144	 m/z = 102	 m/z = 77
 6	 m/e = 362	 m/e = 340	 m/e = 220	 m/e = 179	 m/z = 102	 m/z = 77	-
 7	 m/e = 382.5	 m/e = 360.5	 m/e = 240.5	 m/e = 179	 m/z = 102	 m/z = 77	-

 8	 m/e = 382.5	 m/e = 360.5	 m/e = 240.5	 m/e = 206	 m/e = 179	 m/z = 102	 m/z = 77
 9	 m/e = 461.5	 m/e = 438.5	 m/e = 319.5	 m/e = 291.5	 m/z = 102	 m/z = 77	-
 10	 m/e = 412.5	 m/e = 390.5	 m/e = 270.5	 m/z = 102	 m/z = 77	-	-

 11	 m/e = 396.5	 m/e = 374.5	 m/e = 255.5	 m/e = 144	 m/z = 102	 m/z = 77	-
 12	 m/z = 294	 m/z = 236	 m/z = 130	 m/z = 102	 m/z = 77	-	-
 13	 m/e = 210	 m/e = 188	 m/e = 130	 m/e = 103	 m/z = 77	-	-
 14	 m/e = 224	 m/e = 202	 m/e = 144	 m/e = 117	 m/e = 103	 m/z = 77	-

CONCLUSIONS

CONCLUSIONS

We have demonstrated copper(II) chloride as a novel catalyst for Friedel-Crafts type alkylation of indole and its derivatives with enones at room temperature to give 3-substituted indoles that are potential building blocks for synthesis of natural products. The catalyst used is cheap, easily available and can be removed easily from the reaction mixture. The reaction procedure is quite simple and 3-substituted indoles are formed exclusively. Three types of electrophiles *viz.* chalcones, methyl vinyl ketone and cyclohexenone reacted with different indoles and reactions proceeded smoothly to furnish the products in moderate to very high yields. All the compounds were fully characterized by analytical tools and by comparison of the known data for the available compounds.

SPECTRA

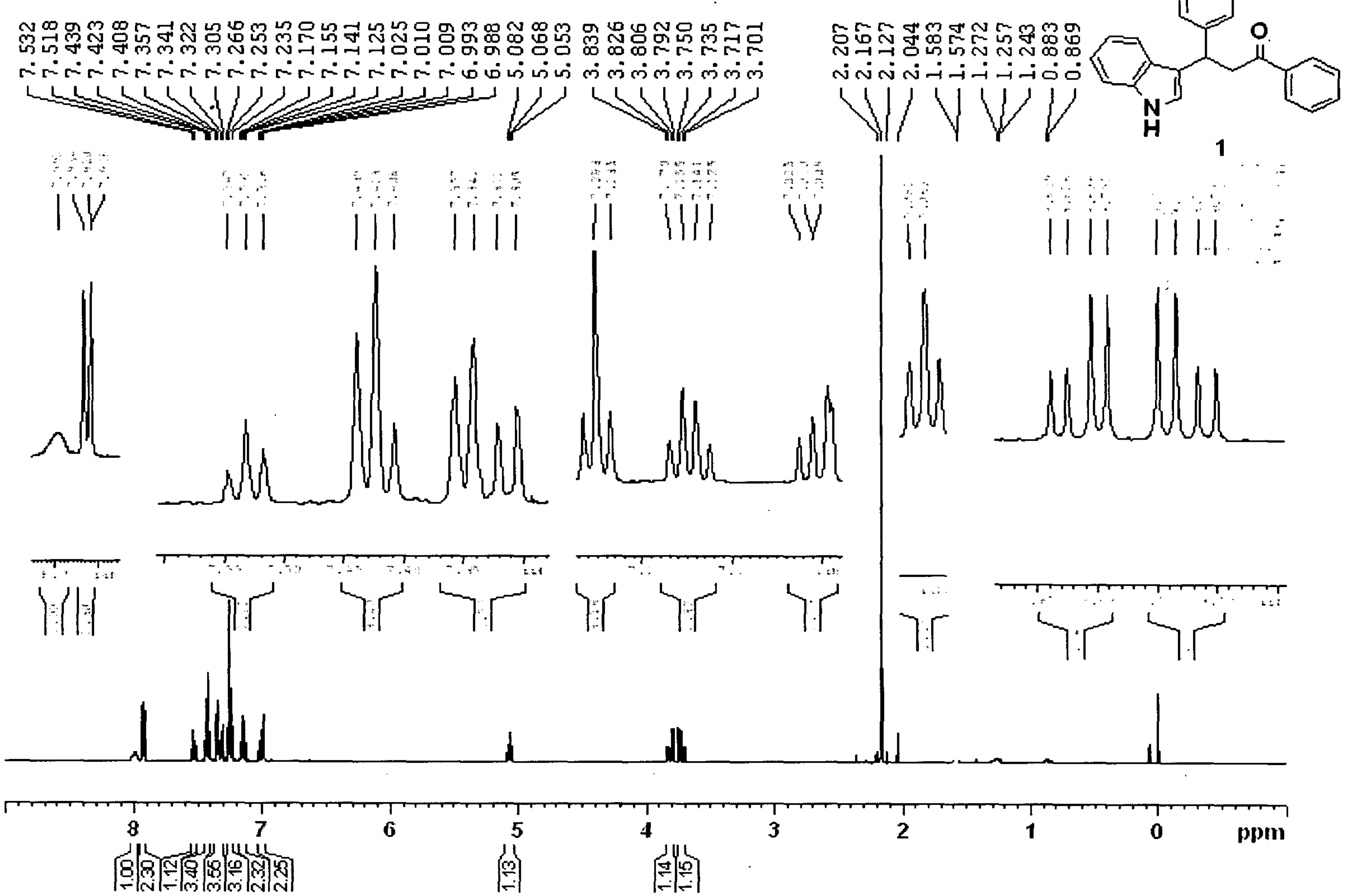


Fig 1. ^{1}H NMR (500 MHz) spectrum of 3-(3-indolyl)-1,3-diphenylpropan-1-one

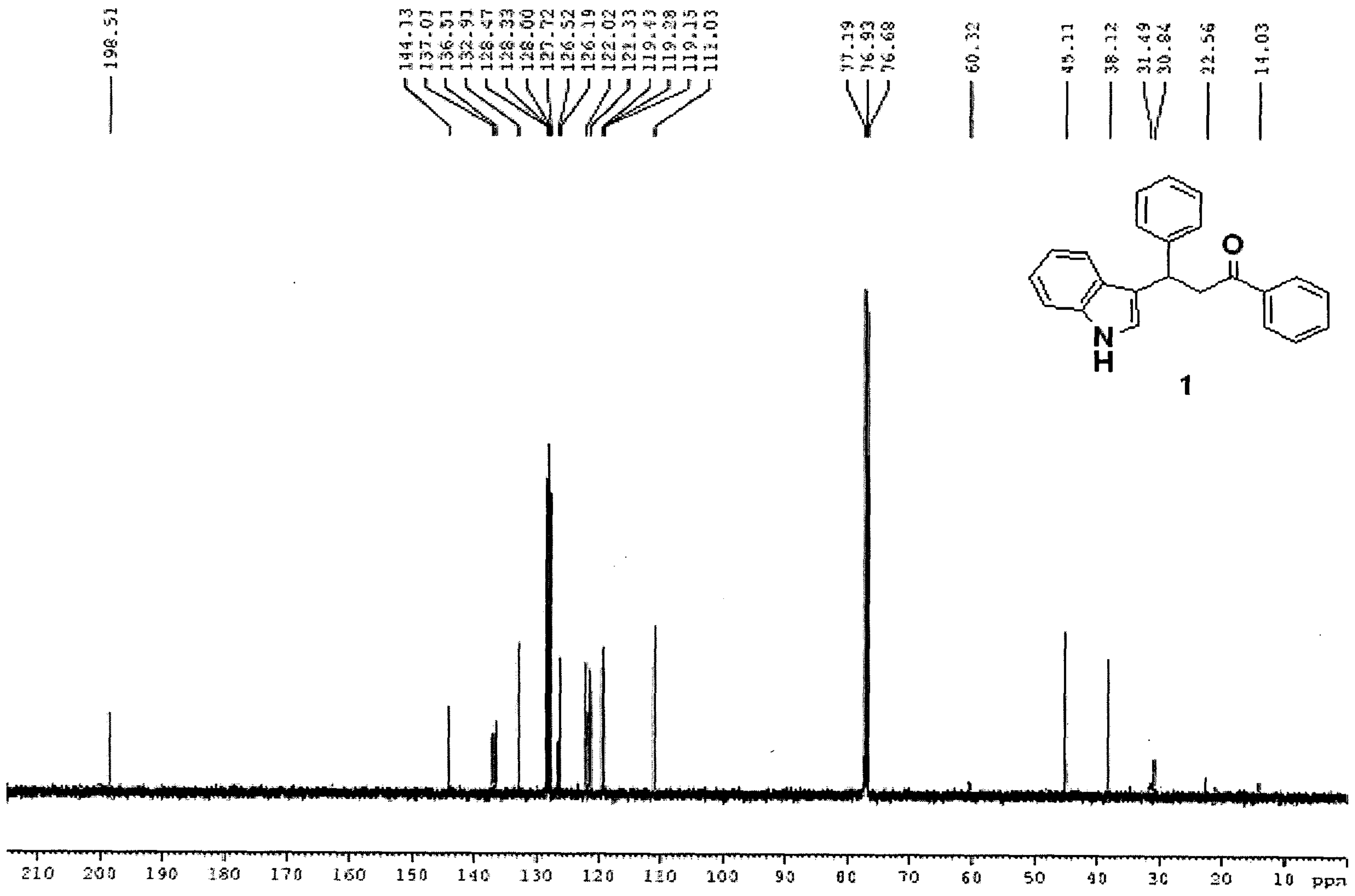


Fig 2. ^{13}C NMR (125 MHz) spectrum of 3-(3-indolyl)-1,3-diphenylpropan-1-one

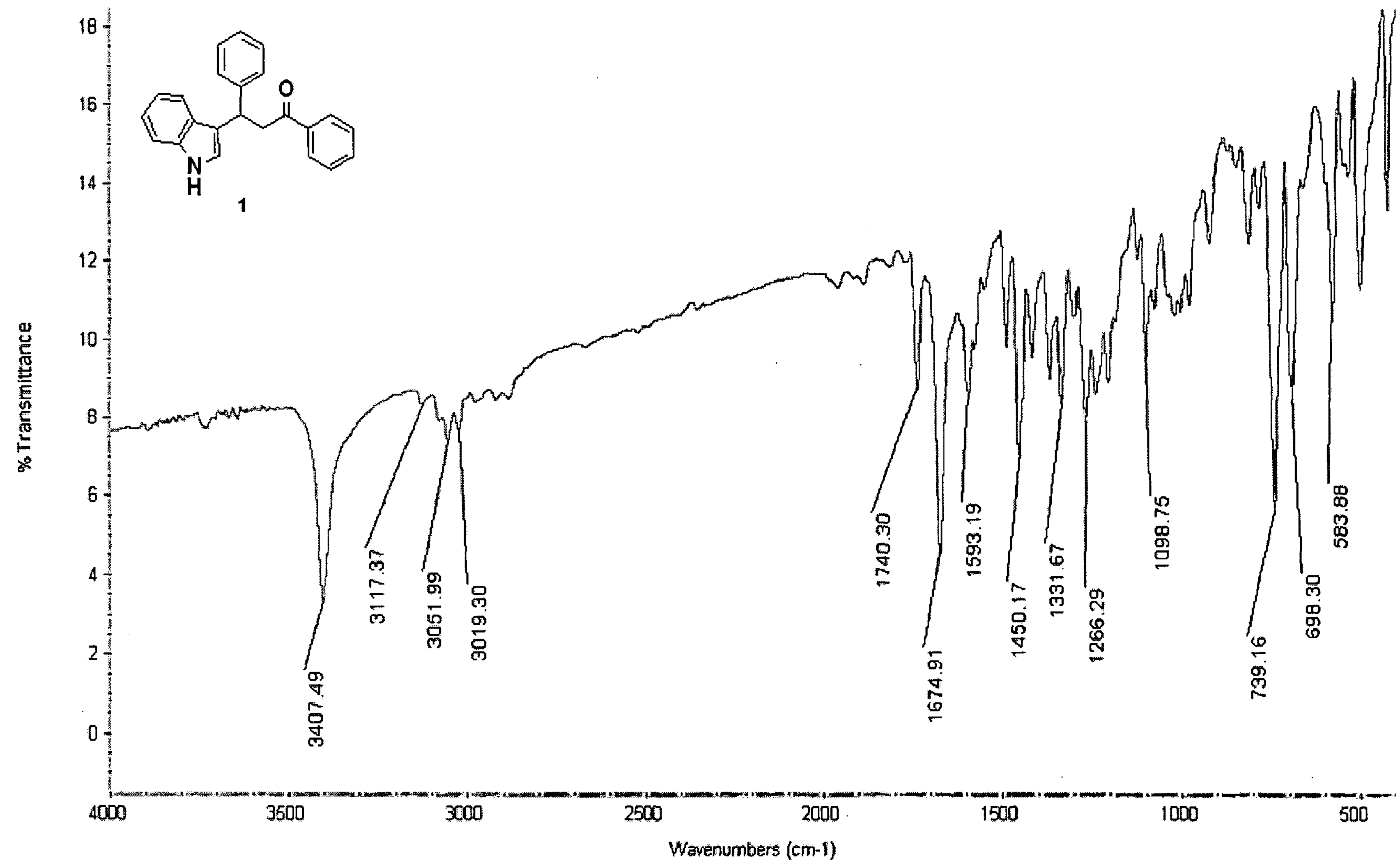


Fig 3. IR spectrum of 3-(3-indolyl)-1,3-diphenylpropan-1-one

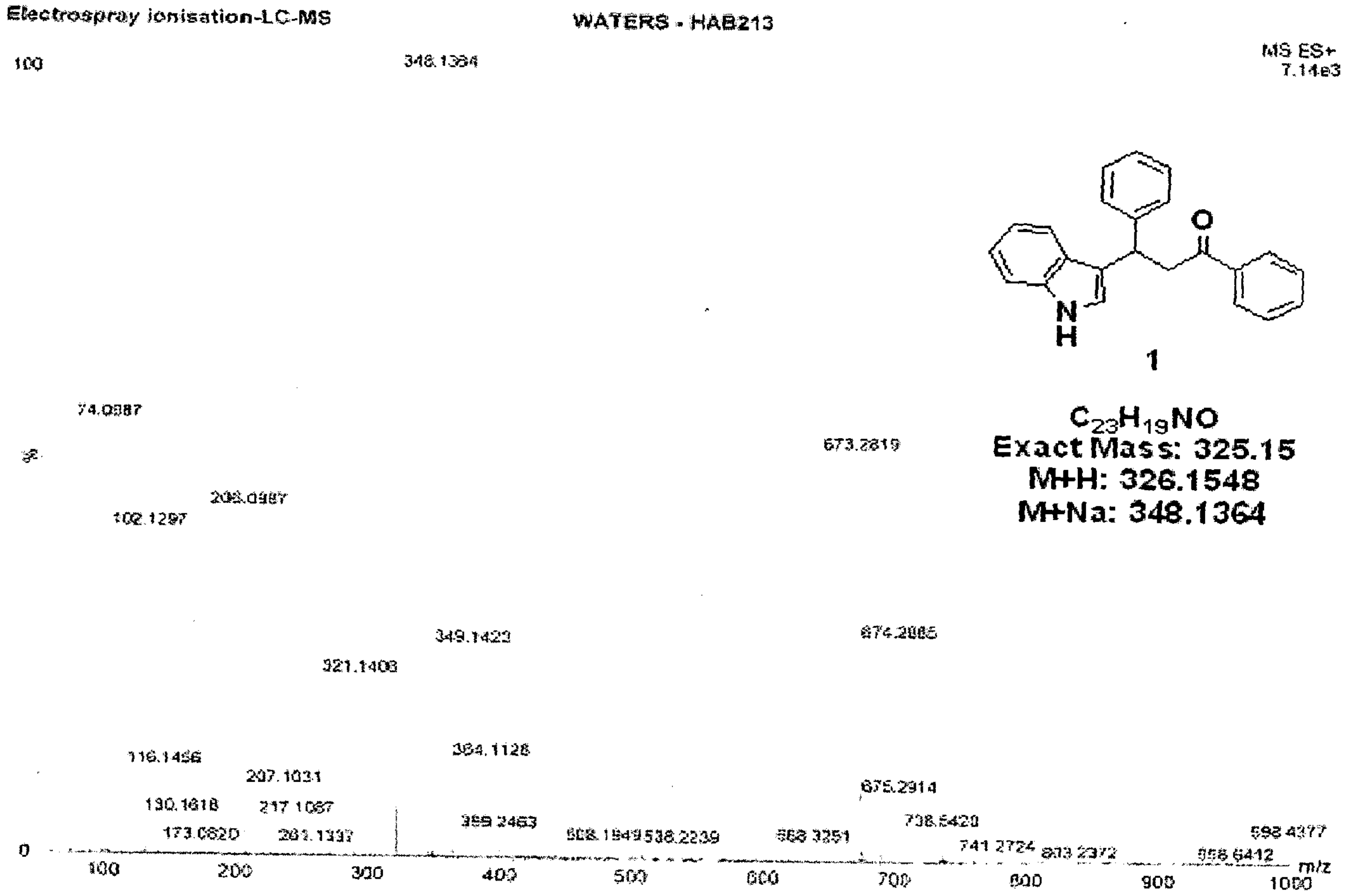


Fig 4. ESI-MS spectrum of 3-(3-indolyl)-1,3-diphenylpropan-1-one

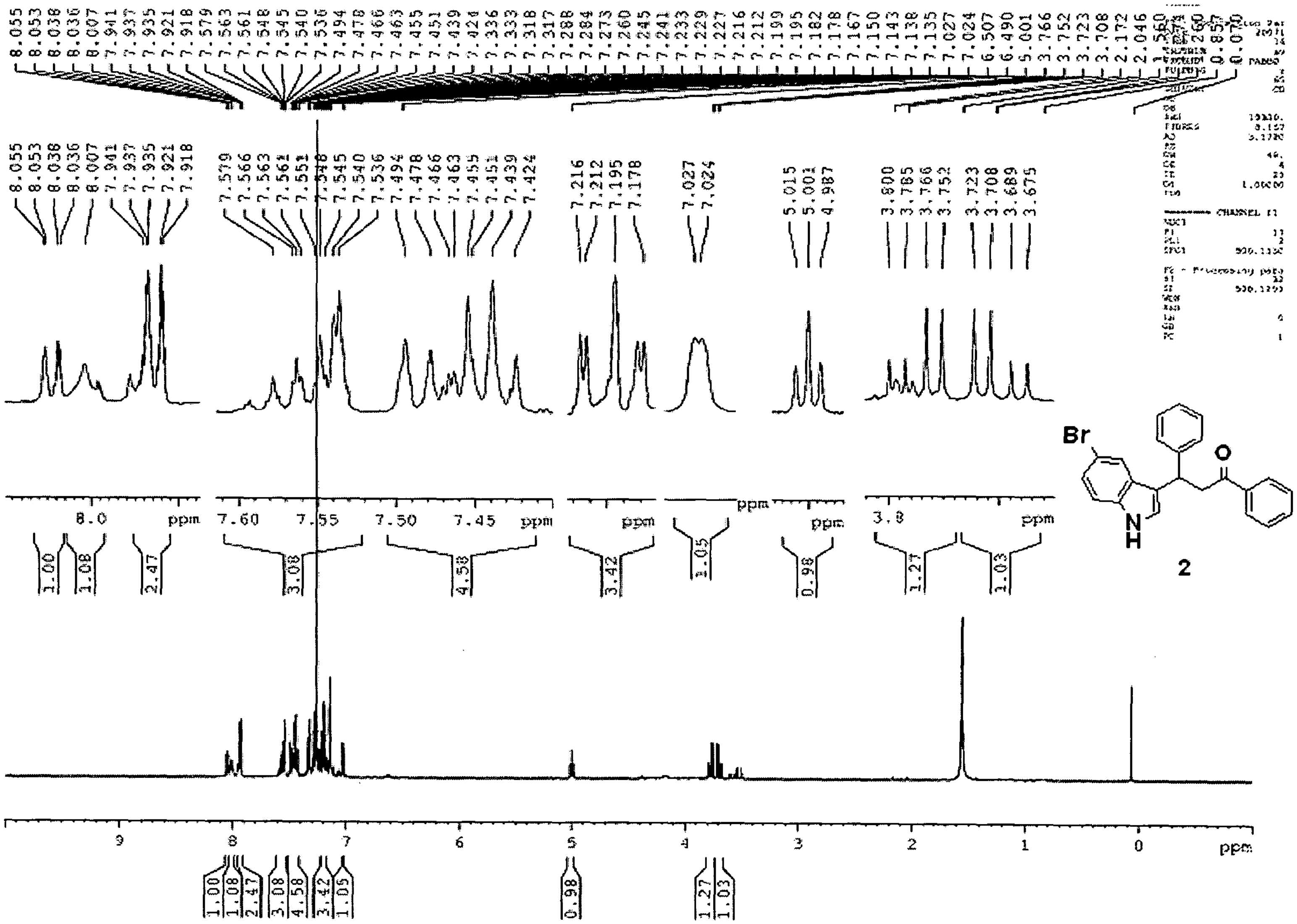


Fig 5. ^{1}H NMR (500 MHz) spectrum of 3-(5-bromo-3-indolyl)-1,3-diphenylpropan-1-one

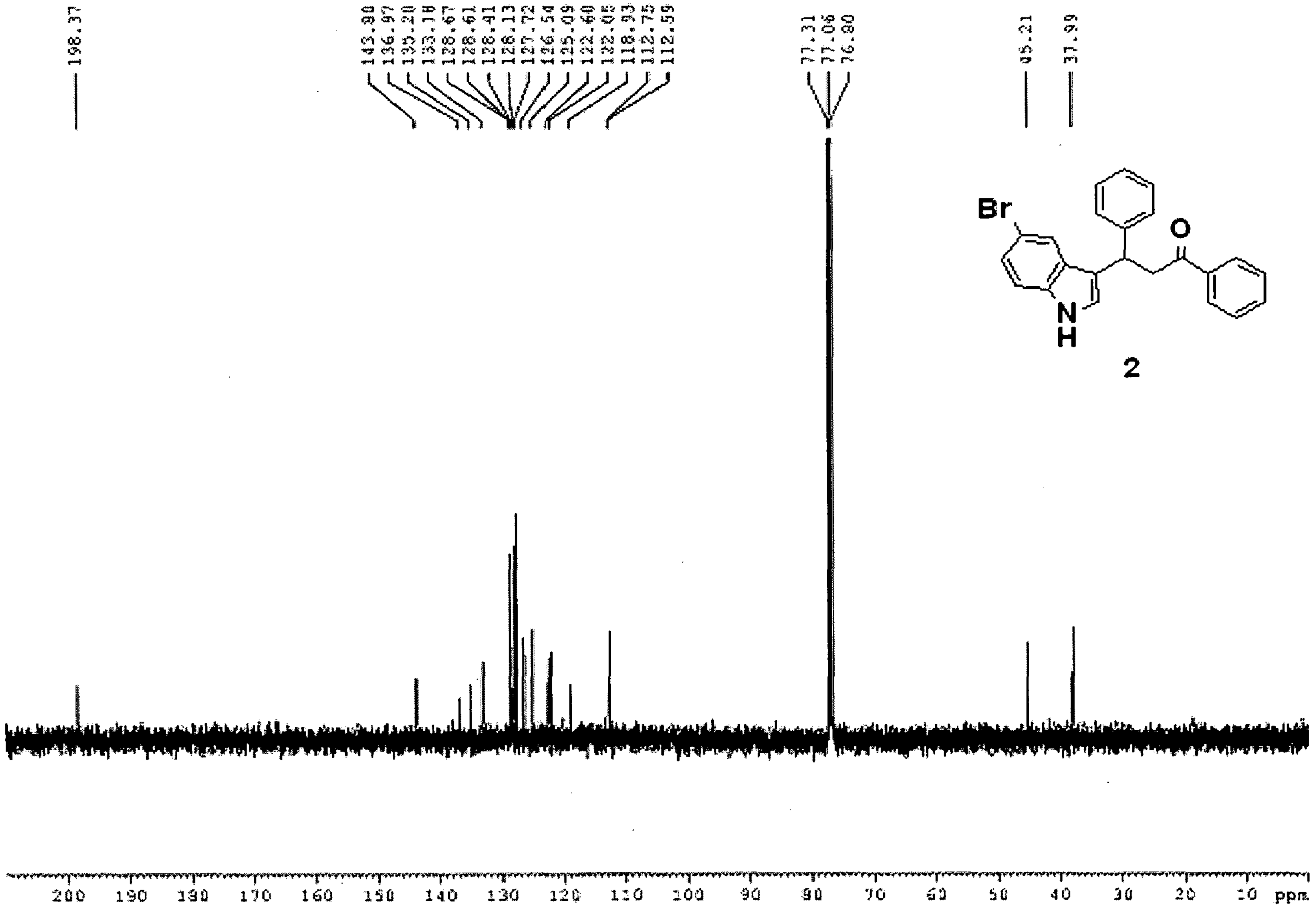


Fig 6. ^{13}C NMR (125 MHz) spectrum of 3-(5-bromo-3-indolyl)-1,3-diphenylpropan-1-one

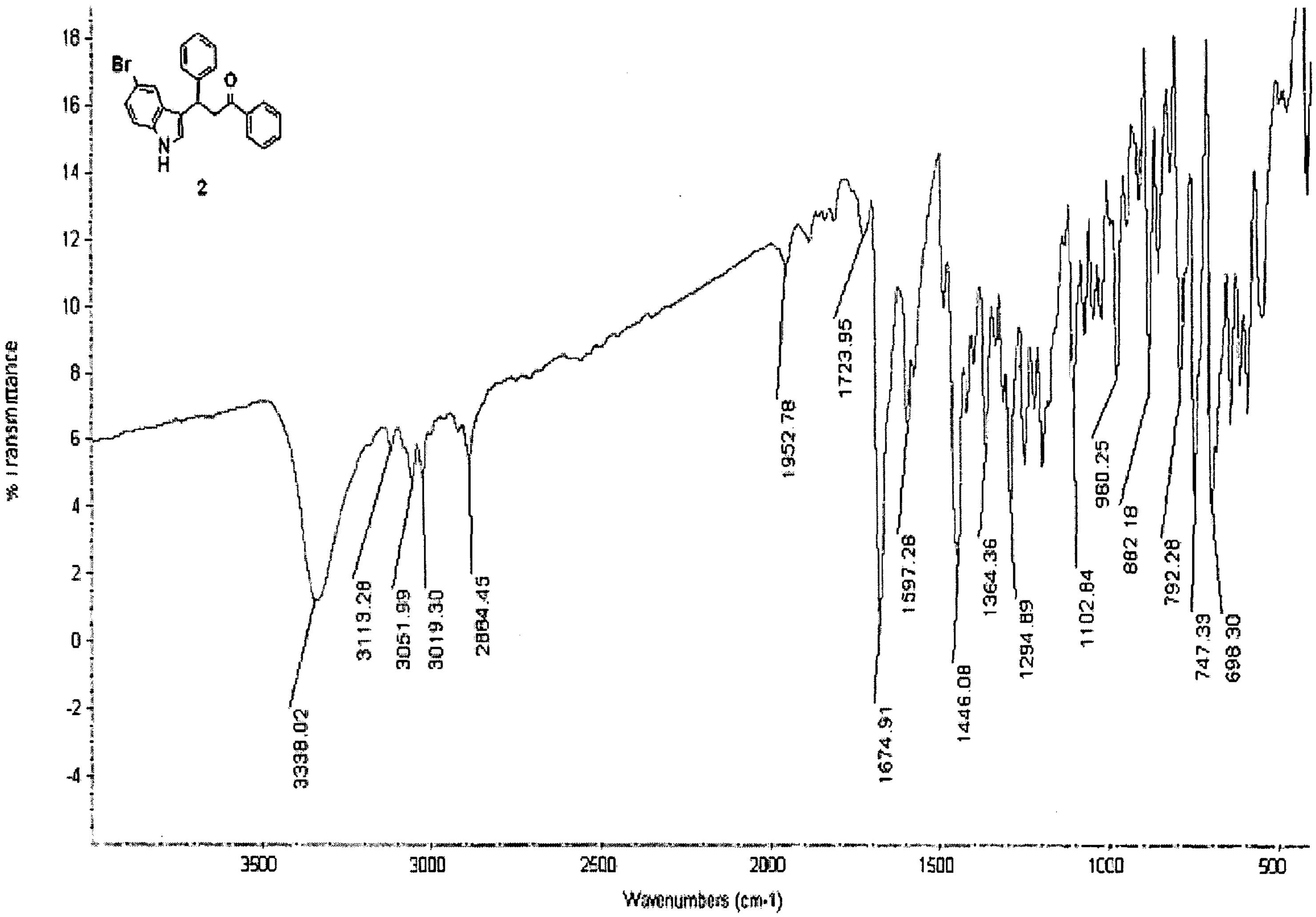


Fig 7. IR spectrum of 3-(5-bromo-3-indolyl)-1,3-diphenylpropan-1-one

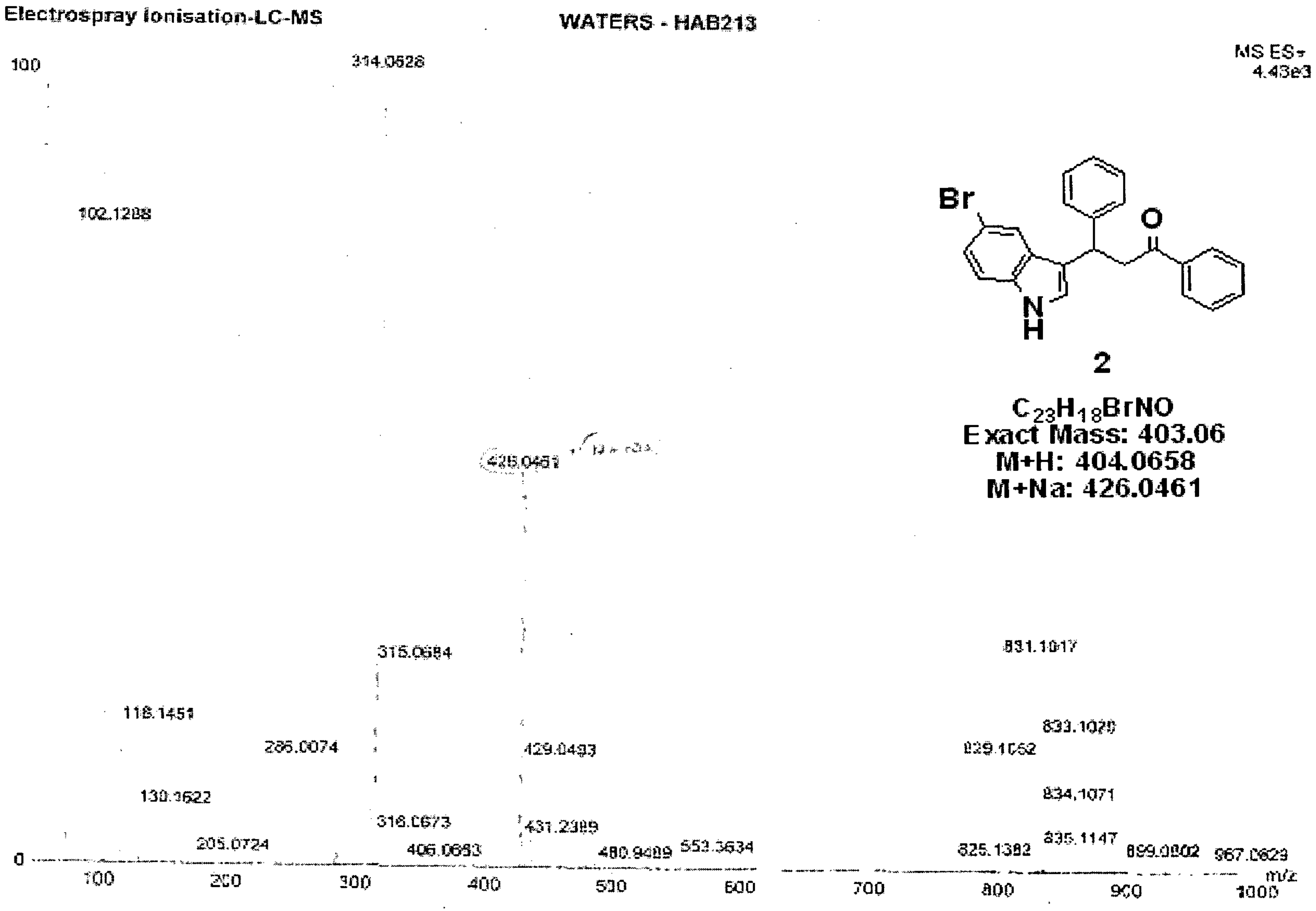


Fig 8. ESI -MS spectrum of 3-(5-bromo-3-indolyl)-1,3-diphenylpropan-1-one

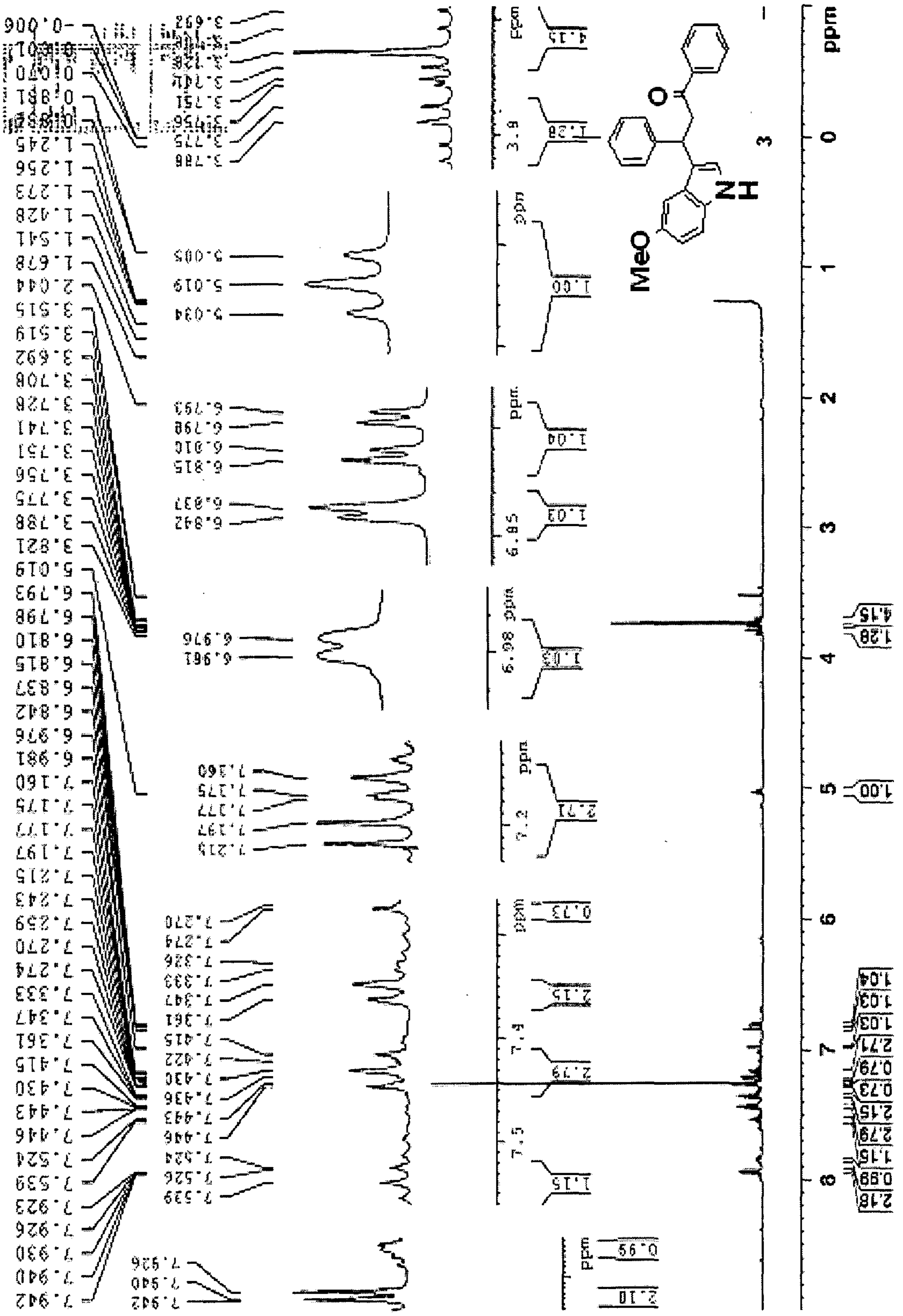


Fig 9. ^{1}H NMR (500 MHz) spectrum of 3-(5-methoxy-3-indolyl)-1,3-diphenylpropan-1-one

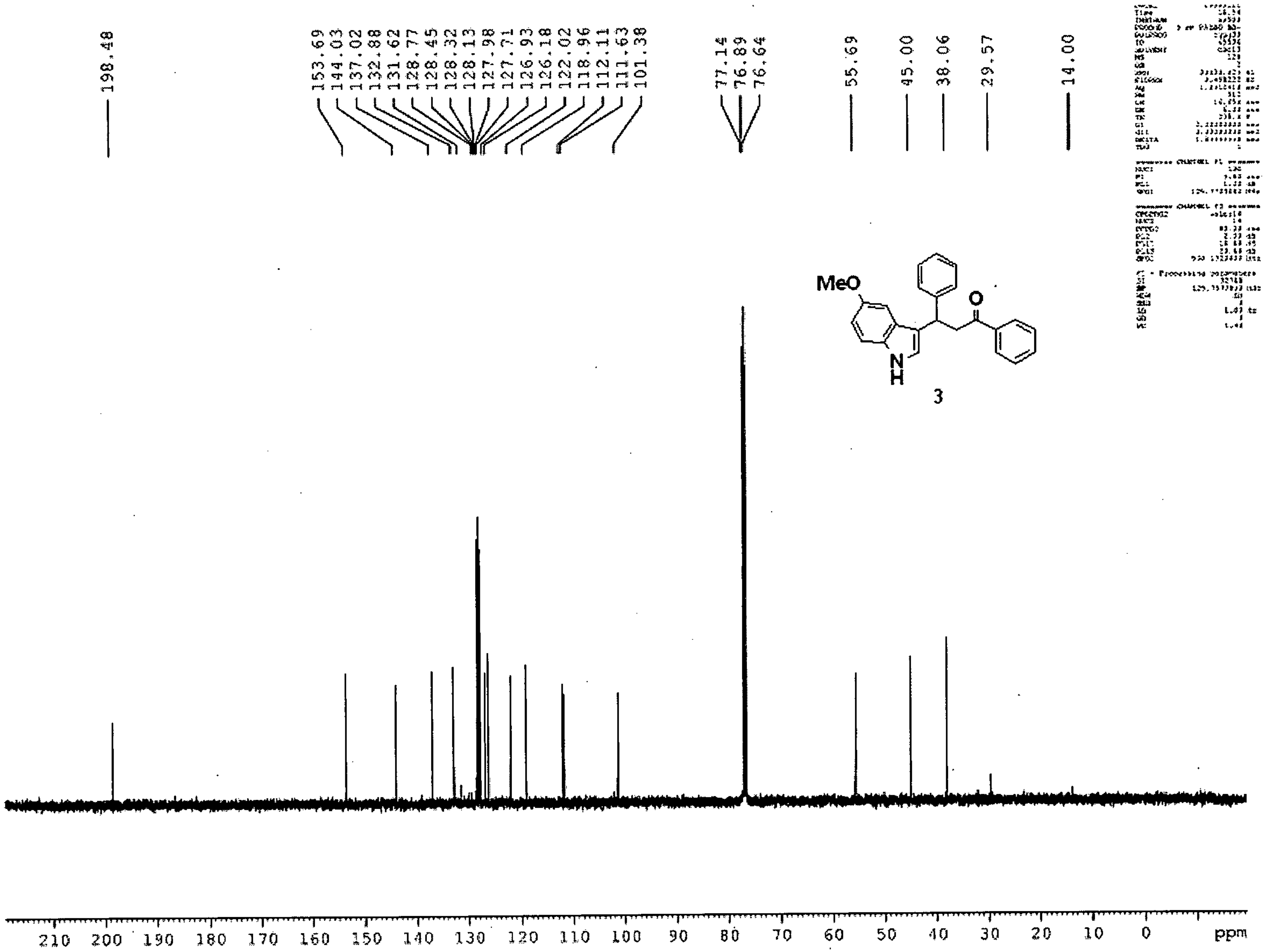


Fig 10. ^{13}C NMR (125 MHz) spectrum of 3-(5-methoxy-3-indolyl)-1,3-diphenylpropan-1-one

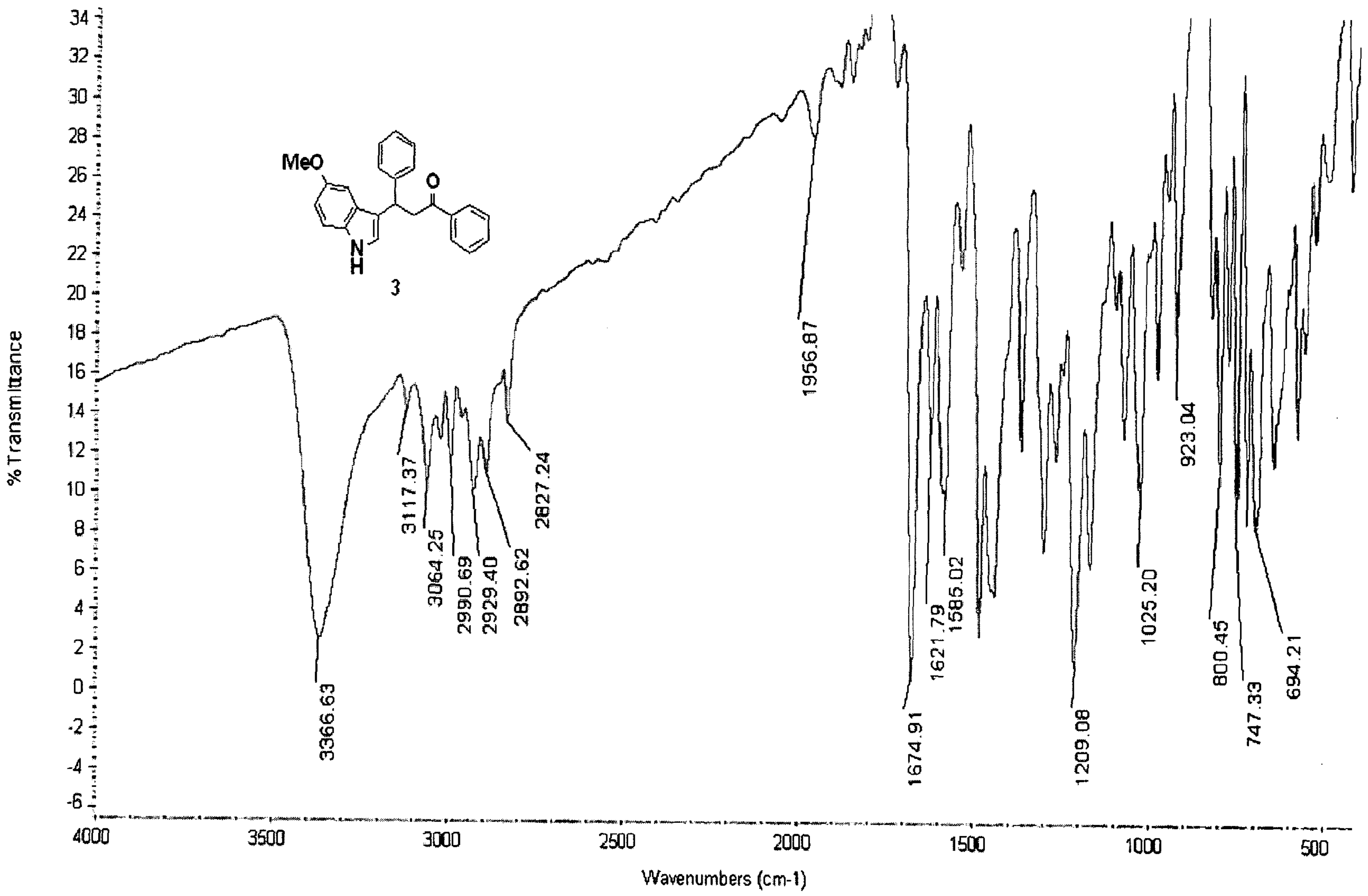


Fig 11. IR spectrum of 3-(5-methoxy-3-indolyl)-1,3-diphenylpropan-1-one

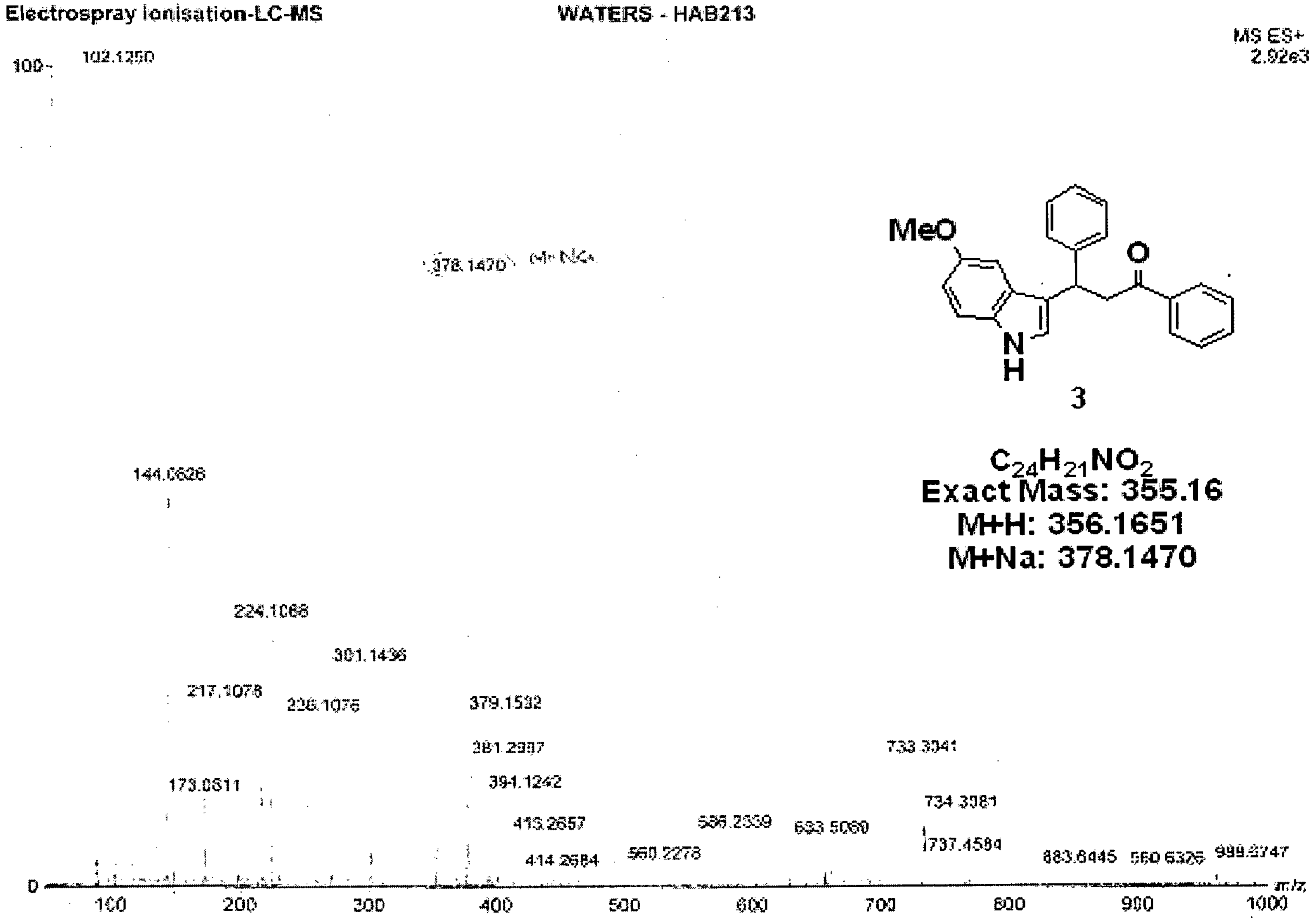


Fig 12. ESI -MS spectrum of 3-(5-methoxy-3-indolyl)-1,3-diphenylpropan-1-one

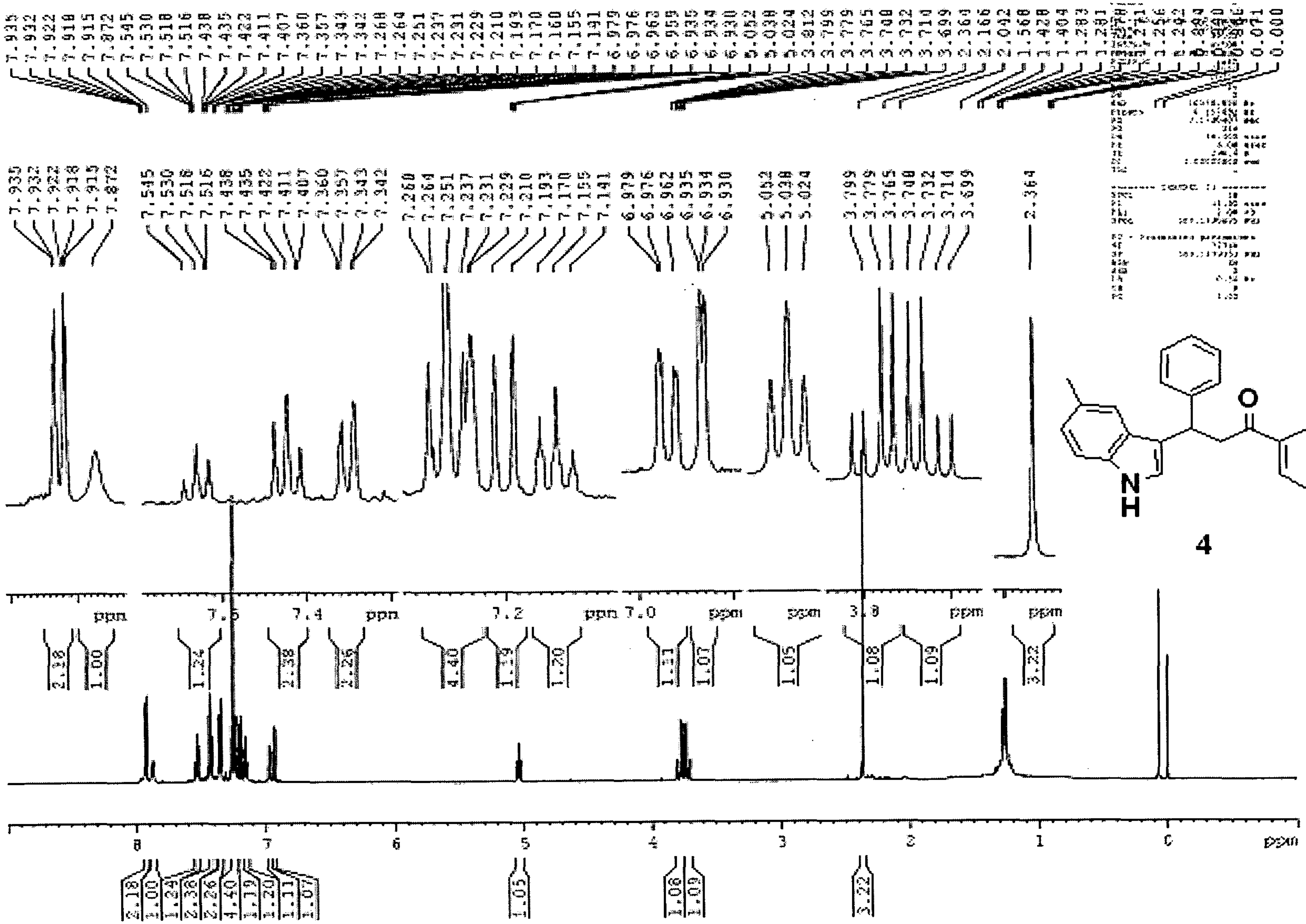


Fig 13. ^{1}H NMR (500 MHz) spectrum of 3-(5-methyl-3-indolyl)-1,3-diphenylpropan-1-one

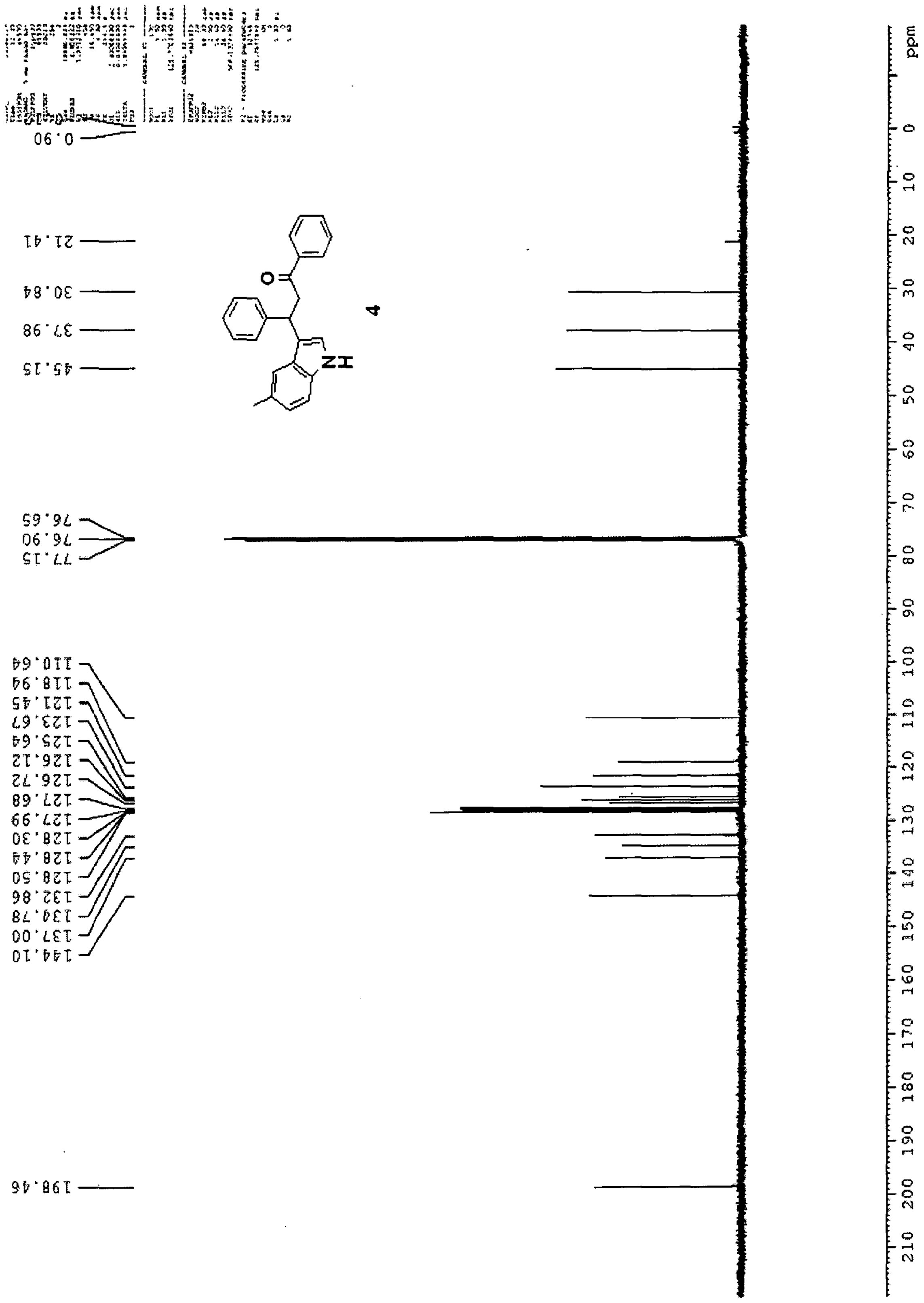


Fig 14. ^{13}C NMR (125 MHz) spectrum of 3-(5-methyl-3-indolyl)-1,3-diphenylpropan-1-one

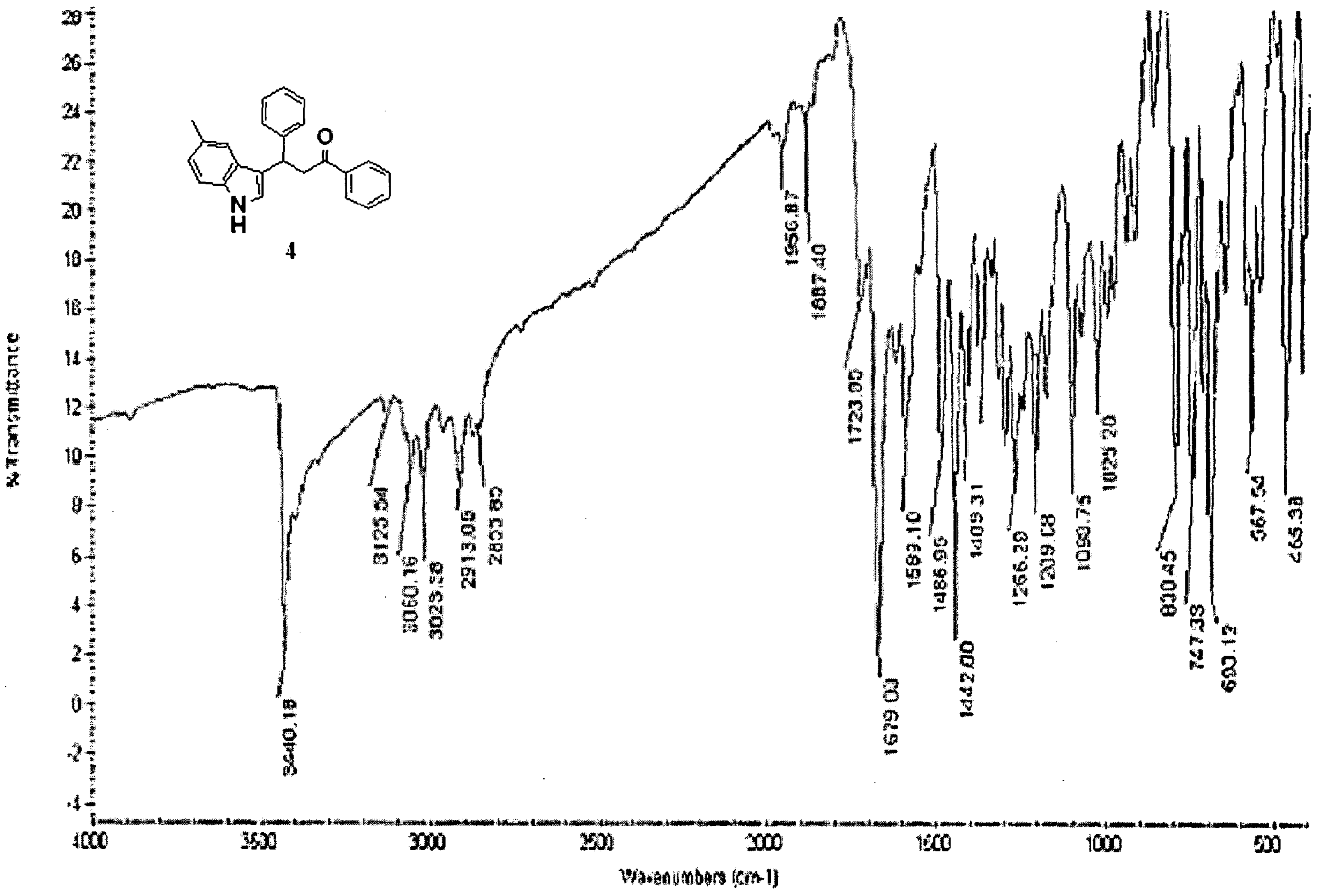


Fig 15. IR spectrum of 3-(5-methyl-3-indolyl)-1,3-diphenylpropan-1-one

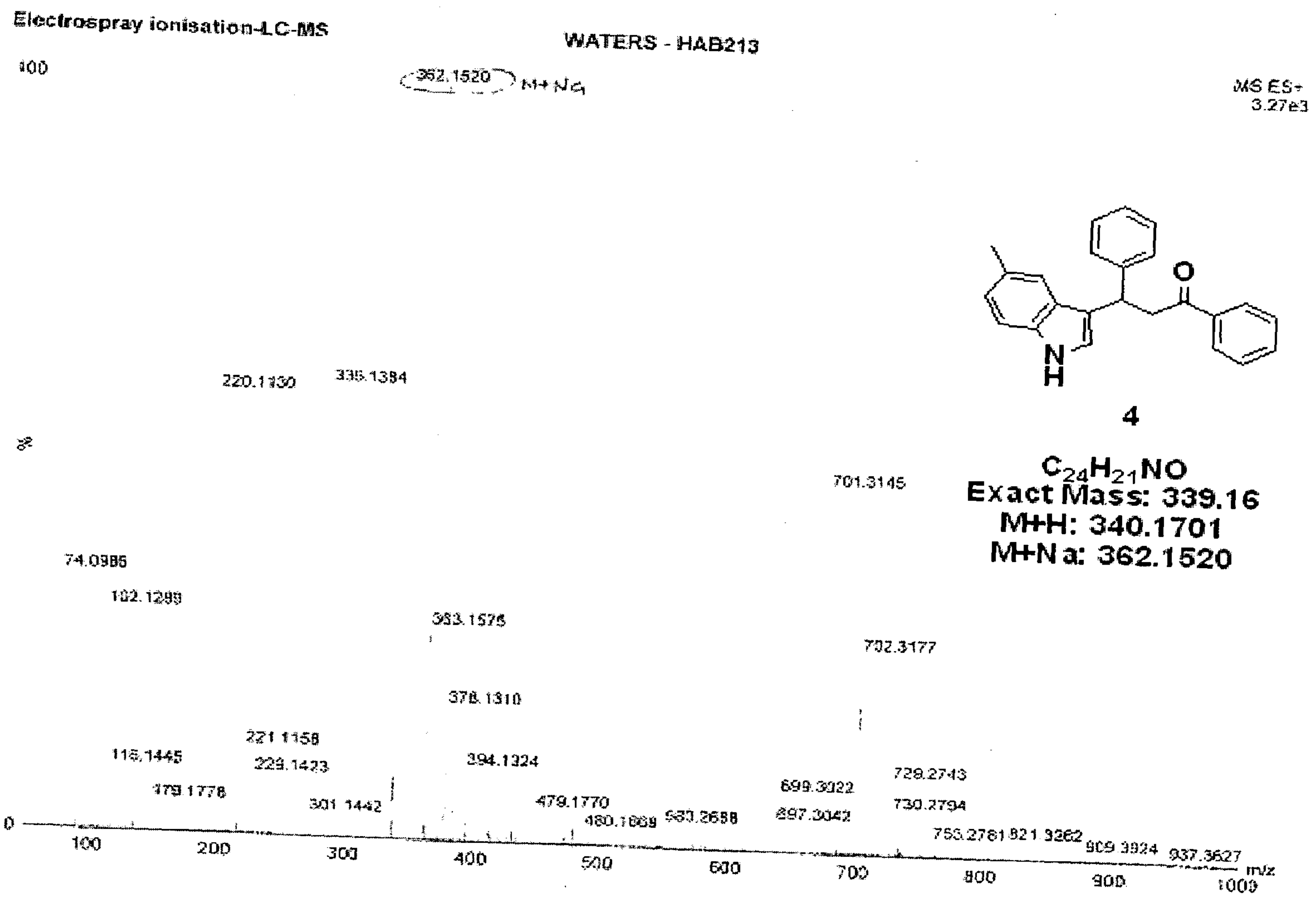


Fig 16. ESI -MS spectrum of 3-(5-methyl-3-indolyl)-1,3-diphenylpropan-1-one

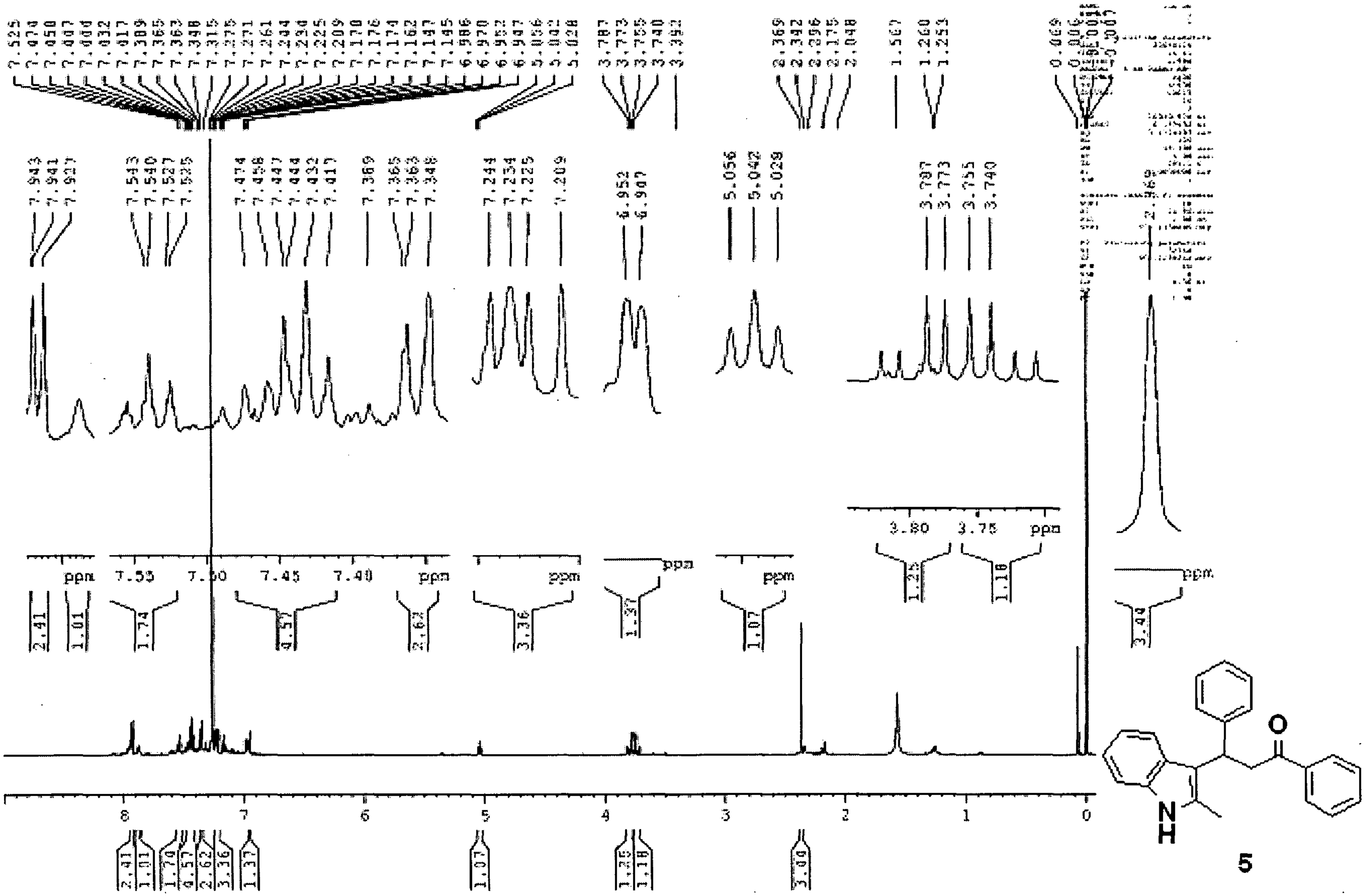


Fig 17. ^{1}H NMR (500 MHz) spectrum of 3-(2-methyl-3-indolyl)-1,3-diphenylpropan-1-one

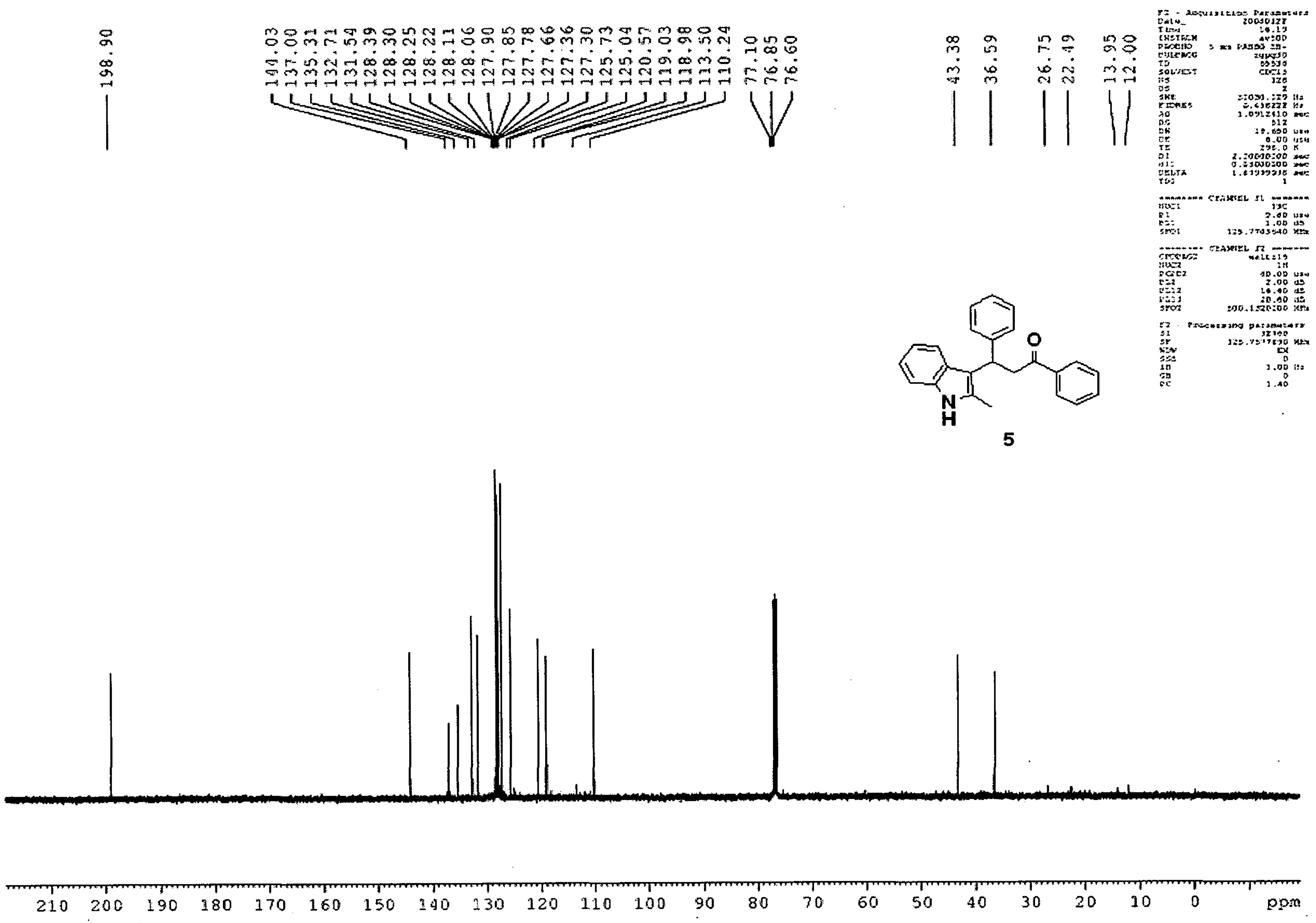


Fig 18. ^{13}C NMR (125 MHz) spectrum of 3-(2-methyl-3-indolyl)-1,3-diphenylpropan-1-one

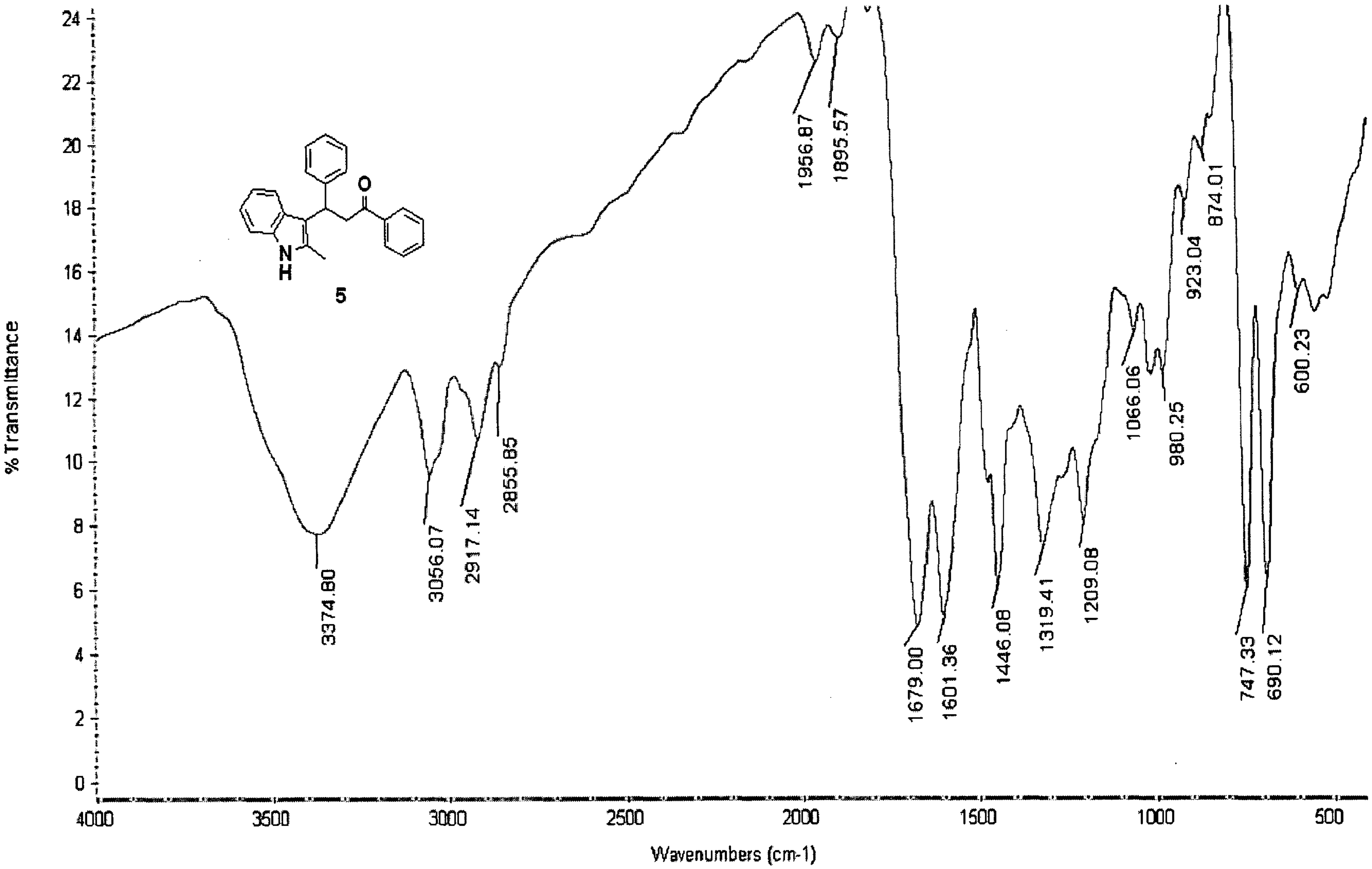


Fig 19. IR spectrum of 3-(2-methyl-3-indolyl)-1,3-diphenylpropan-1-one

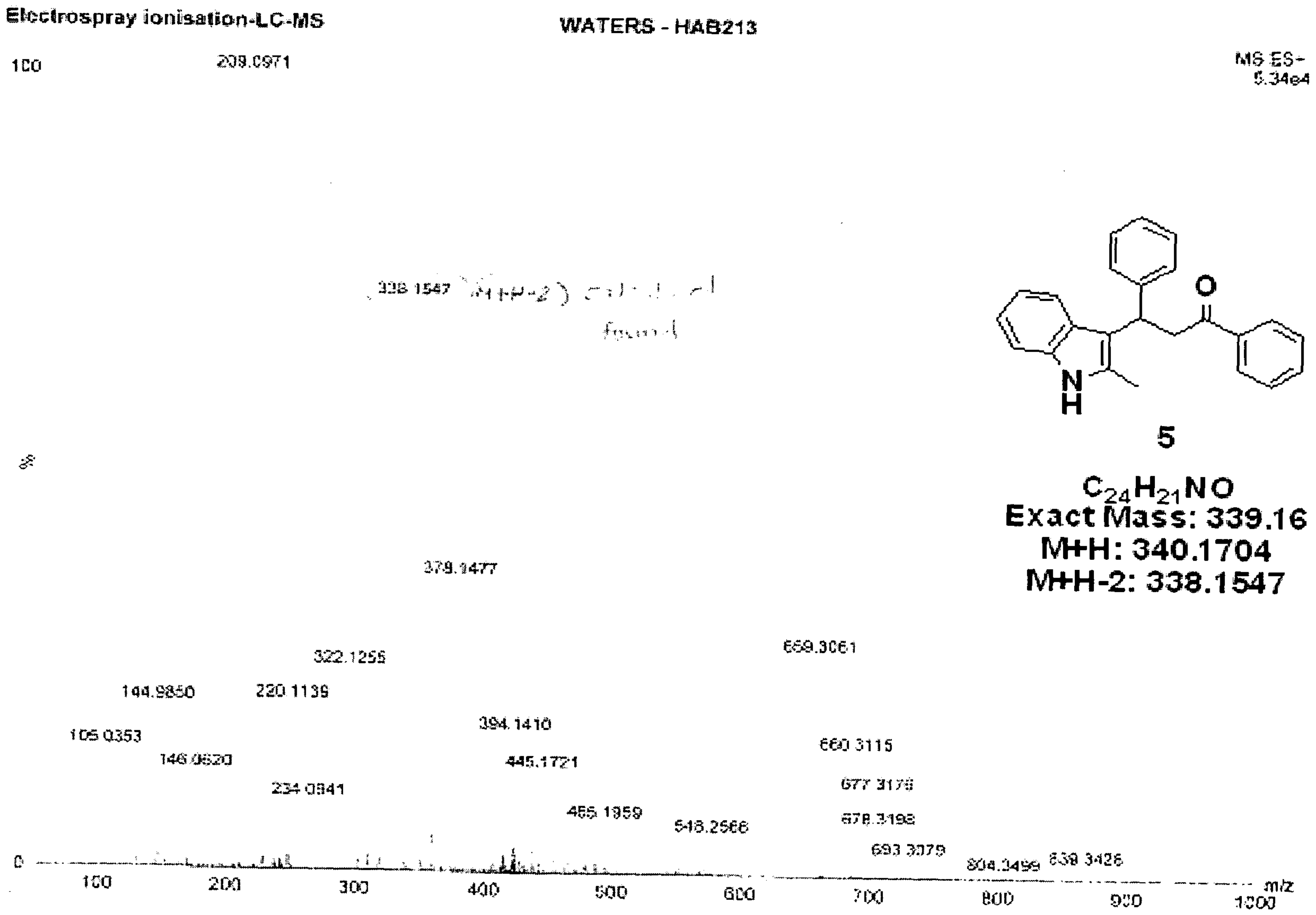


Fig 20. ESI -MS spectrum of 3-(2-methyl-3-indolyl)-1,3-diphenylpropan-1-one

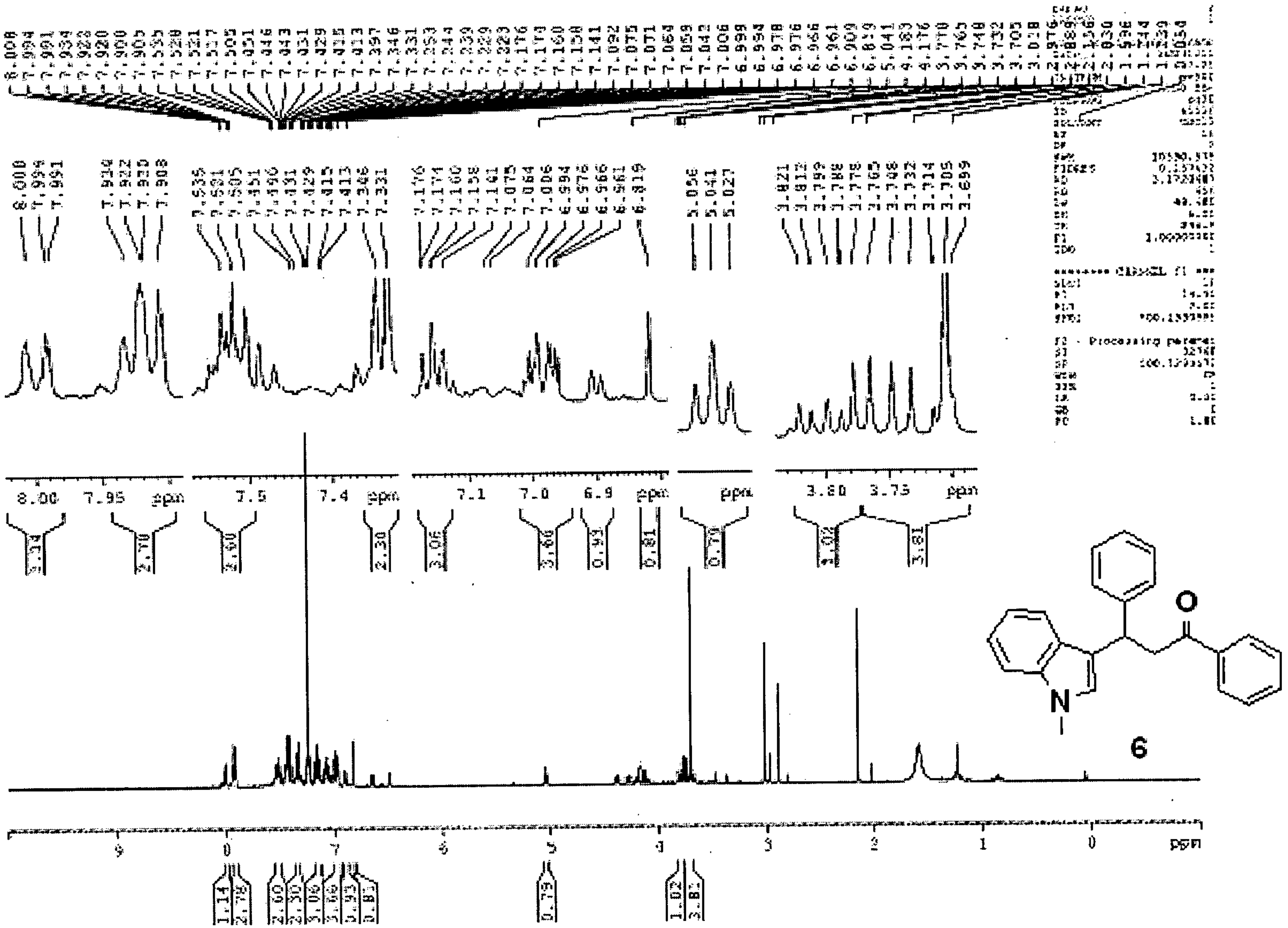


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Fig 21. ^{1}H NMR (500 MHz) spectrum of 3-(1-methyl-3-indolyl)-1,3-diphenylpropan-1-one

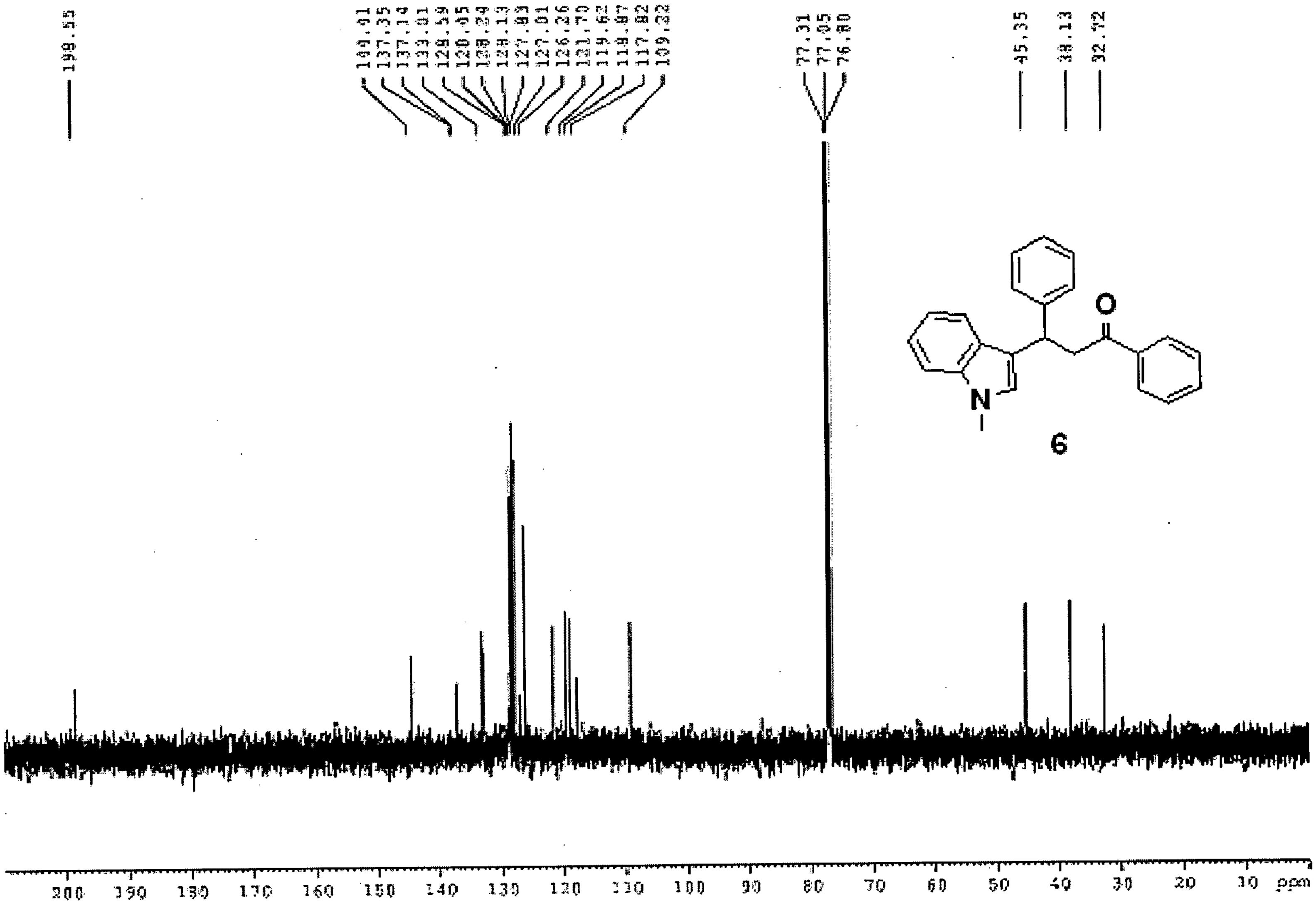


Fig 22. ^{13}C NMR (125 MHz) spectrum of 3-(1-methyl-3-indolyl)-1,3-diphenylpropan-1-one

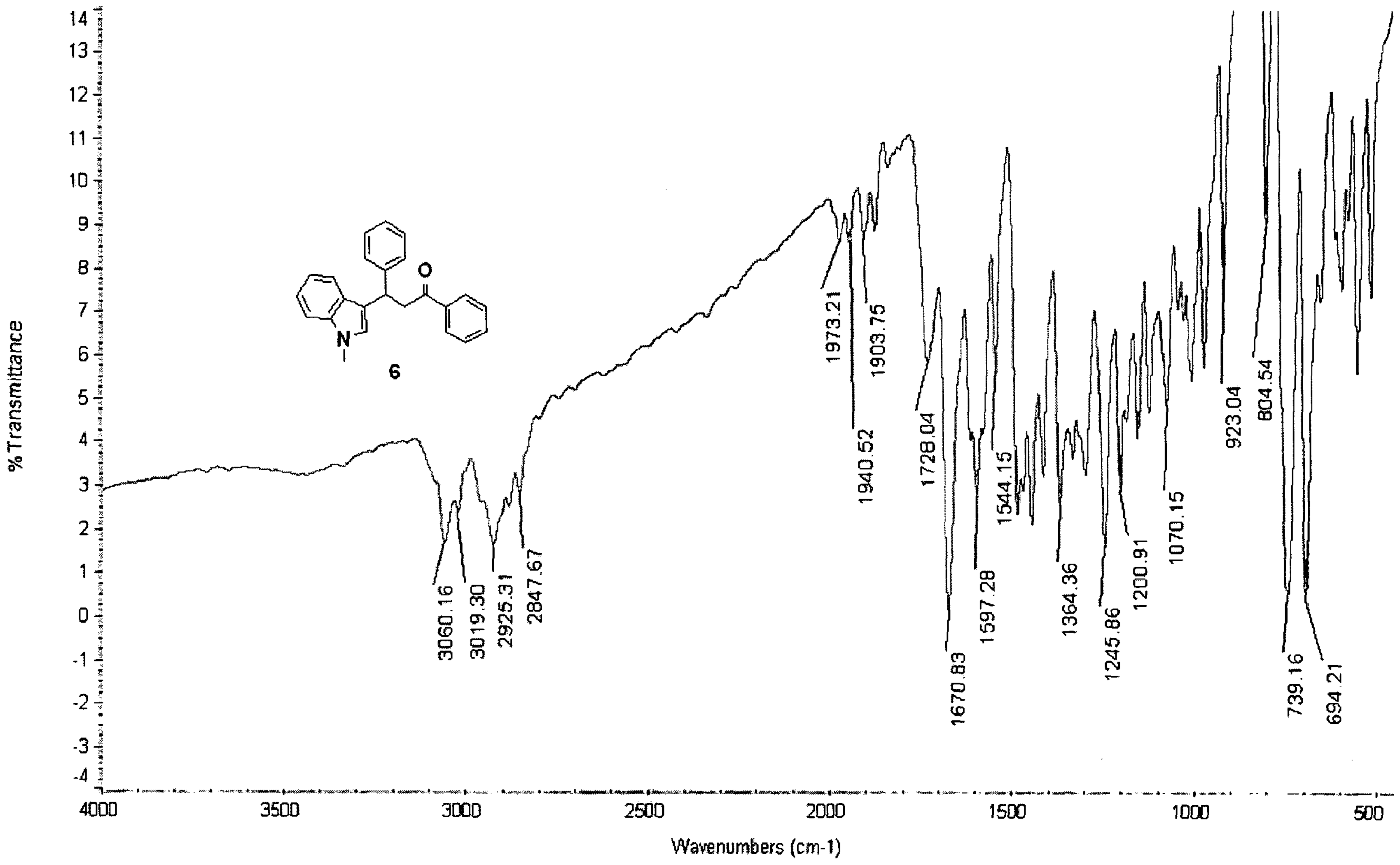


Fig 23. IR spectrum of 3-(1-methyl-3-indolyl)-1,3-diphenylpropan-1-one

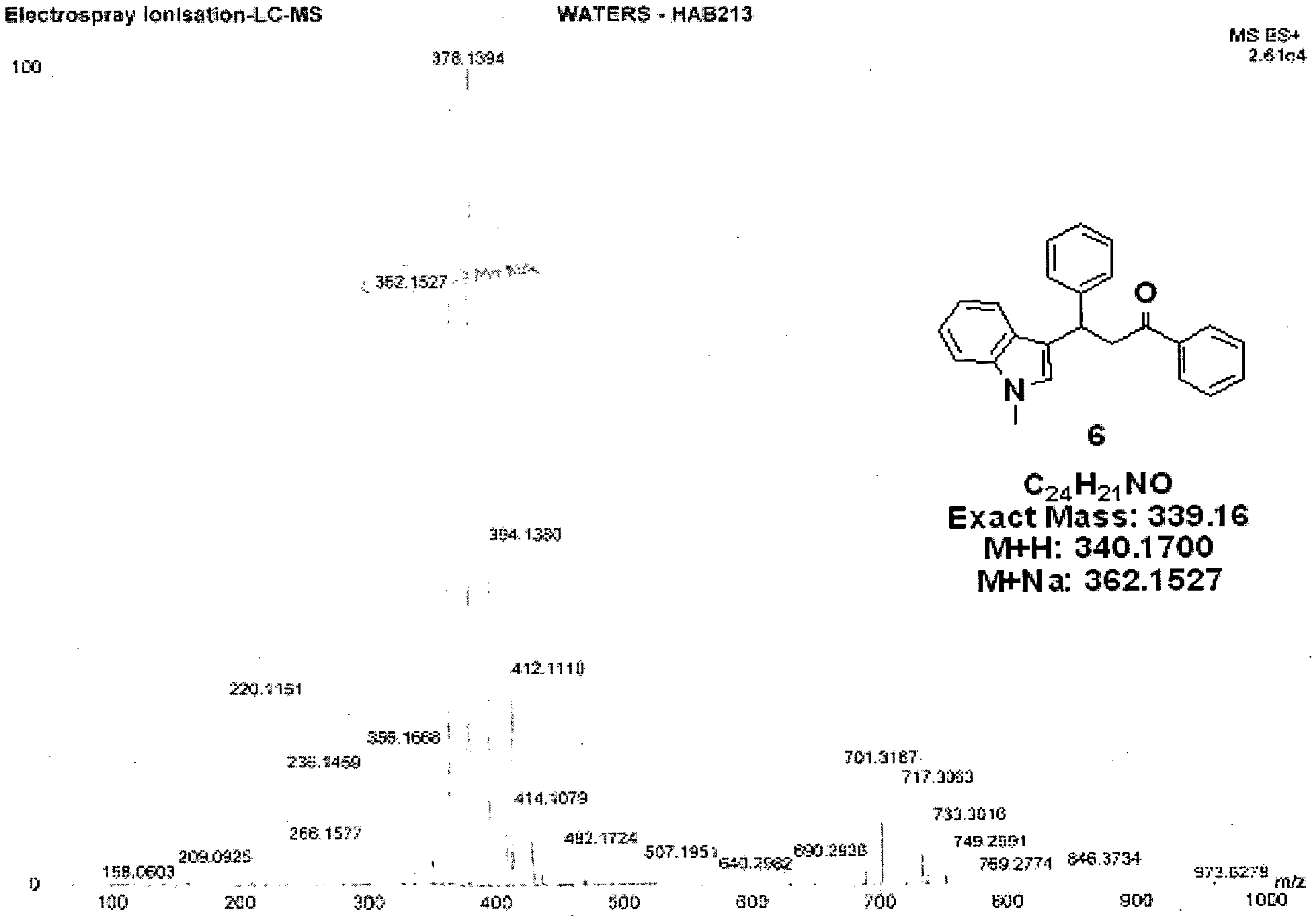


Fig 24. ESI -MS spectrum of 3-(1-methyl-3-indolyl)-1,3-diphenylpropan-1-one

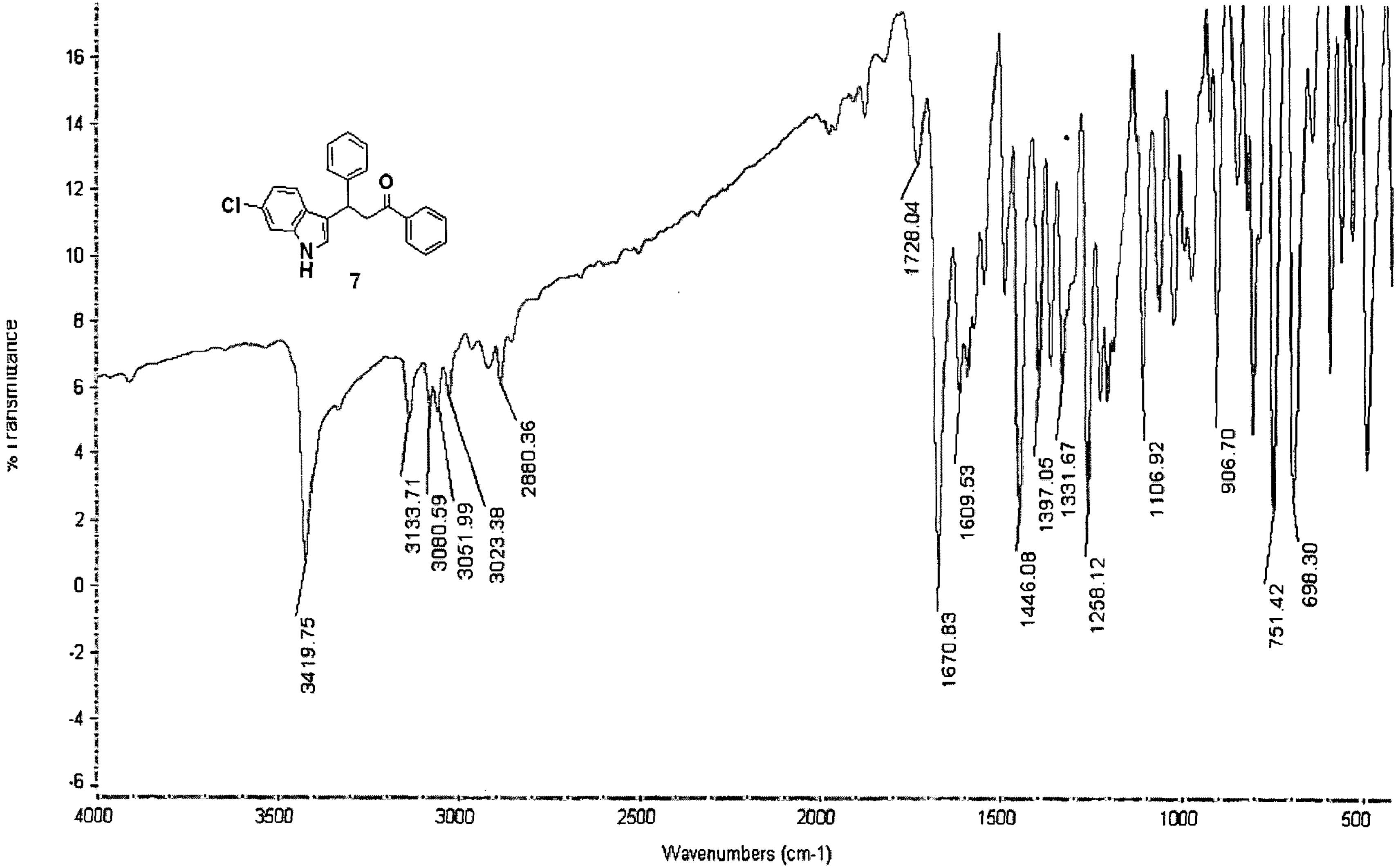


Fig 27. IR spectrum of 3-(6-chloro-3-indolyl)-1,3-diphenylpropan-1-one

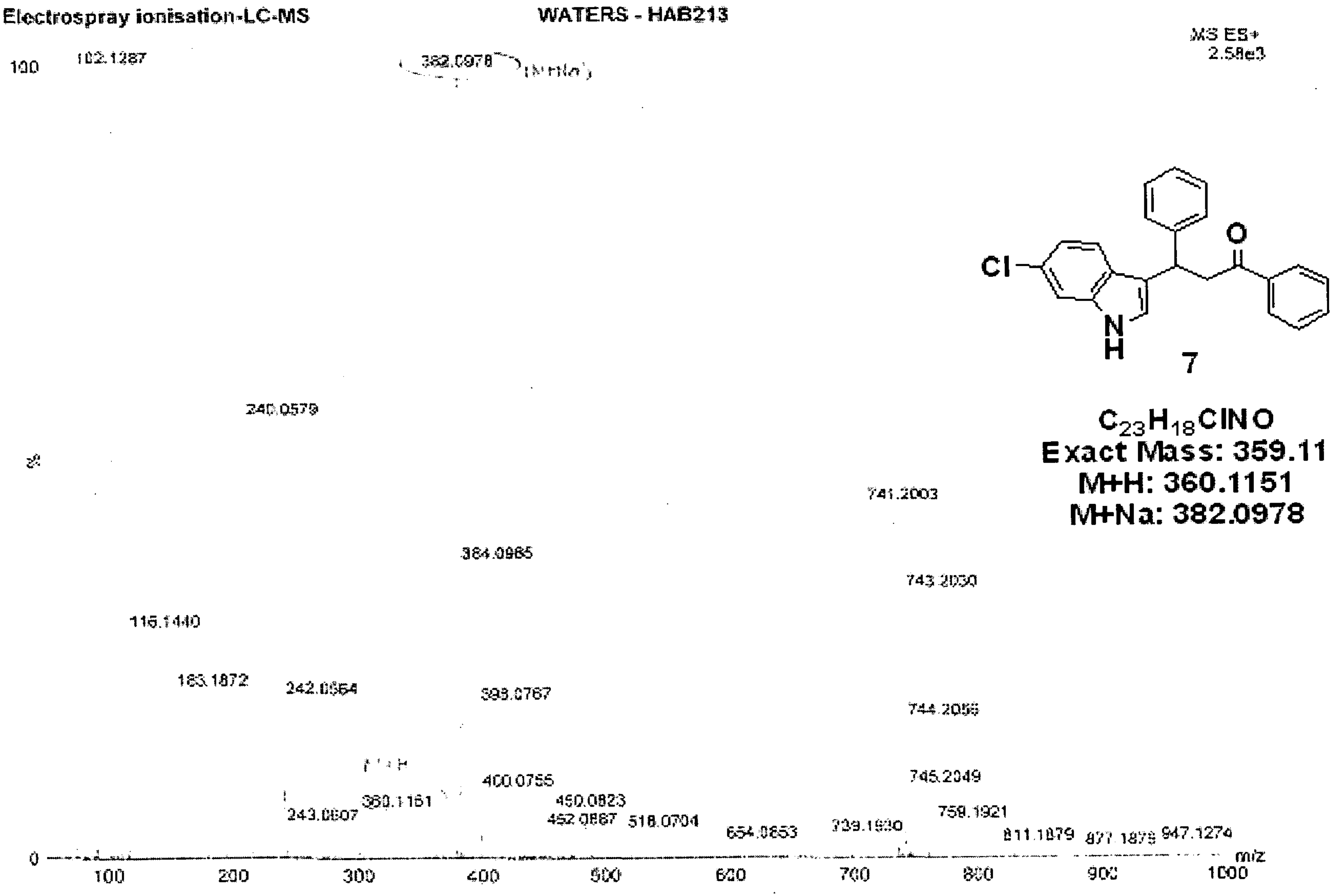


Fig 28. ESI -MS spectrum of 3-(6-chloro-3-indolyl)-1,3-diphenylpropan-1-one

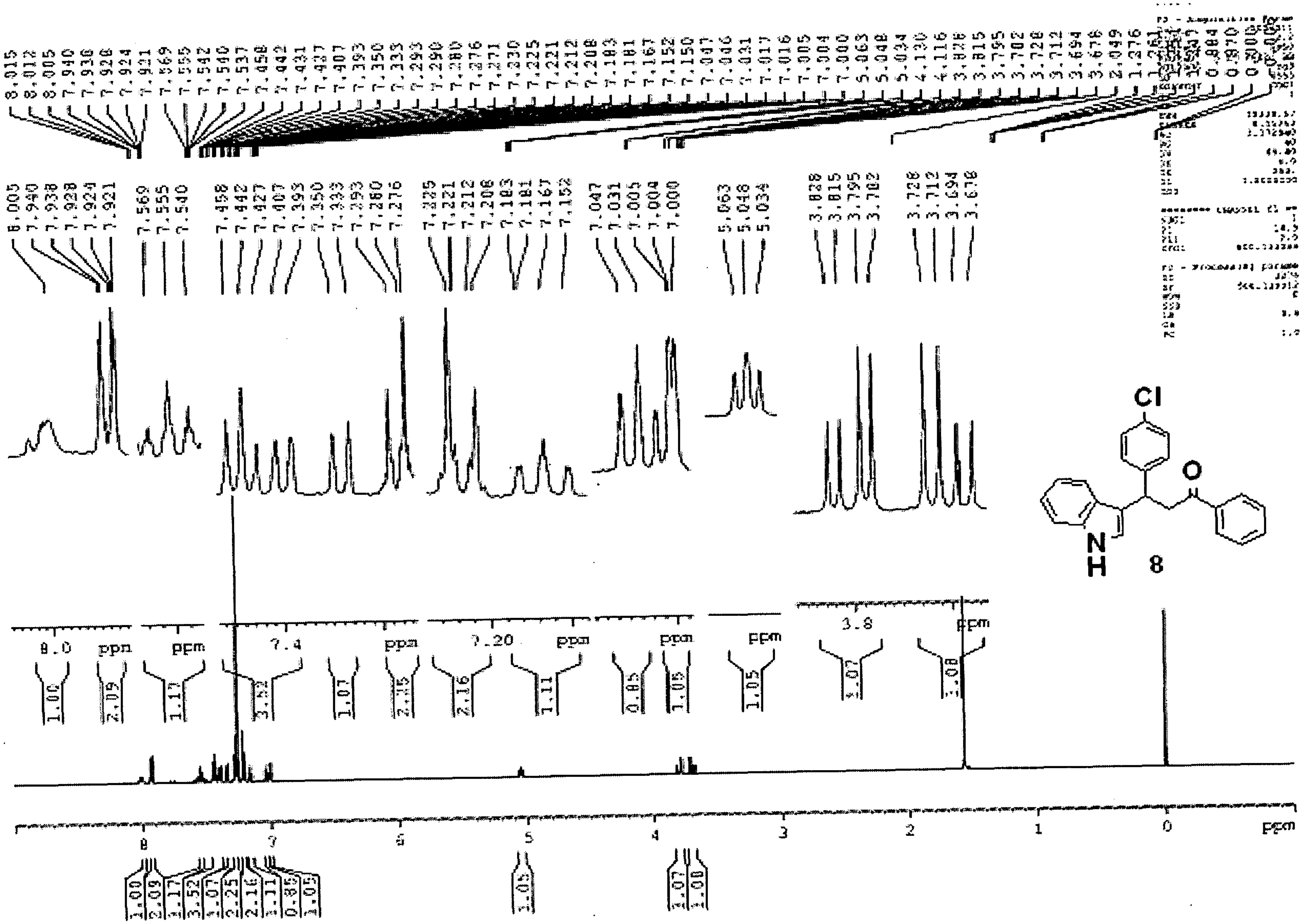


Fig 29. ^{1}H NMR (500 MHz) spectrum of 3-(3-indolyl)-3-(4-chlorophenyl)-1-phenylpropan-1-one

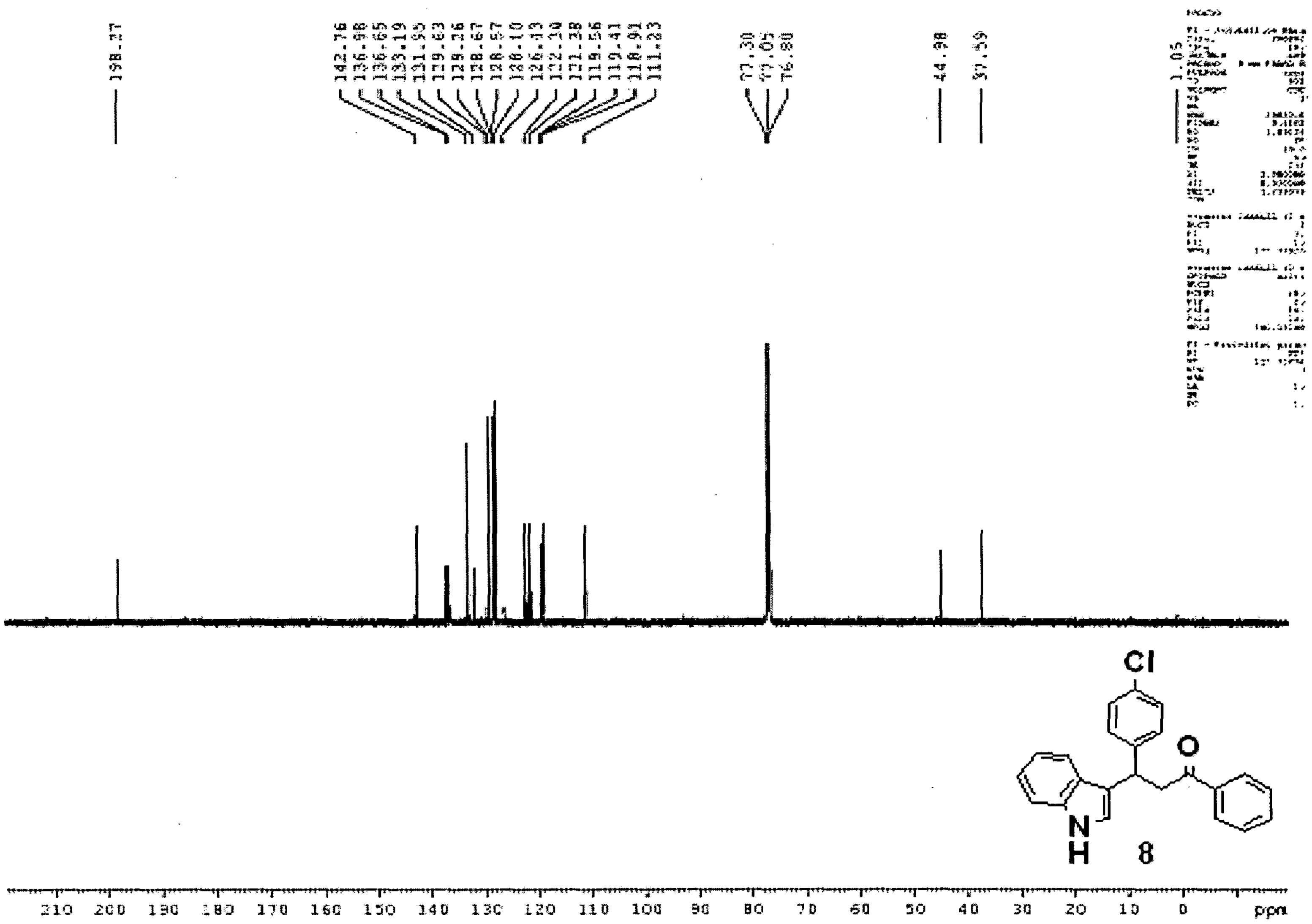


Fig 30. ^{13}C NMR (125 MHz) spectrum of 3-(3-indolyl)-3-(4-chlorophenyl)-1-phenylpropan-1-one

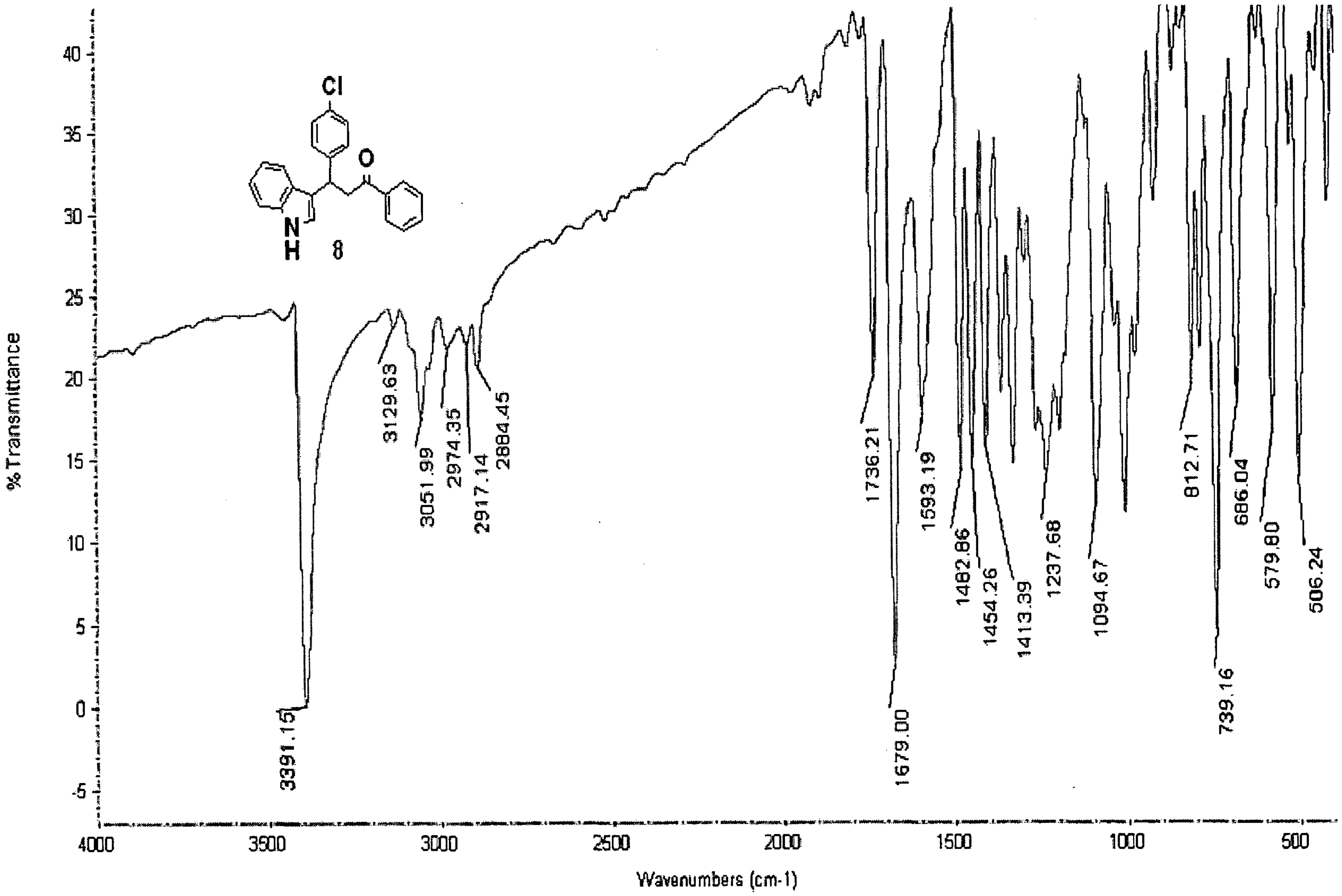


Fig 31. IR spectrum of 3-(3-indolyl)-3-(4-chlorophenyl)-1-phenylpropan-1-one

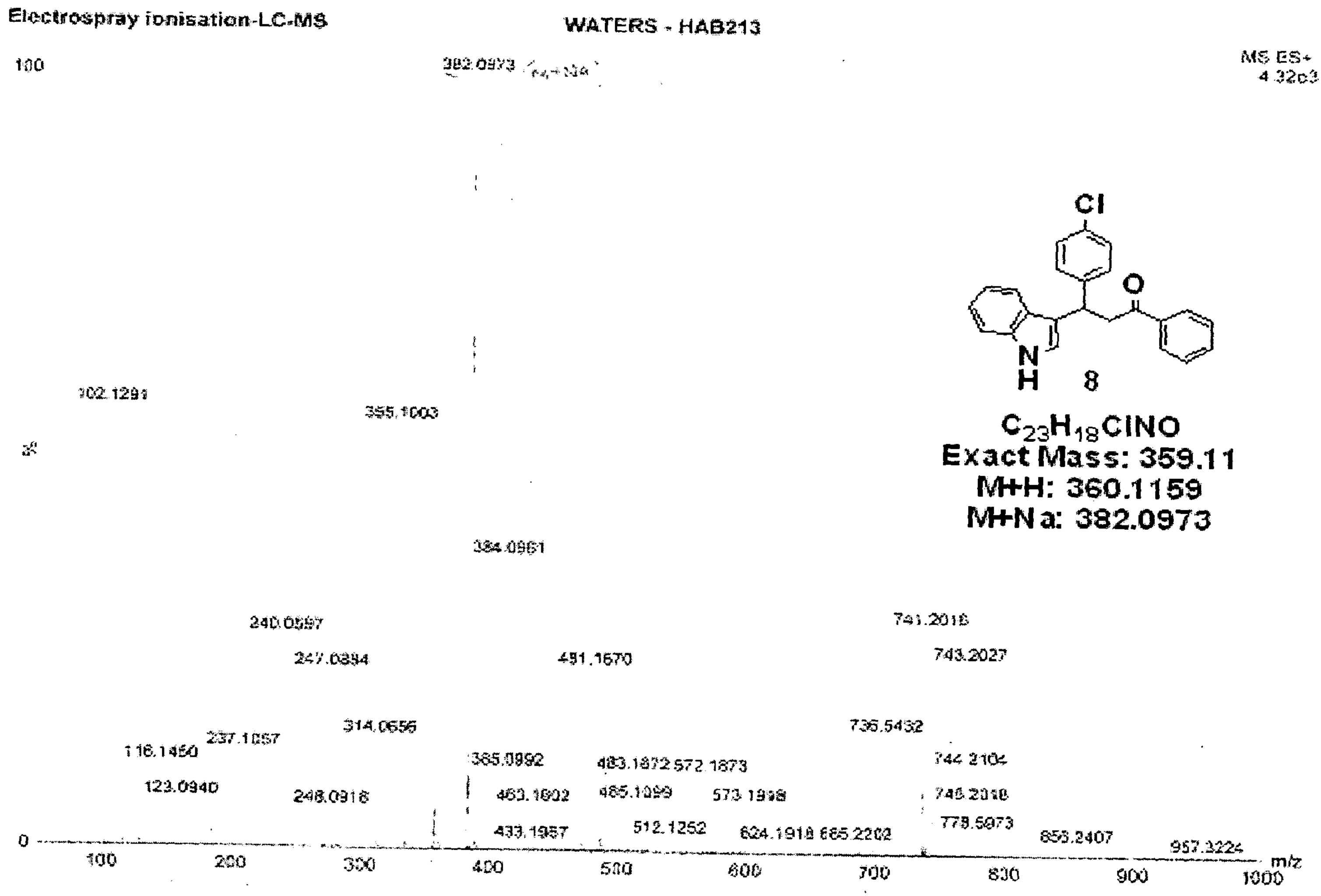


Fig 32. ESI -MS spectrum of 3-(3-indolyl)-3-(4-chlorophenyl)-1-phenylpropan-1-one

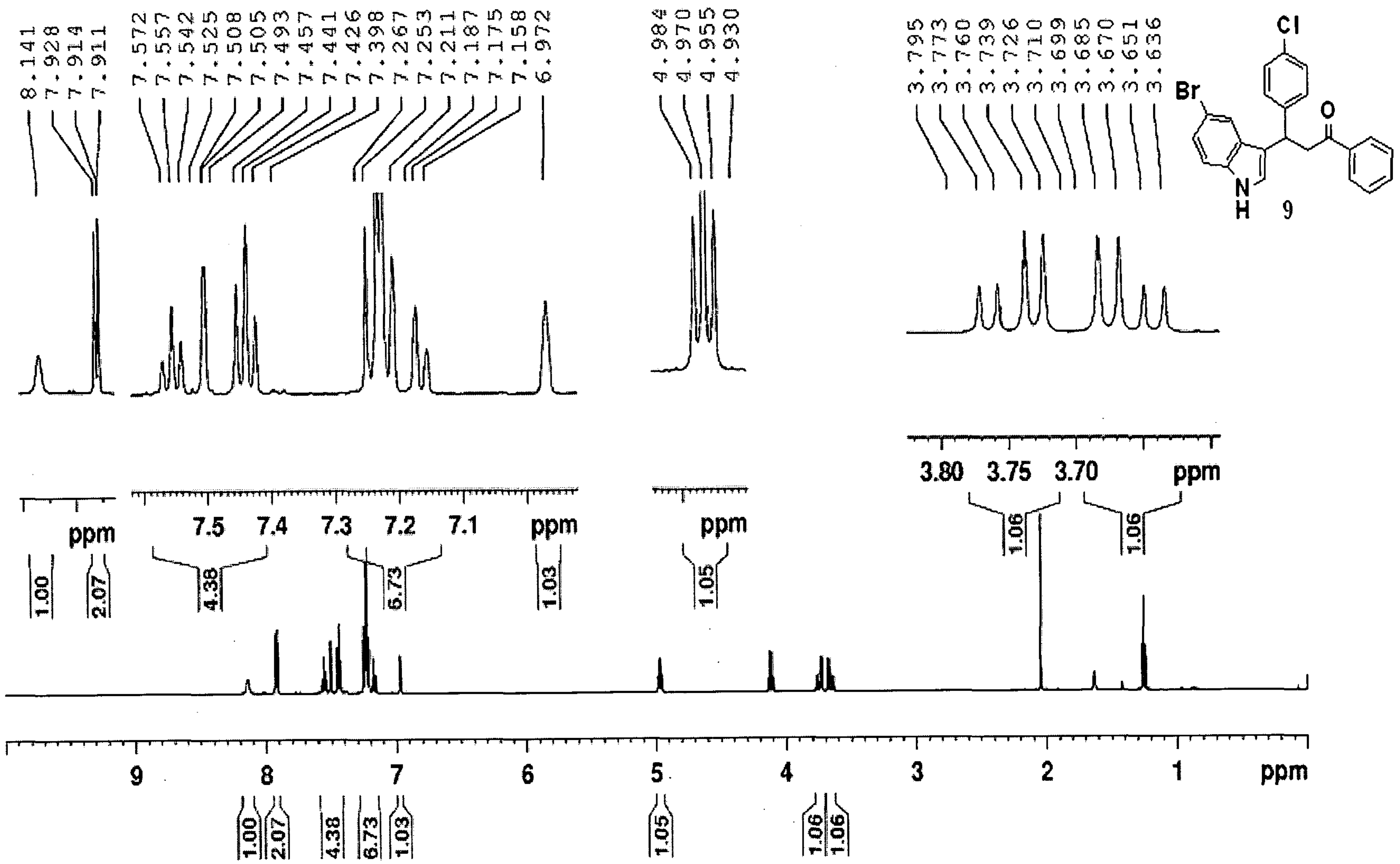


Fig 33. ^{1}H NMR (500 MHz) spectrum of 3-(5-bromo-3-indolyl)-3-(4-chlorophenyl)-1-phenylpropan-1-one

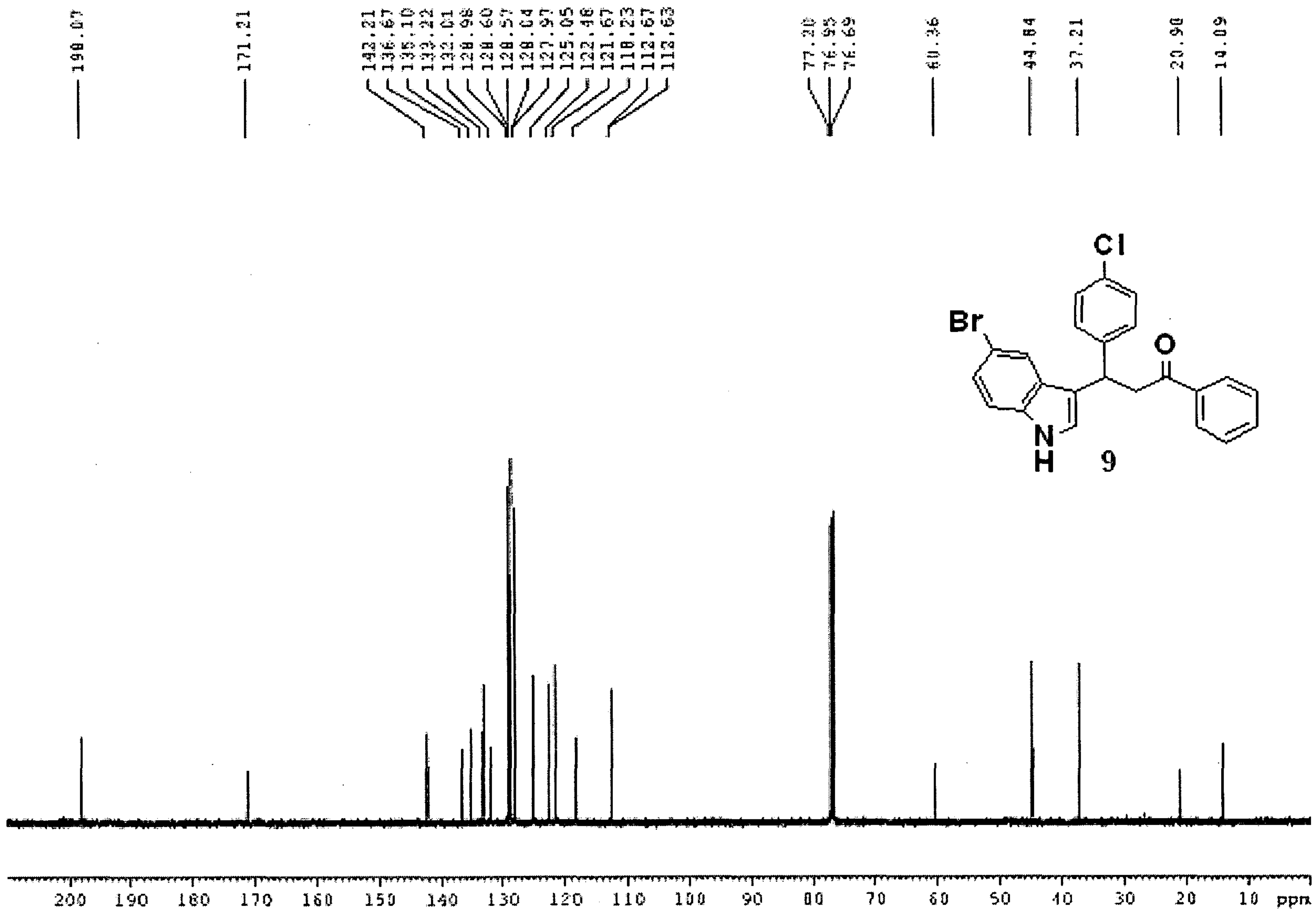


Fig 34. ^{13}C NMR (125 MHz) spectrum of 3-(5-bromo-3-indolyl)-3-(4-chlorophenyl)-1-phenylpropan-1-one

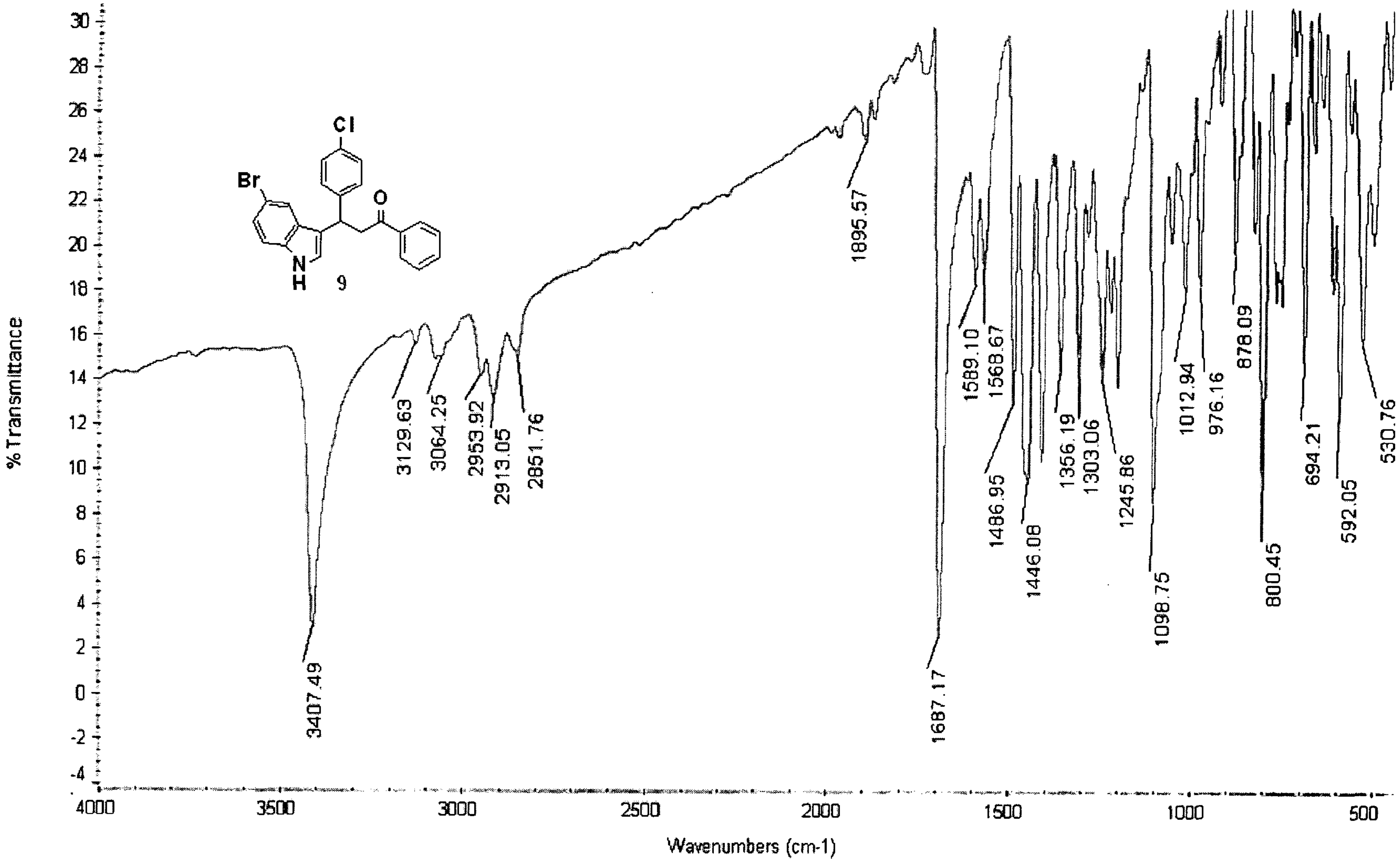


Fig 35. IR spectrum of 3-(5-bromo-3-indolyl)-3-(4-chlorophenyl)-1-phenylpropan-1-one

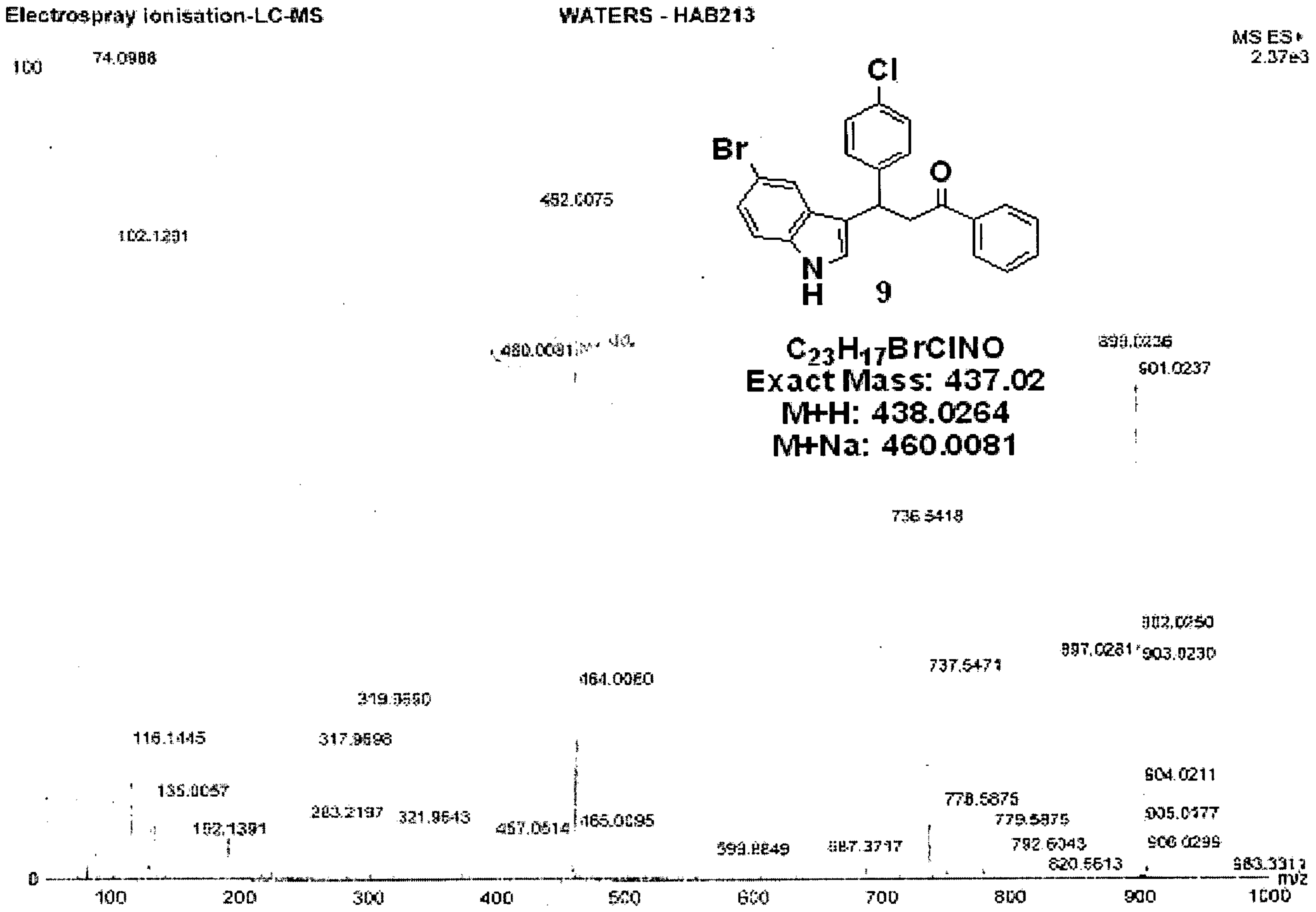


Fig 36. ESI -MS spectrum of 3-(5-bromo-3-indolyl)-3-(4-chlorophenyl)-1-phenylpropan-1-one

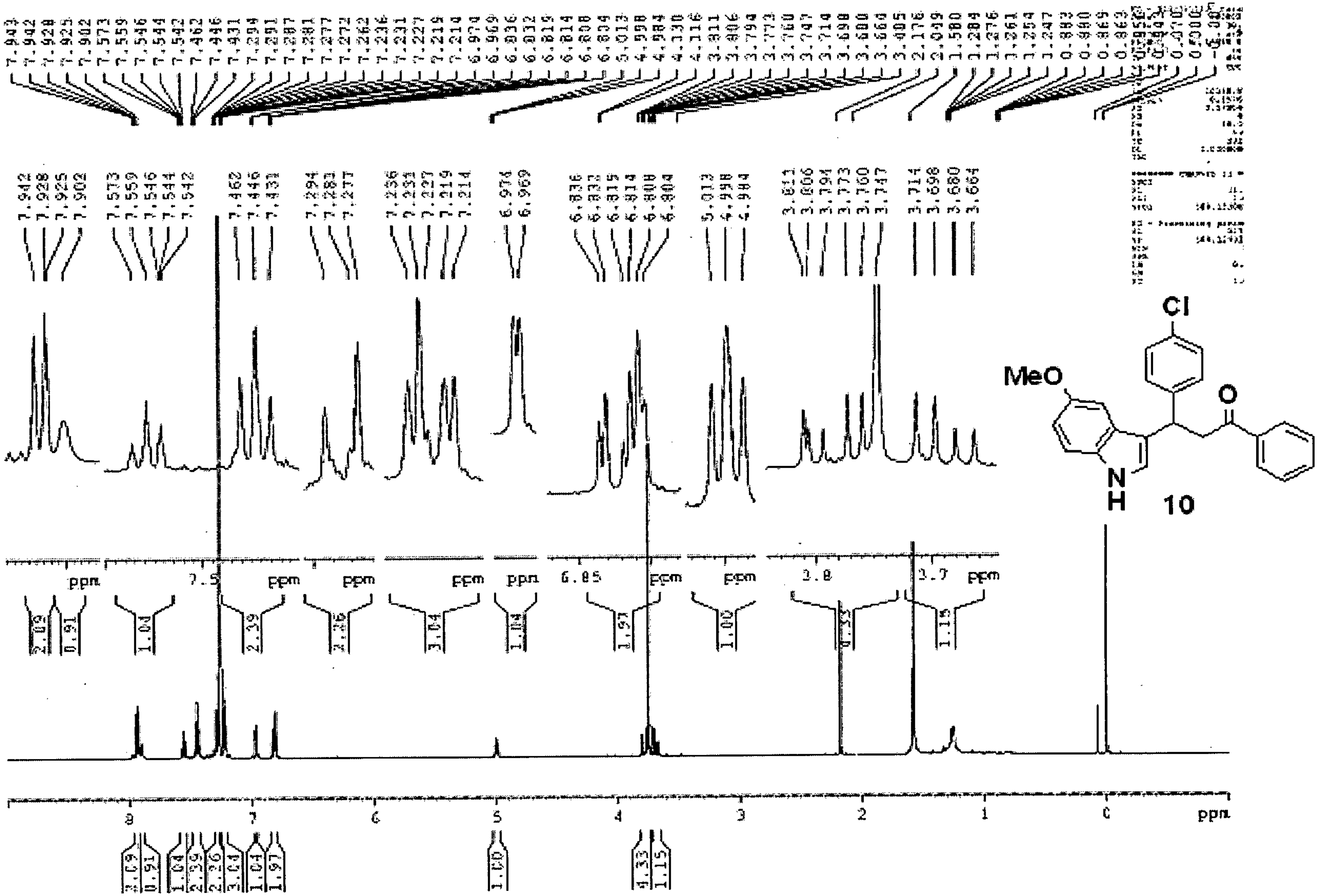


Fig 37. ^{1}H NMR (500 MHz) spectrum of 3-(5-methoxy-3-indolyl)-3-(4-chlorophenyl)-1-phenylpropan-1-one

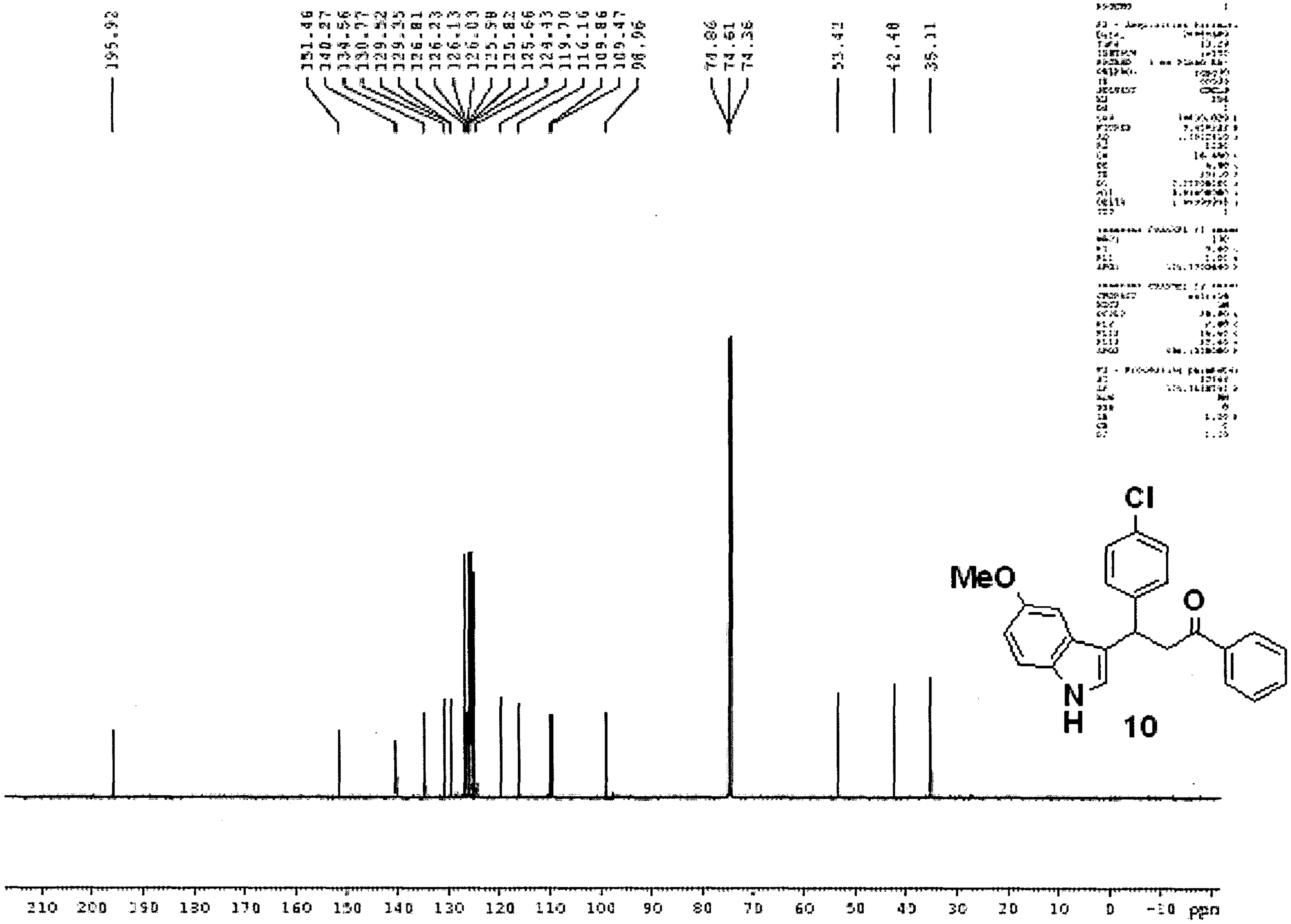


Fig 38. ^{13}C NMR (125 MHz) spectrum of 3-(5-methoxy-3-indolyl)-3-(4-chlorophenyl)-1-phenylpropan-1-one

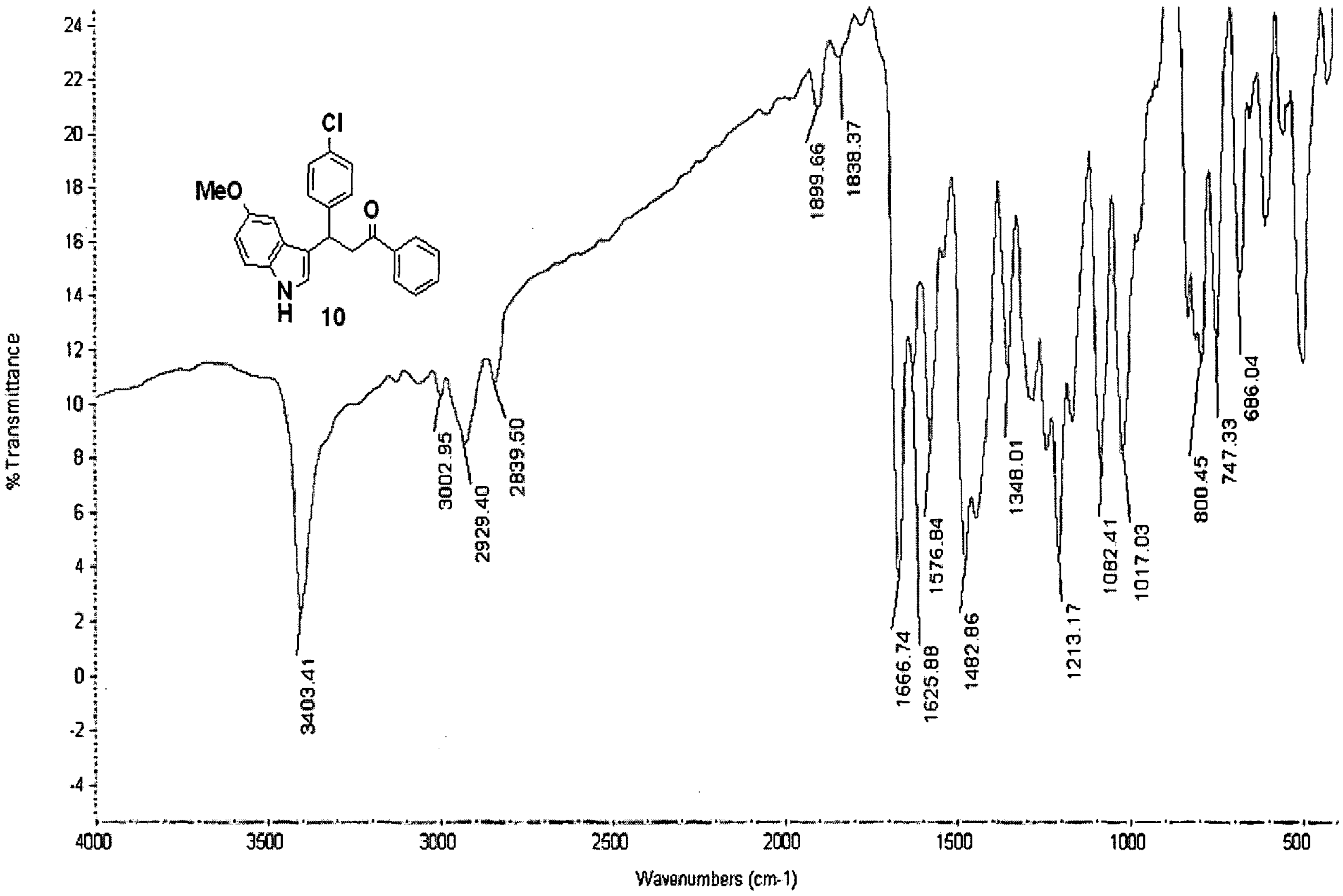


Fig 39. IR spectrum of 3-(5-methoxy-3-indolyl)-3-(4-chlorophenyl)-1-phenylpropan-1-one

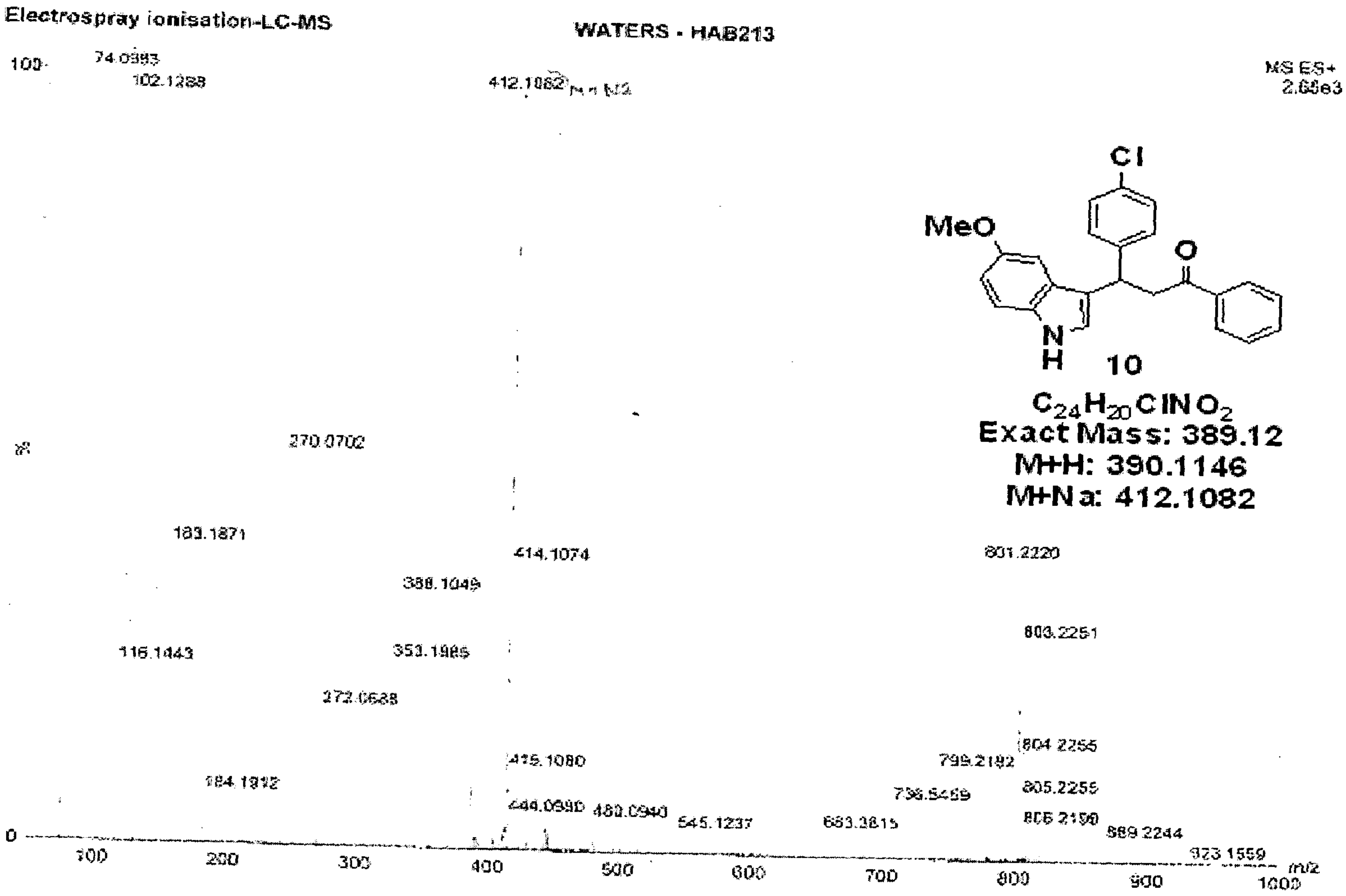


Fig 40. ESI -MS spectrum of 3-(5-methoxy-3-indolyl)-3-(4-chlorophenyl)-1-phenylpropan-1-one

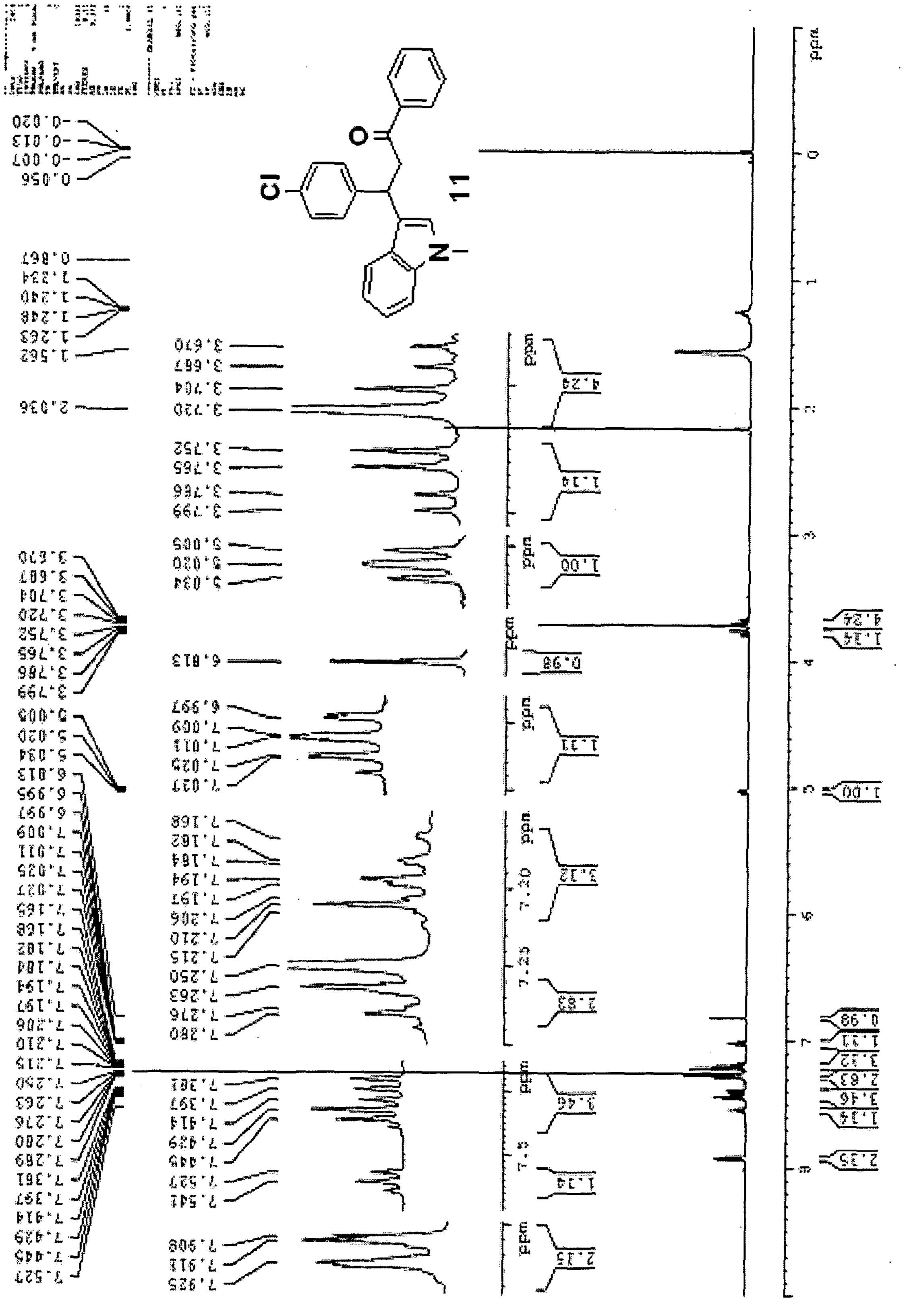


Fig 41. ^{1}H NMR (500 MHz) spectrum of 3-(1-methyl-3-indolyl)-3-(4-chlorophenyl)-1-phenylpropan-1-one

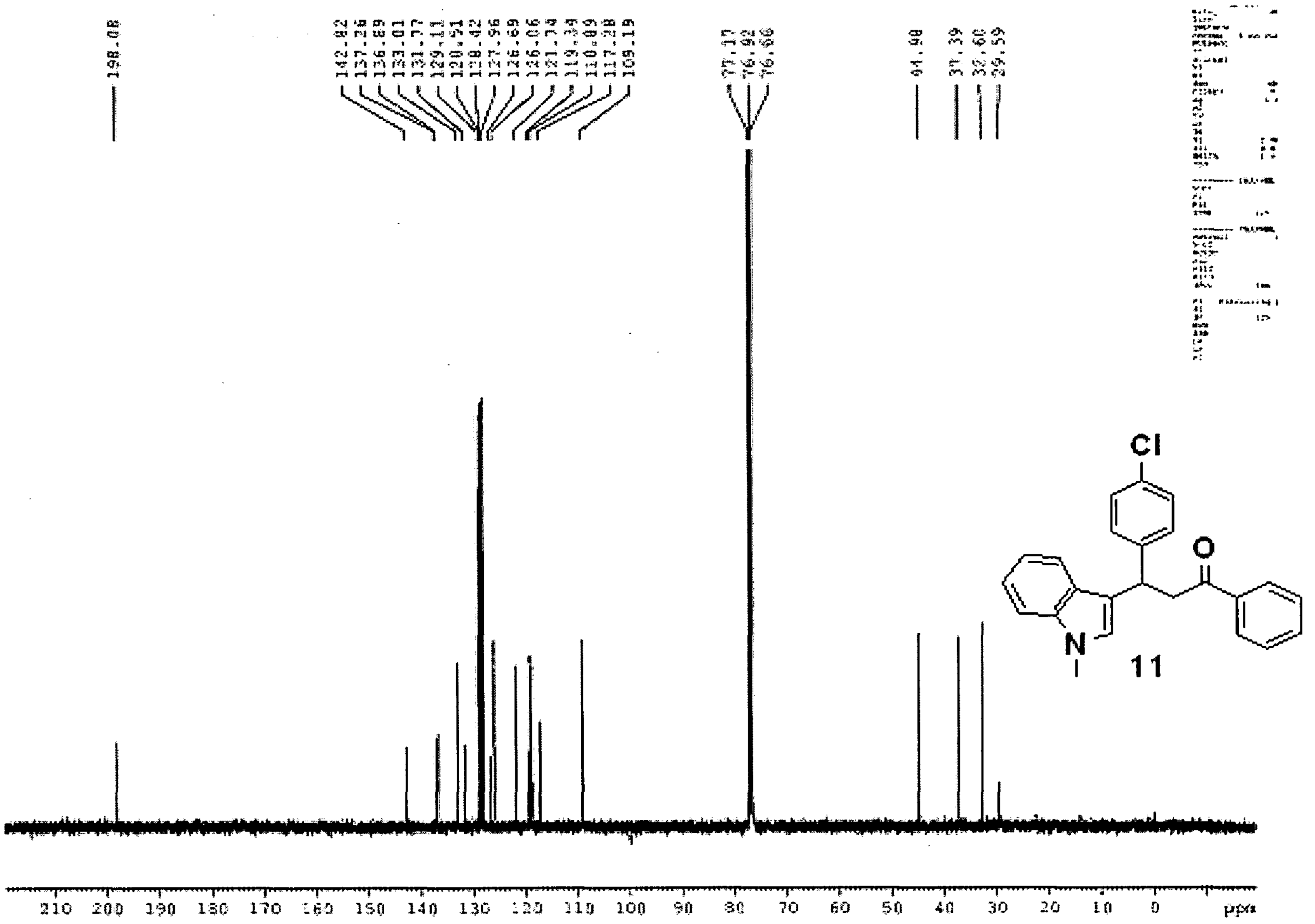


Fig 42. ^{13}C NMR (125 MHz) spectrum of 3-(1-methyl-3-indolyl)-3-(4-chlorophenyl)-1-phenylpropan-1-one

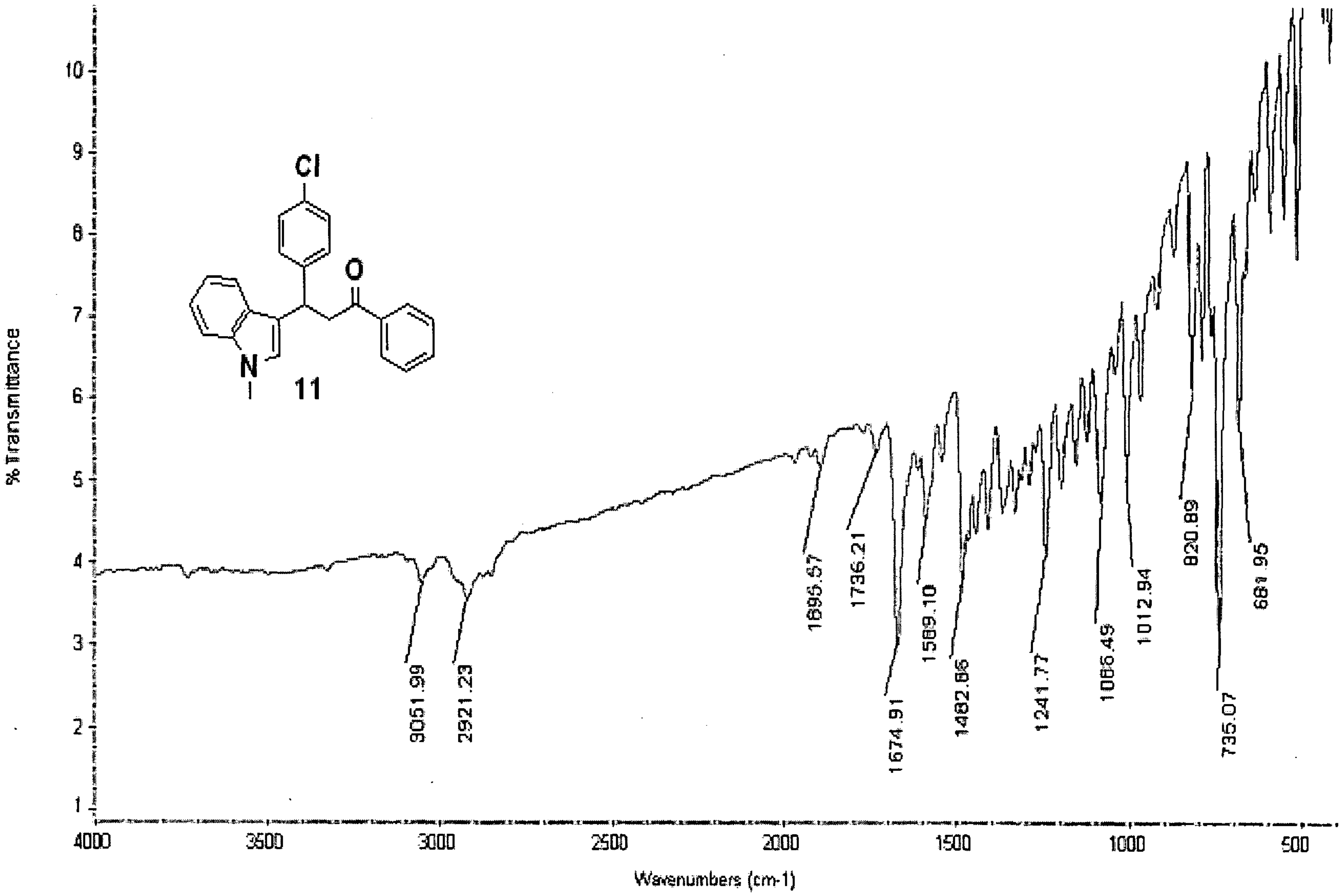


Fig 43. IR spectrum of 3-(1-methyl-3-indolyl)-3-(4-chlorophenyl)-1-phenylpropan-1-one

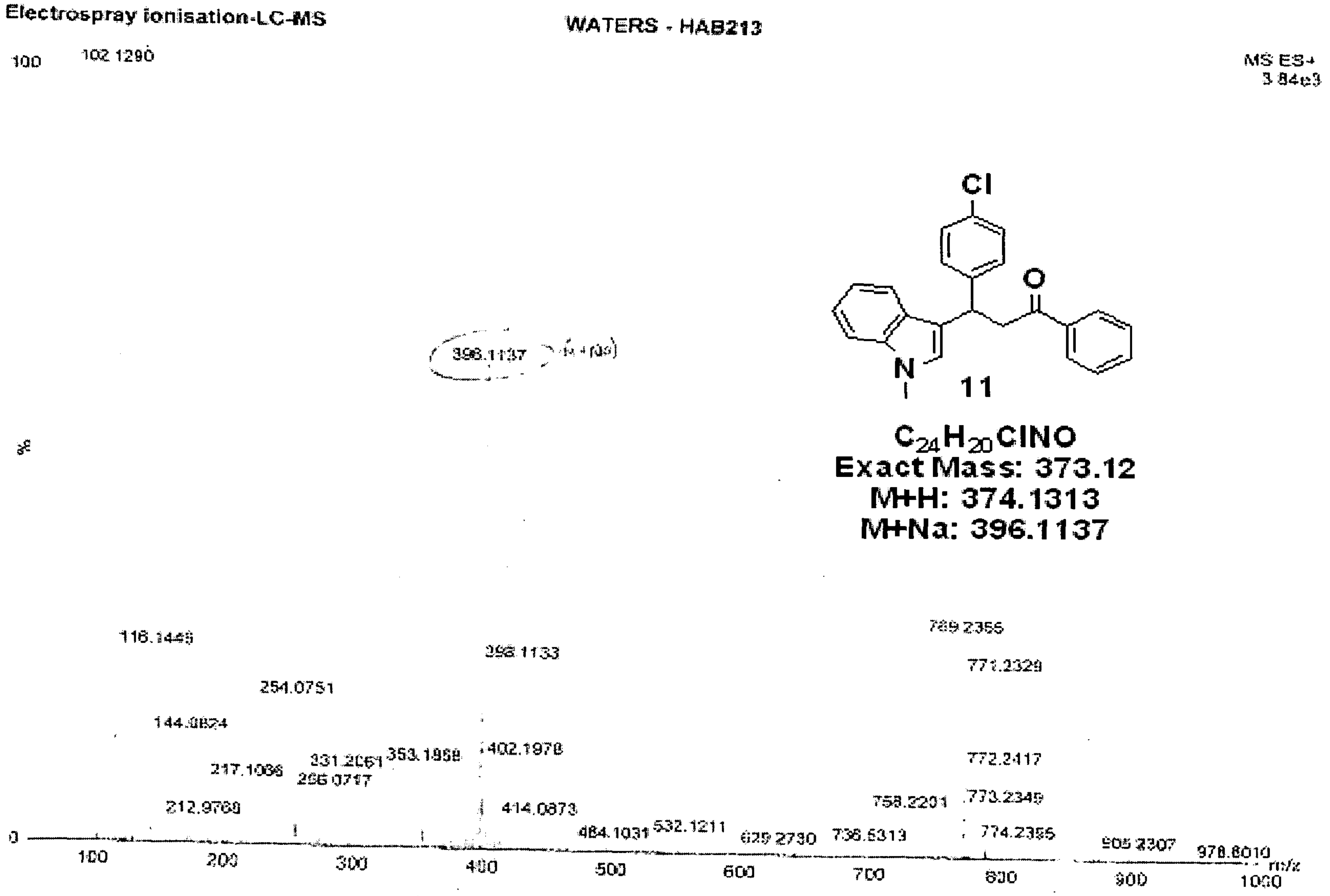


Fig 44. ESI -MS spectrum of 3-(1-methyl-3-indolyl)-3-(4-chlorophenyl)-1-phenylpropan-1-one

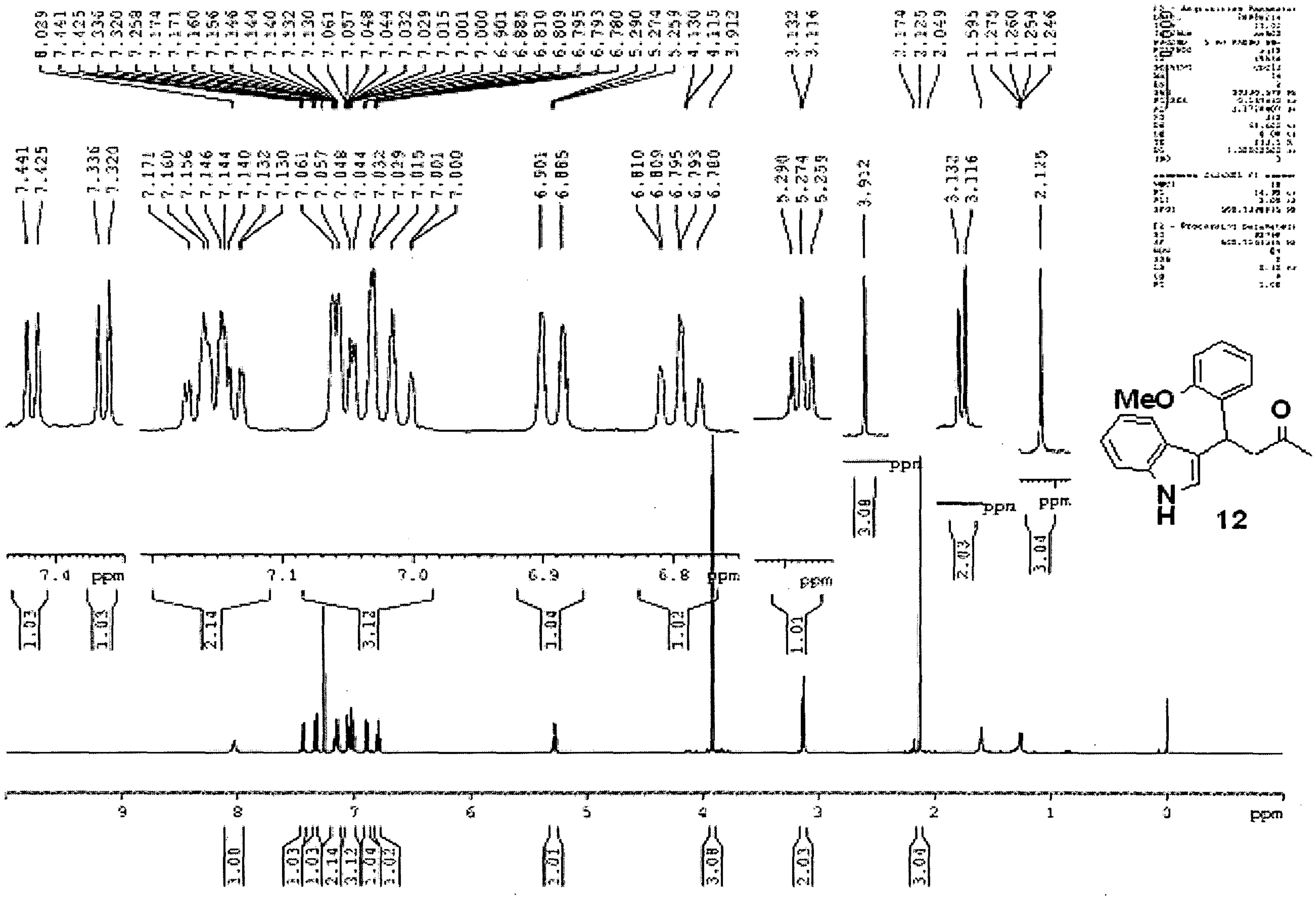


Fig 45. ^{1}H NMR (500 MHz) spectrum of 4-(3-indolyl)-4-(2-methoxyphenyl)butan-2-one

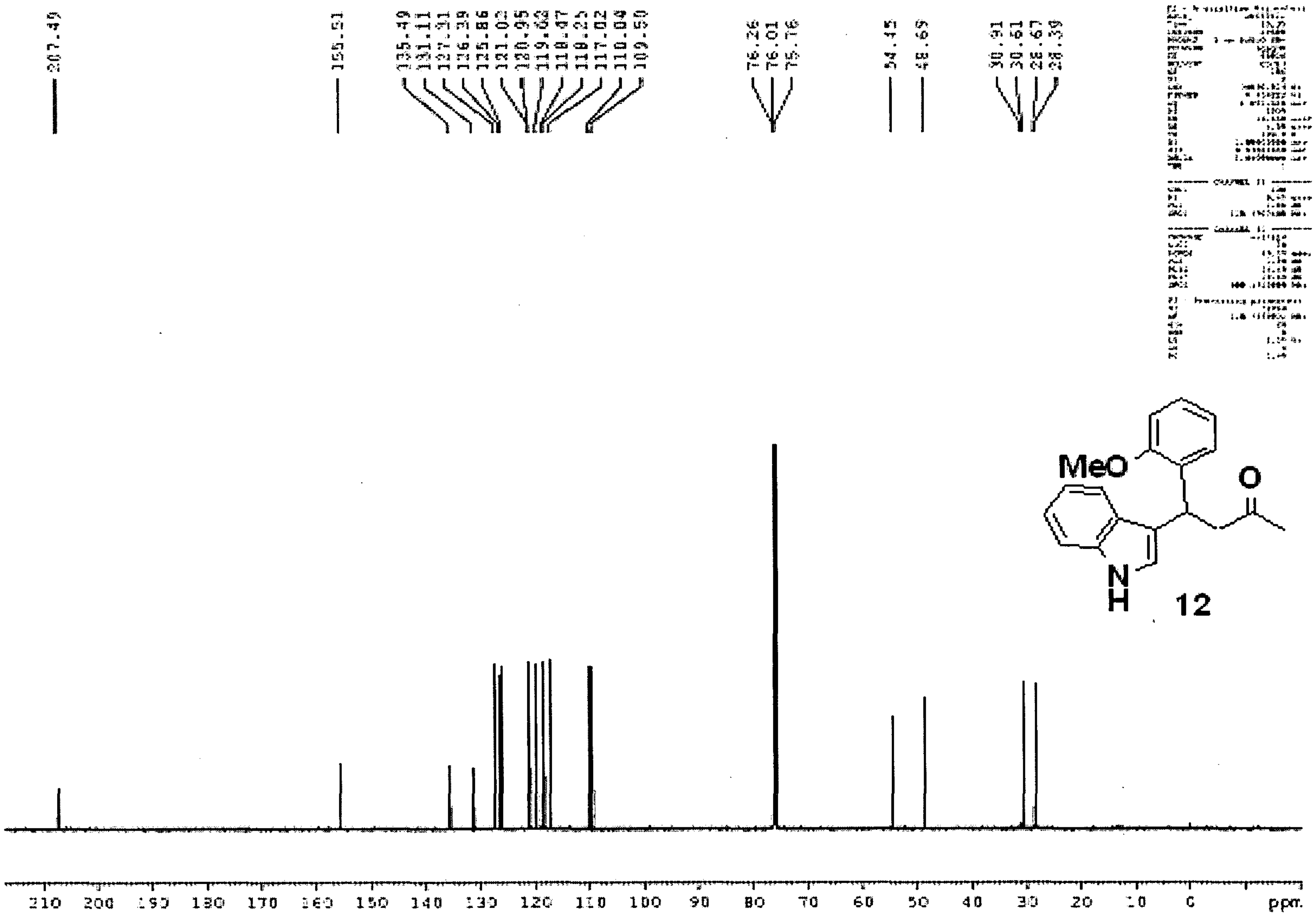


Fig 46. ^{13}C NMR (125 MHz) spectrum of 4-(3-indolyl)-4-(2-methoxyphenyl)butan-2-one

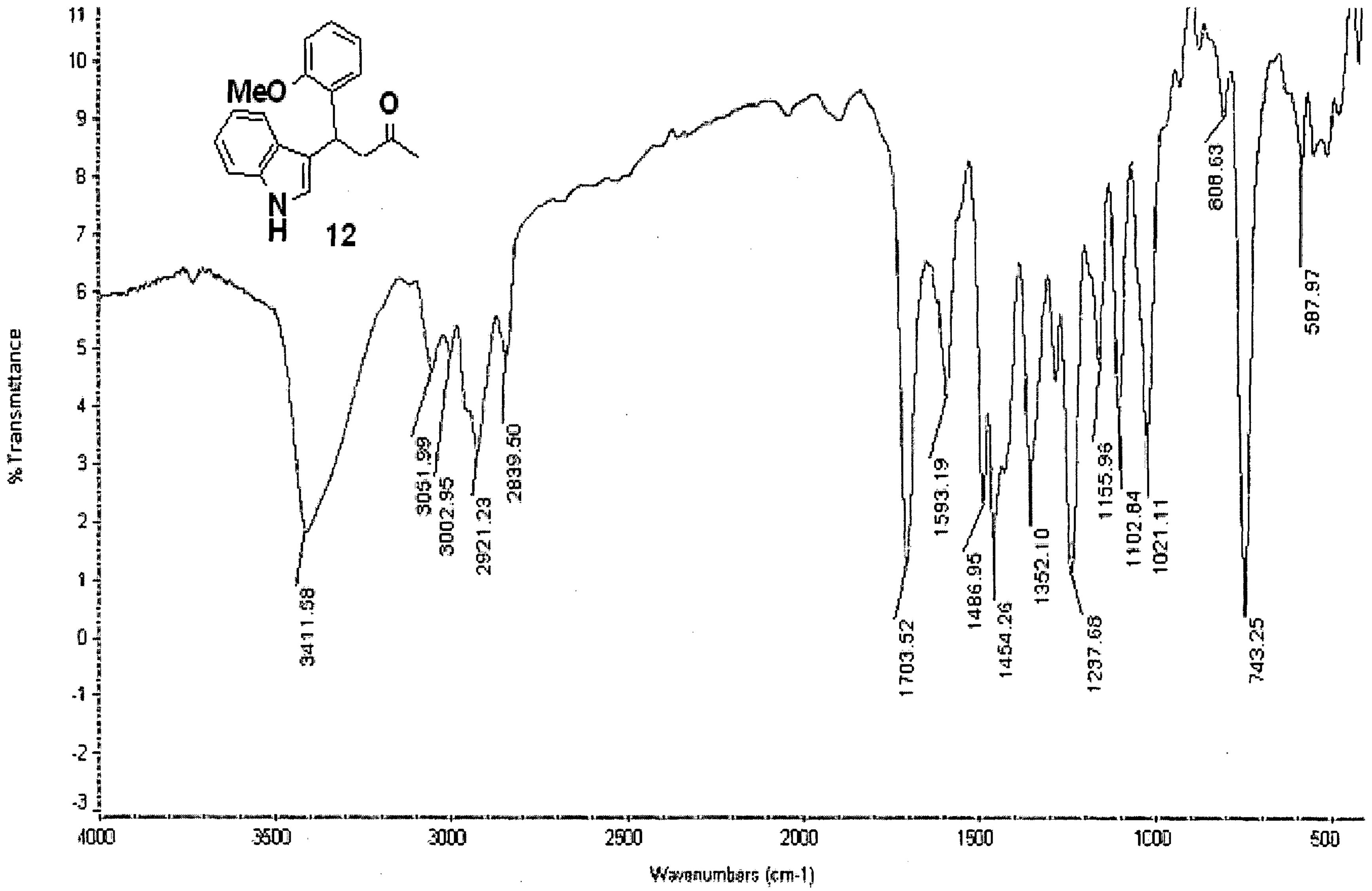
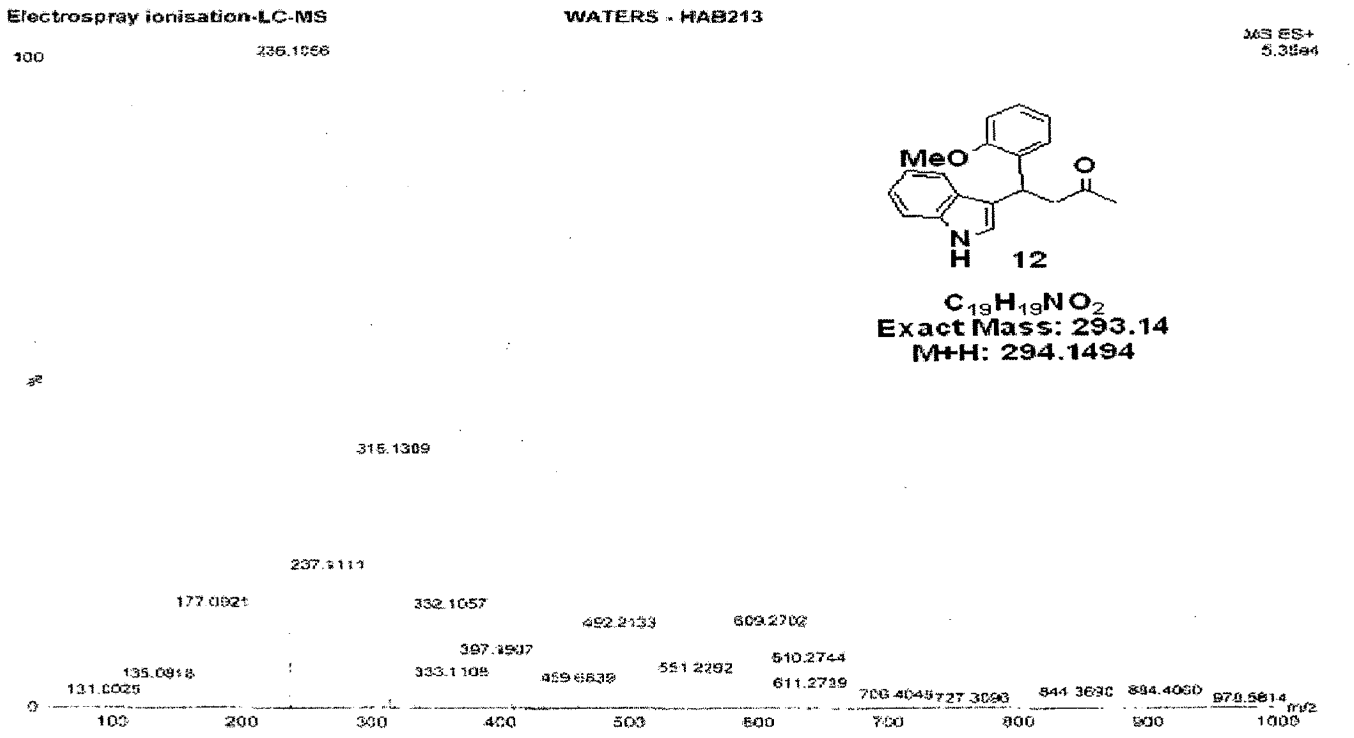


Fig 47. IR spectrum of 4-(3-indolyl)-4-(2-methoxyphenyl)butan-2-one



$C_{19}H_{19}NO_2$
Exact Mass: 293.14
M+H: 294.1494

Fig 48. ESI -MS spectrum of 4-(3-indolyl)-4-(2-methoxyphenyl)butan-2-one

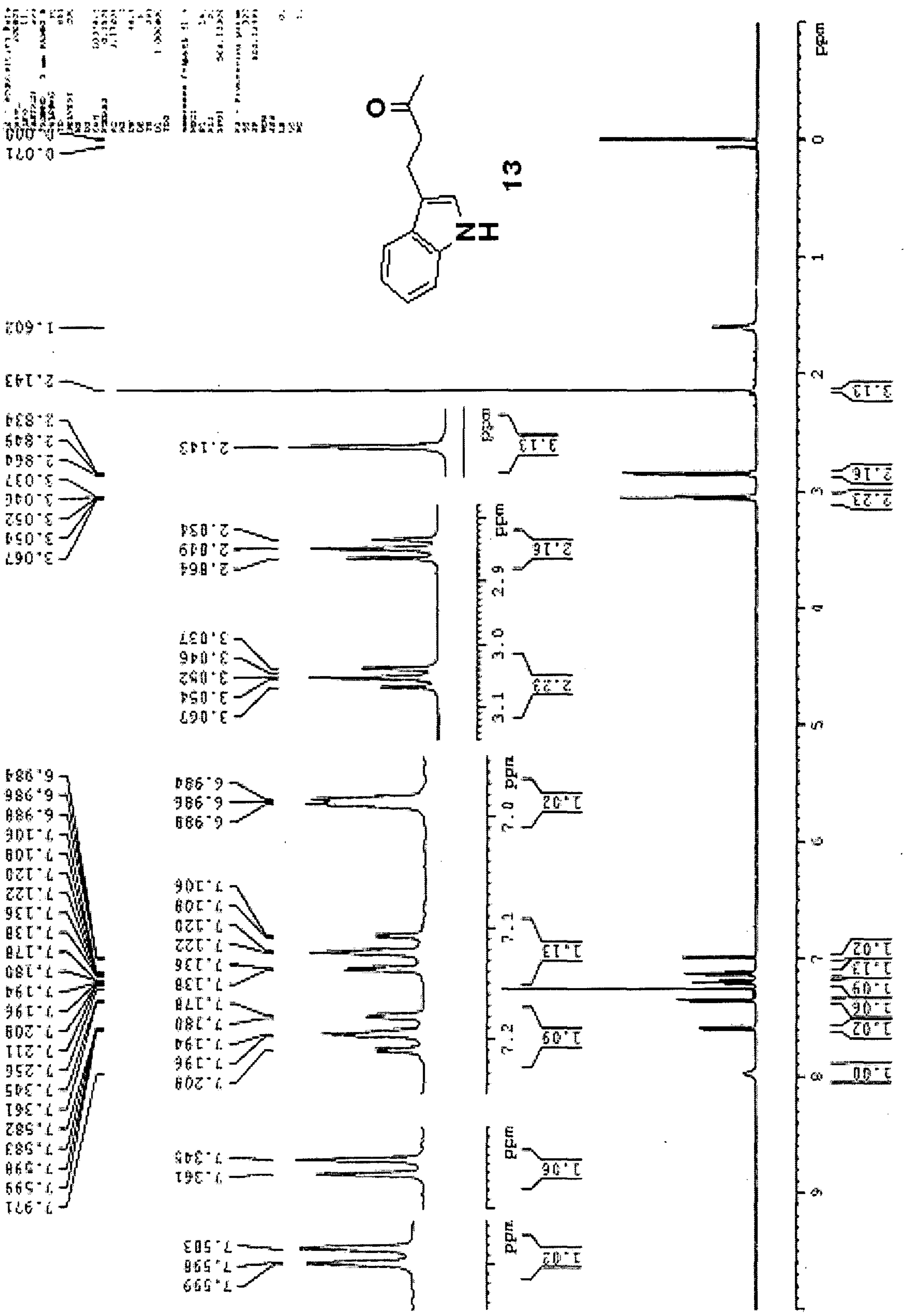


Fig 49. ¹H NMR (500 MHz) spectrum of 4-(3-indolyl)butan-2-one

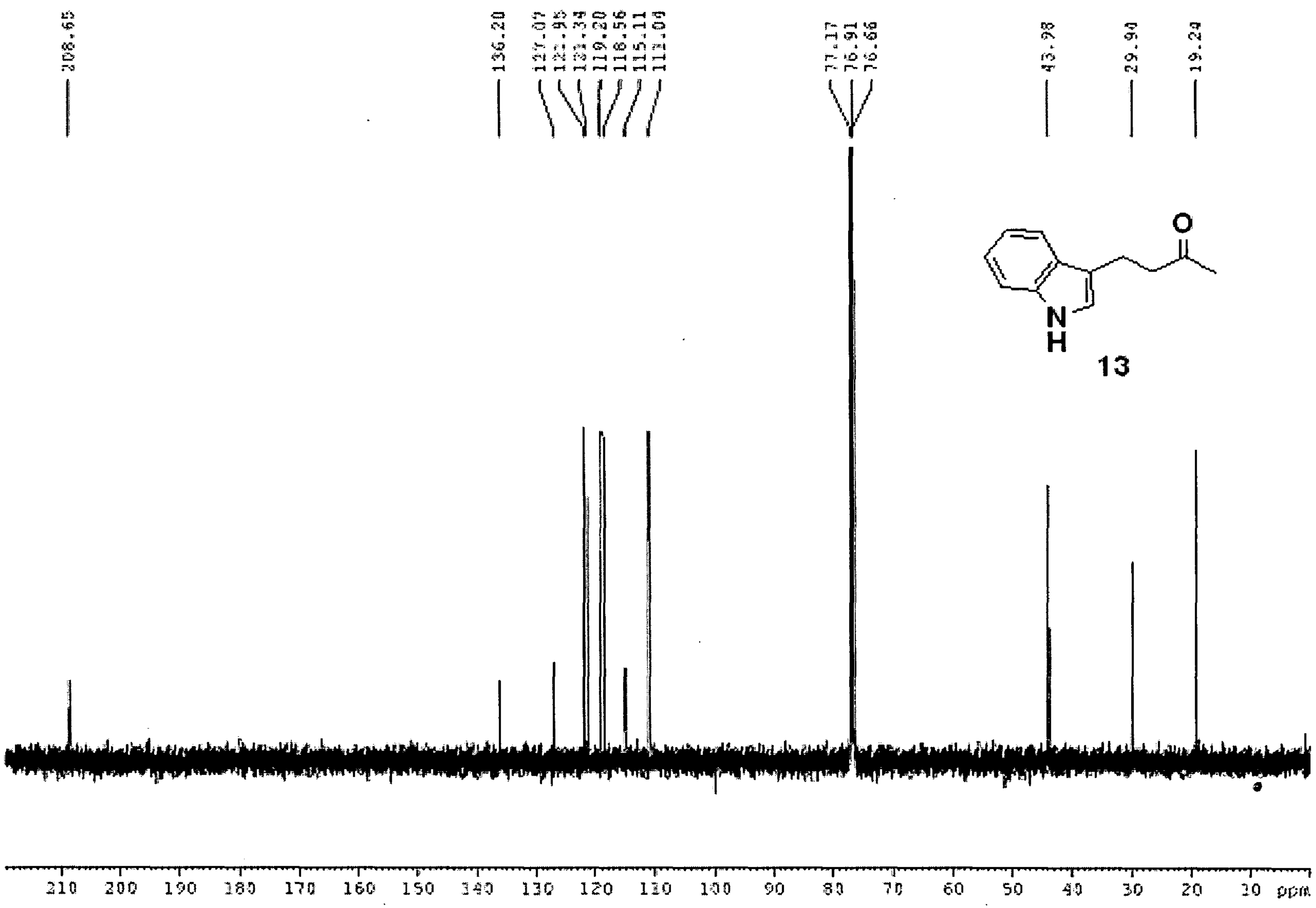


Fig 50. ^{13}C NMR (125 MHz) spectrum of 4-(3-indolyl)butan-2-one

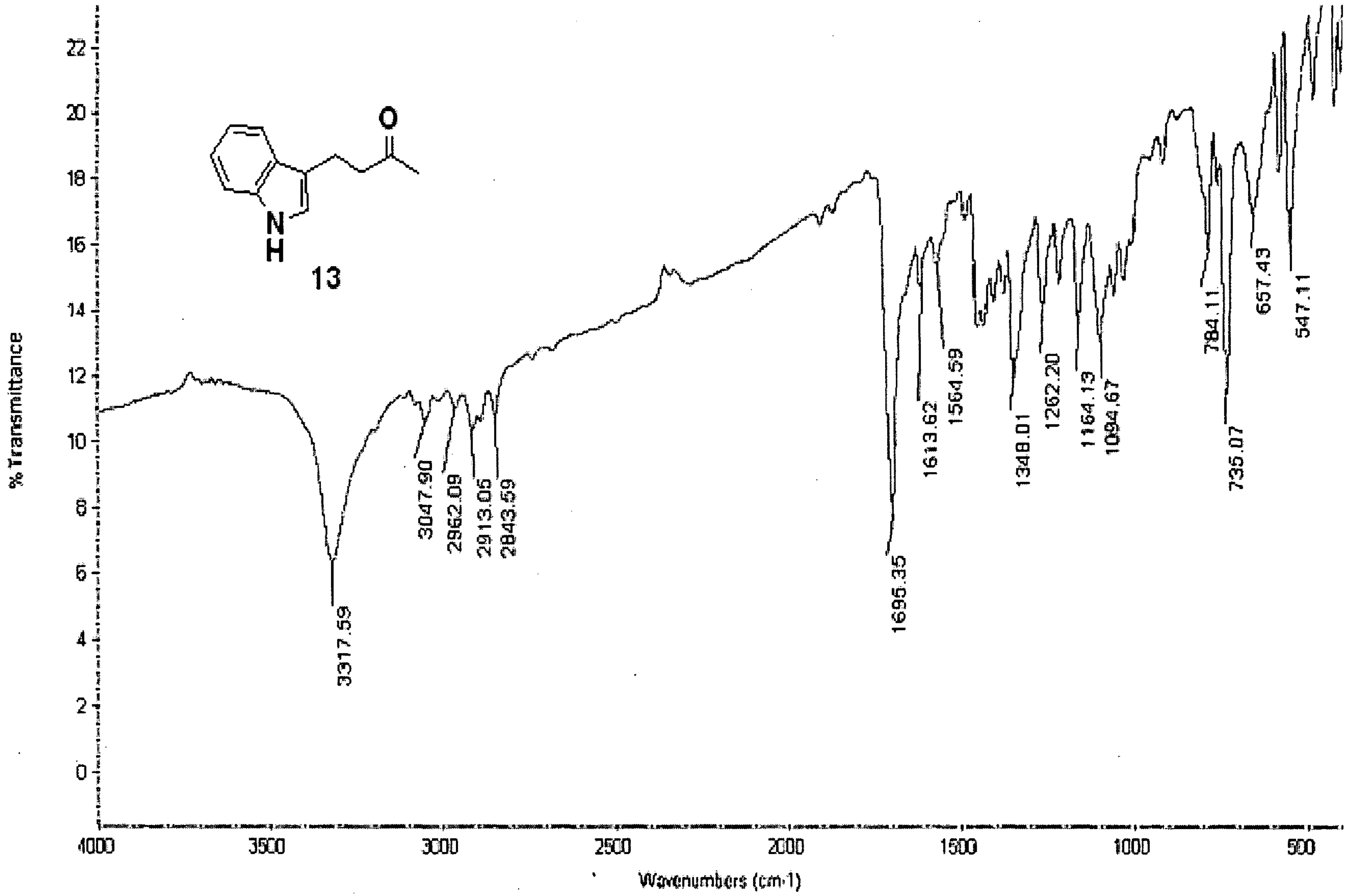


Fig 51. IR spectrum of 4-(3-indolyl)butan-2-one

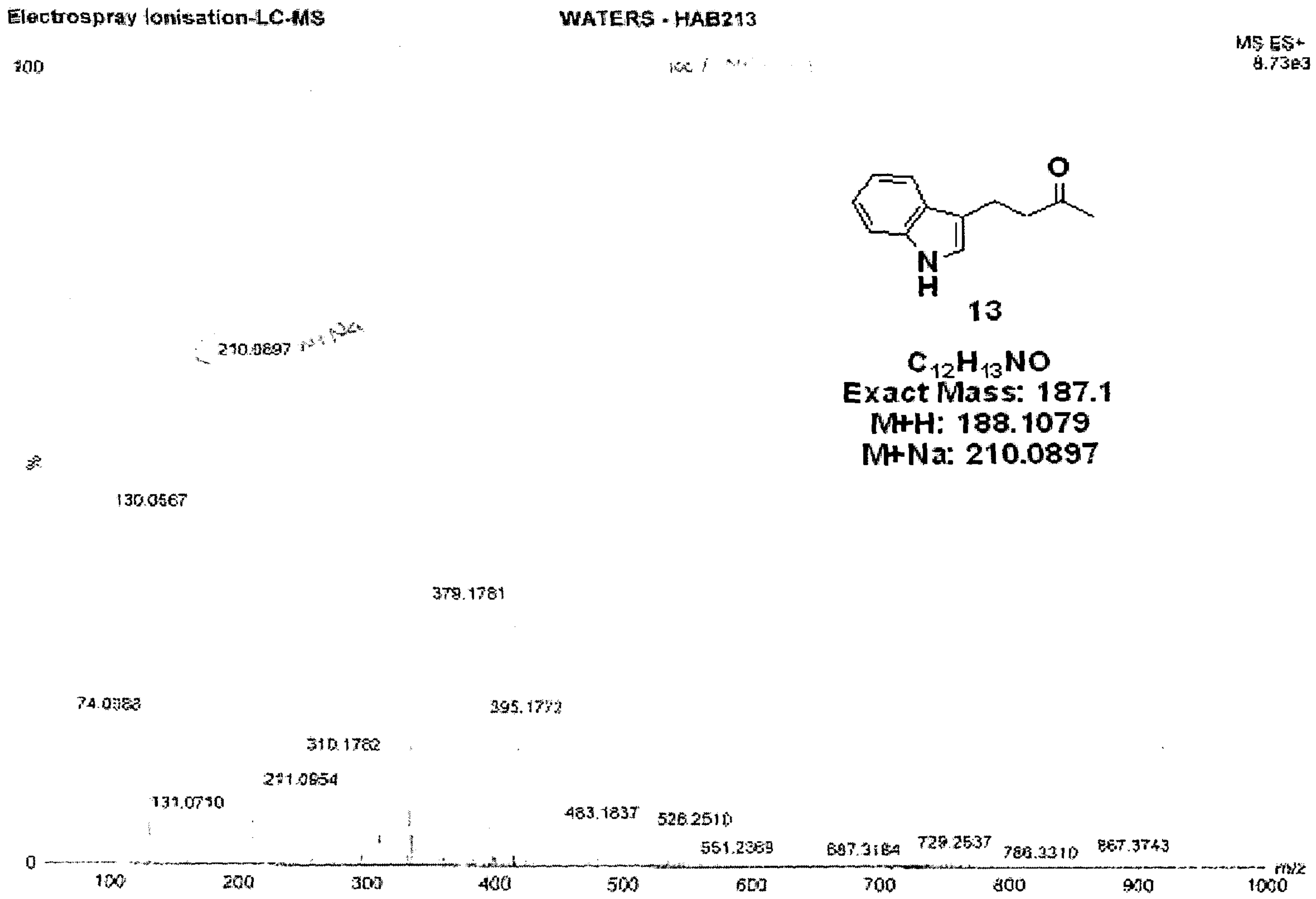


Fig 52. ESI -MS spectrum of 4-(3-indolyl)butan-2-one

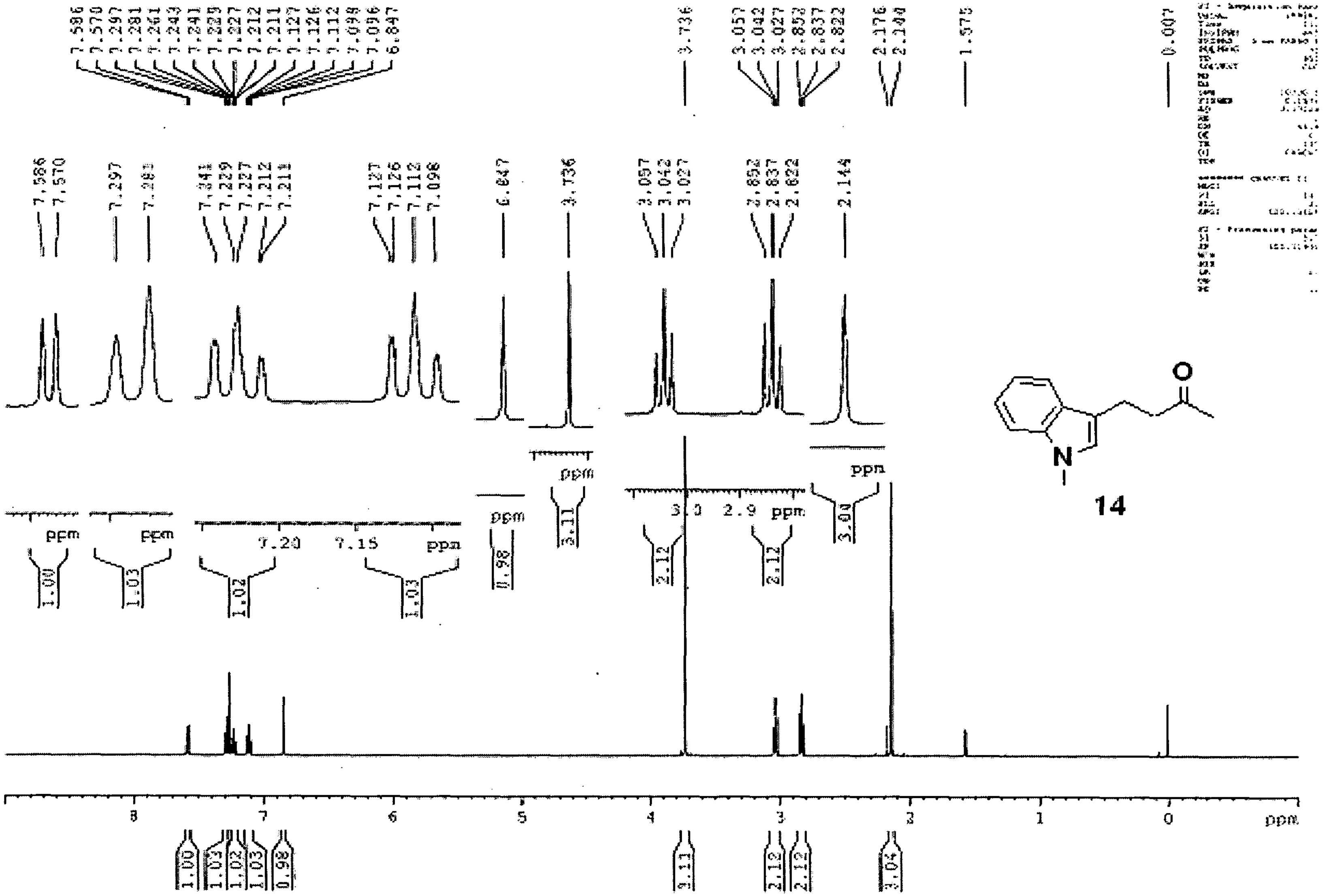


Fig 53. ^{1}H NMR (500 MHz) spectrum of 4-(1-methyl-3-indolyl)butan-2-one

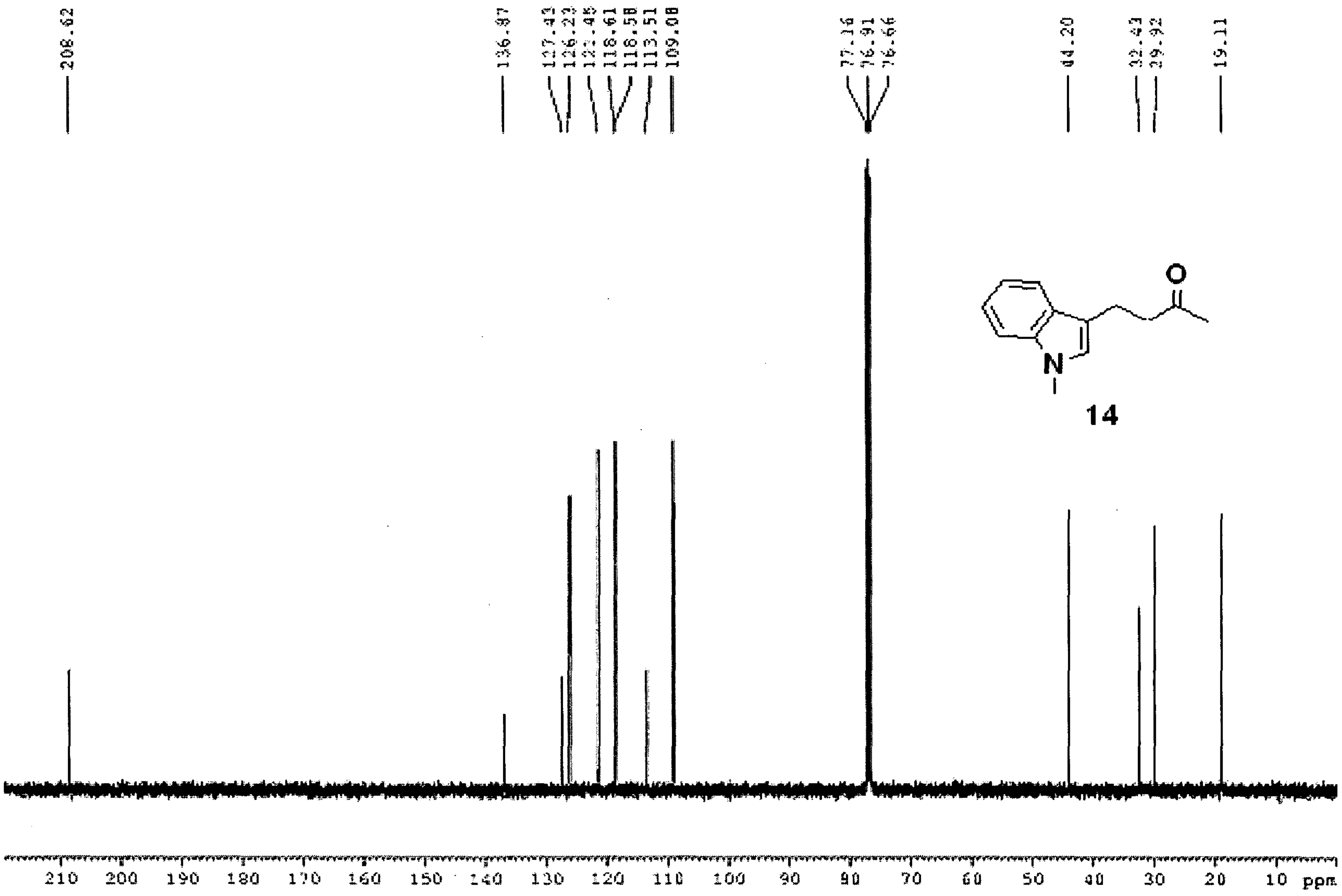


Fig 54. ^{13}C NMR (125 MHz) spectrum of 4-(1-methyl-3-indolyl)butan-2-one

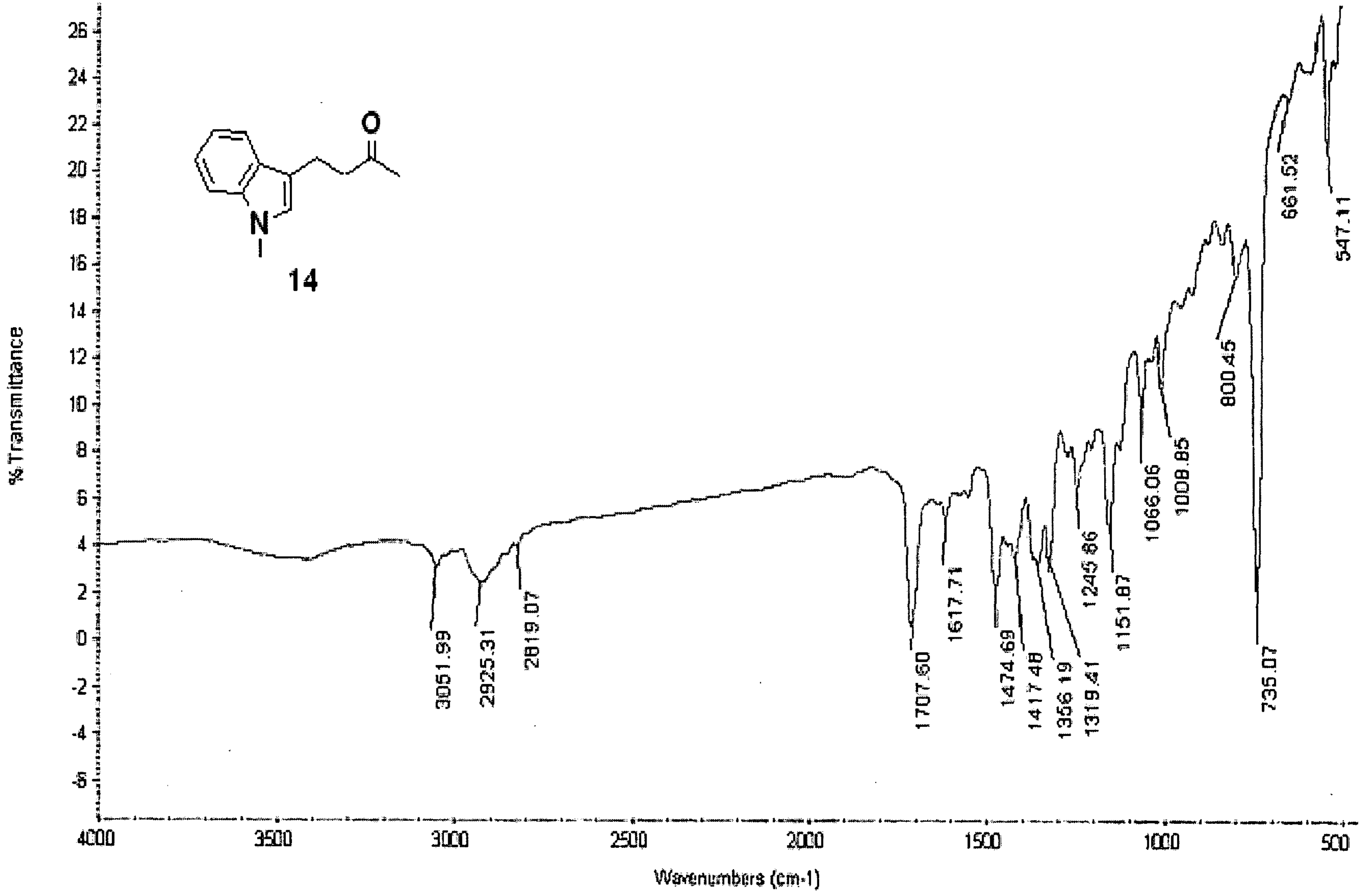


Fig 55. IR spectrum of 4-(1-methyl-3-indolyl)butan-2-one

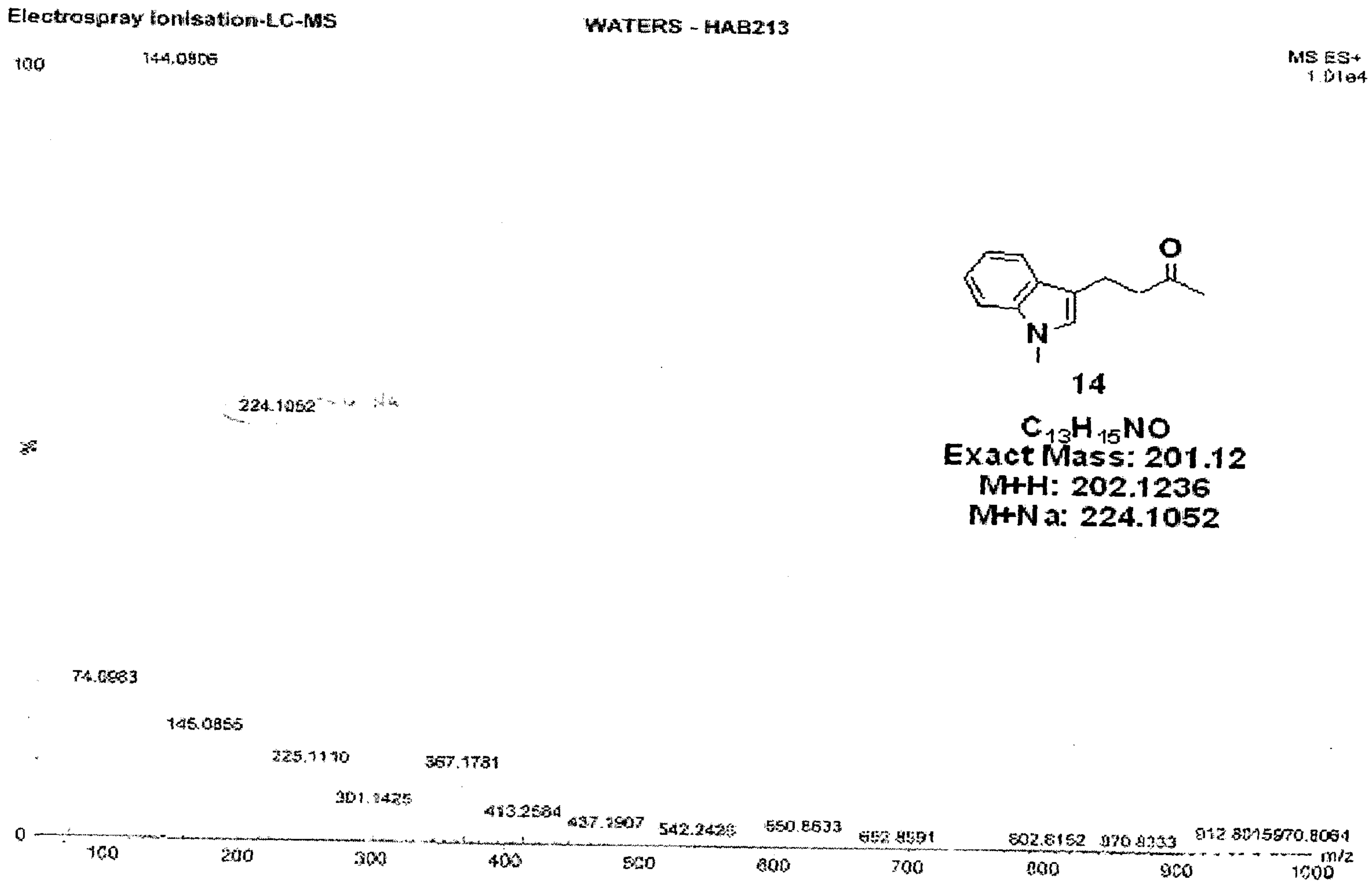


Fig 56. ESI -MS spectrum of 4-(1-methyl-3-indolyl)butan-2-one

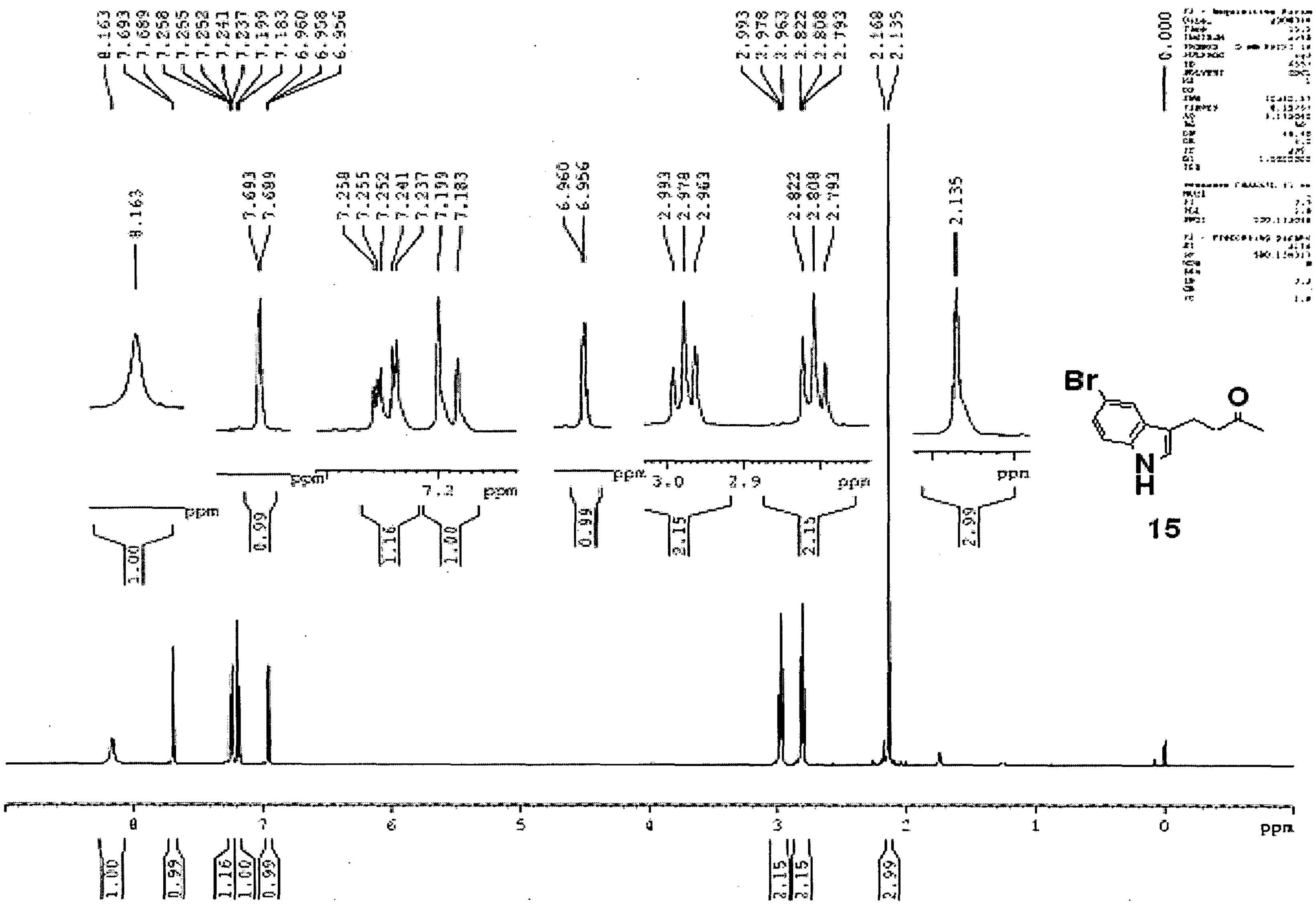


Fig 57. ^{1}H NMR (500 MHz) spectrum of 4-(5-bromo-3-indolyl)butan-2-one

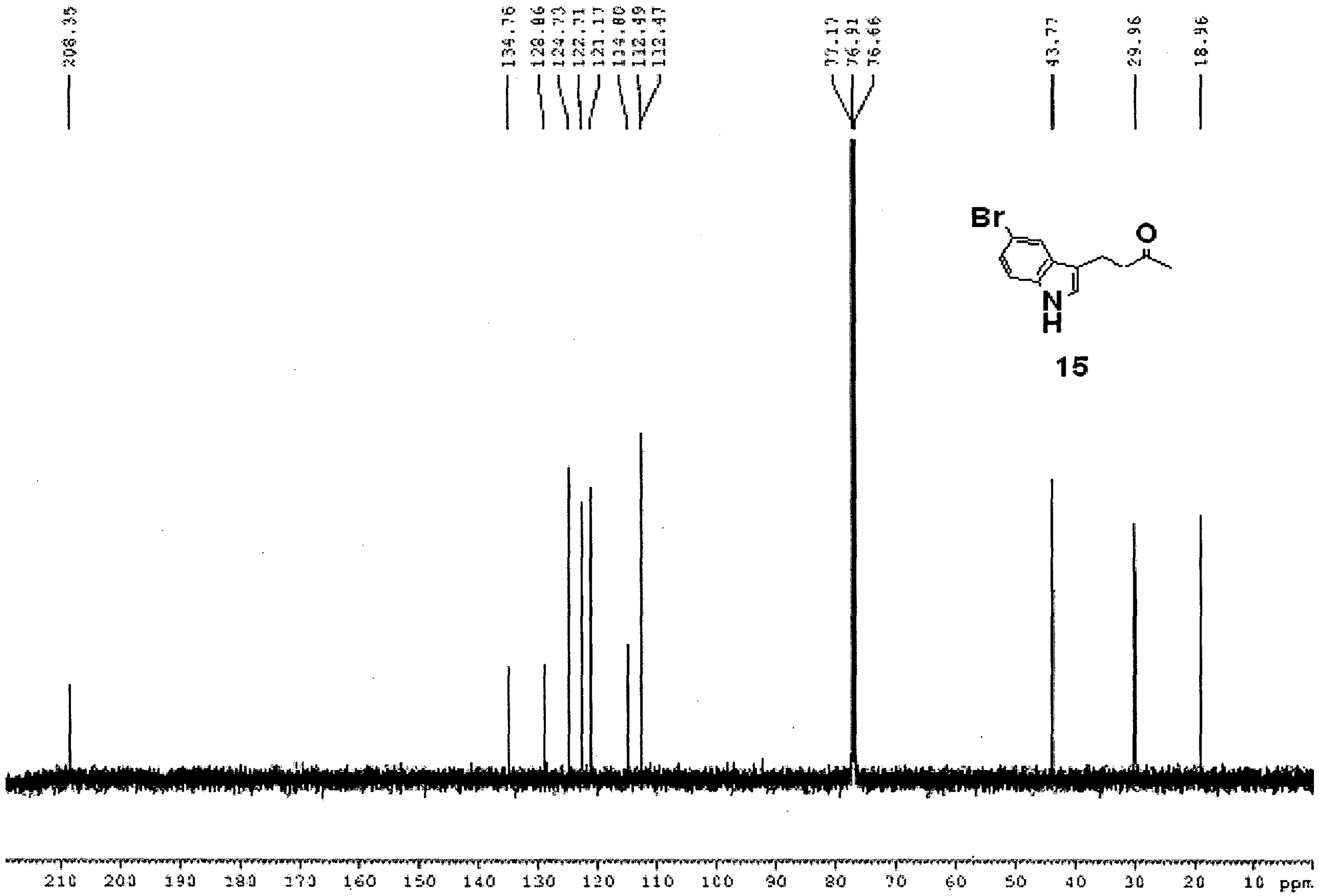


Fig 58. ^{13}C NMR (125 MHz) spectrum of 4-(5-bromo-3-indolyl)butan-2-one

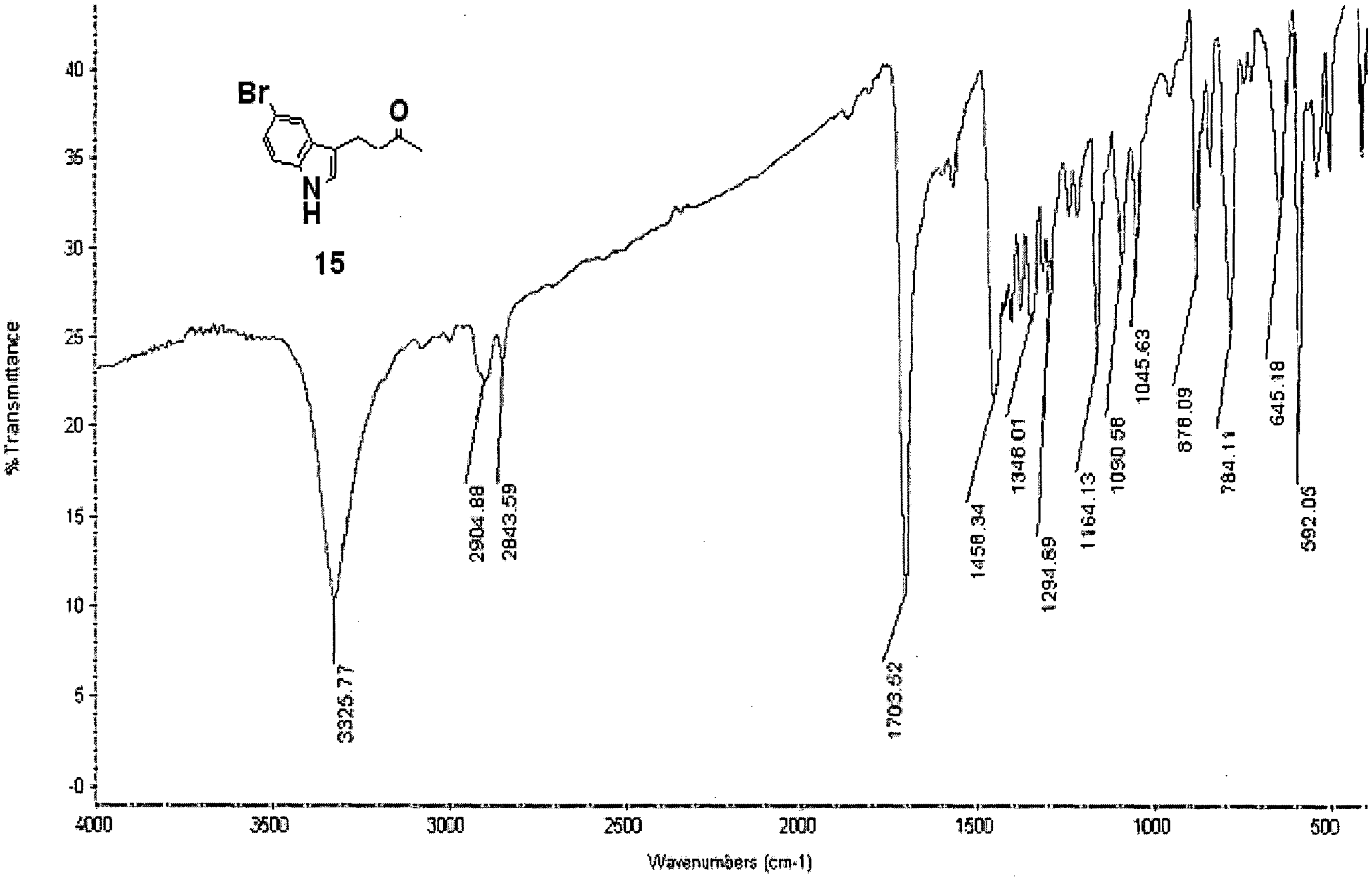


Fig 59. IR spectrum of 4-(5-bromo-3-indolyl)butan-2-one

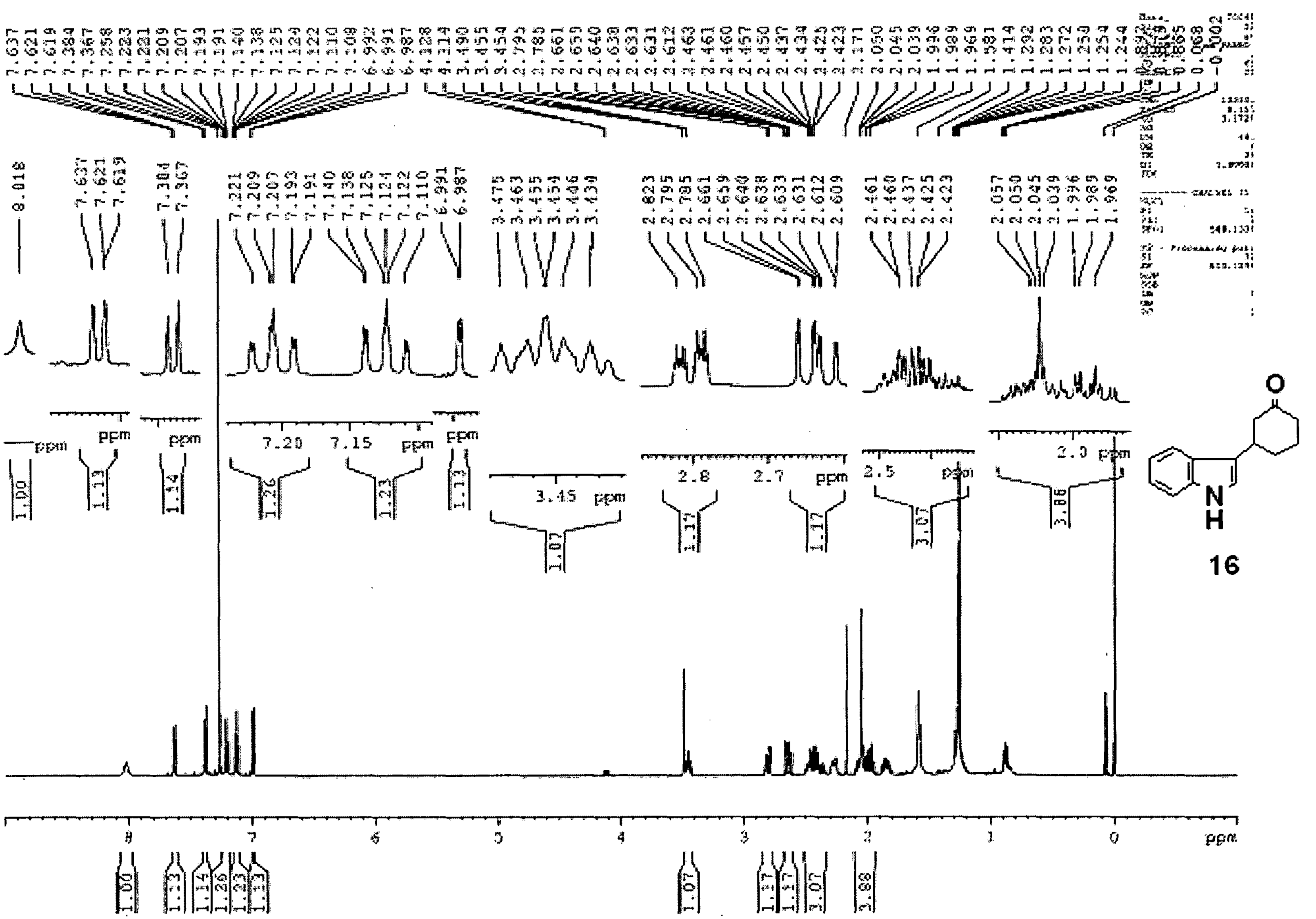


Fig 60. ^{1}H NMR (500 MHz) spectrum of 3-(3-indolyl)cyclohexan-1-one

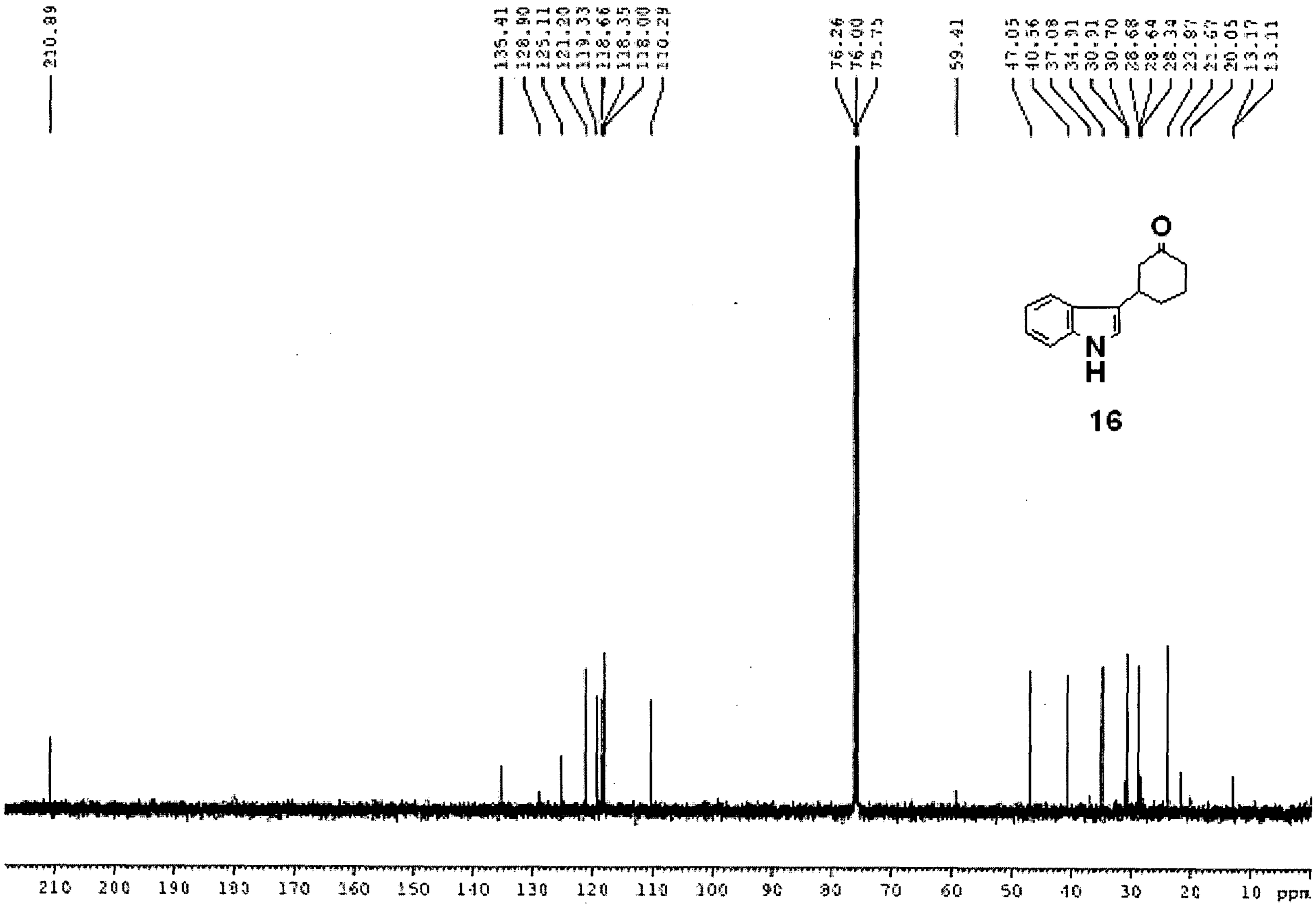


Fig 61. ^{13}C NMR (125 MHz) spectrum of 3-(3-indolyl)cyclohexan-1-one

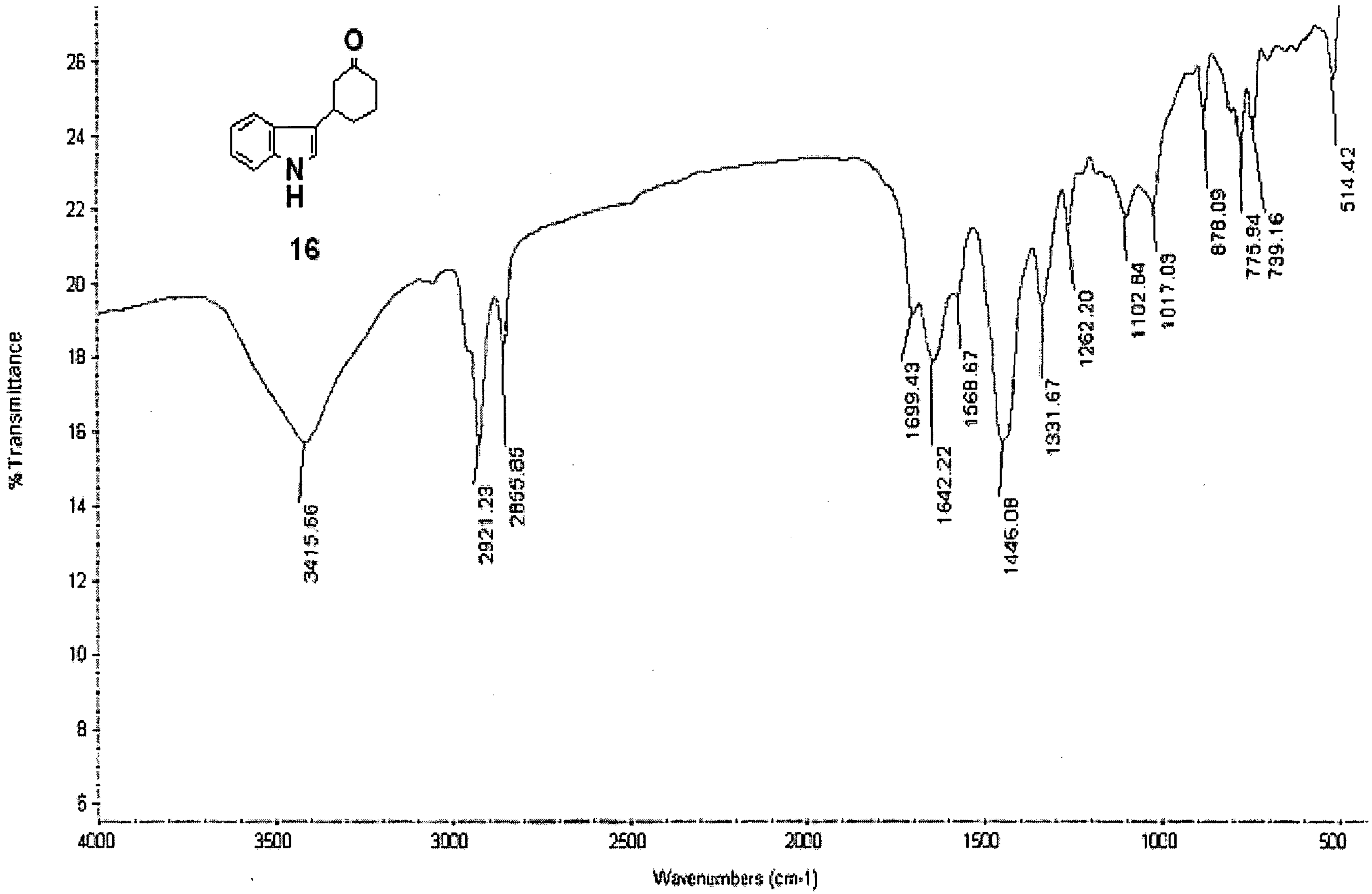


Fig 62. IR spectrum of 3-(3-indolyl)cyclohexan-1-one

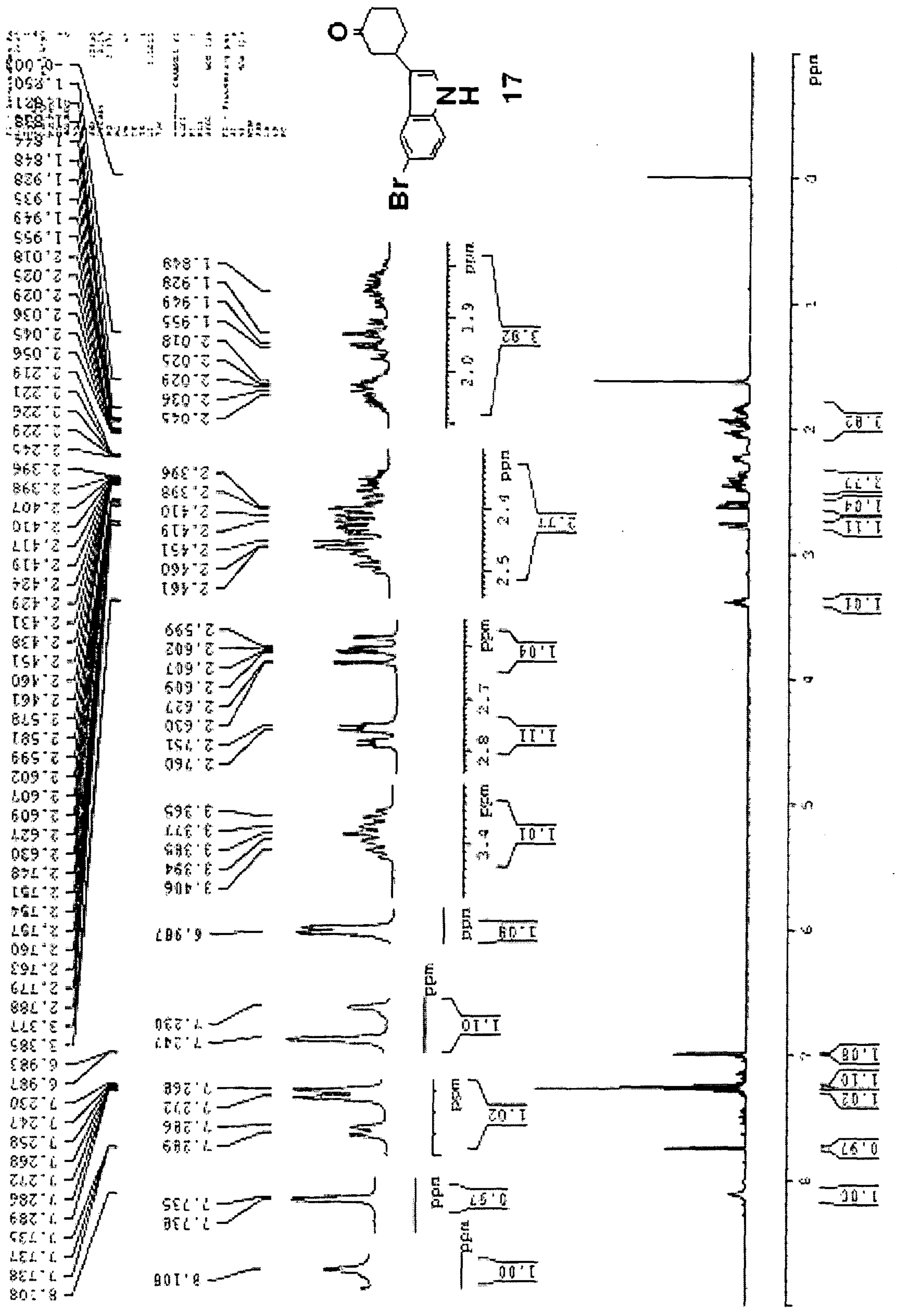


Fig 63. ^{1}H NMR (500 MHz) spectrum of 3-(5-bromo-3-indolyl)cyclohexan-1-one

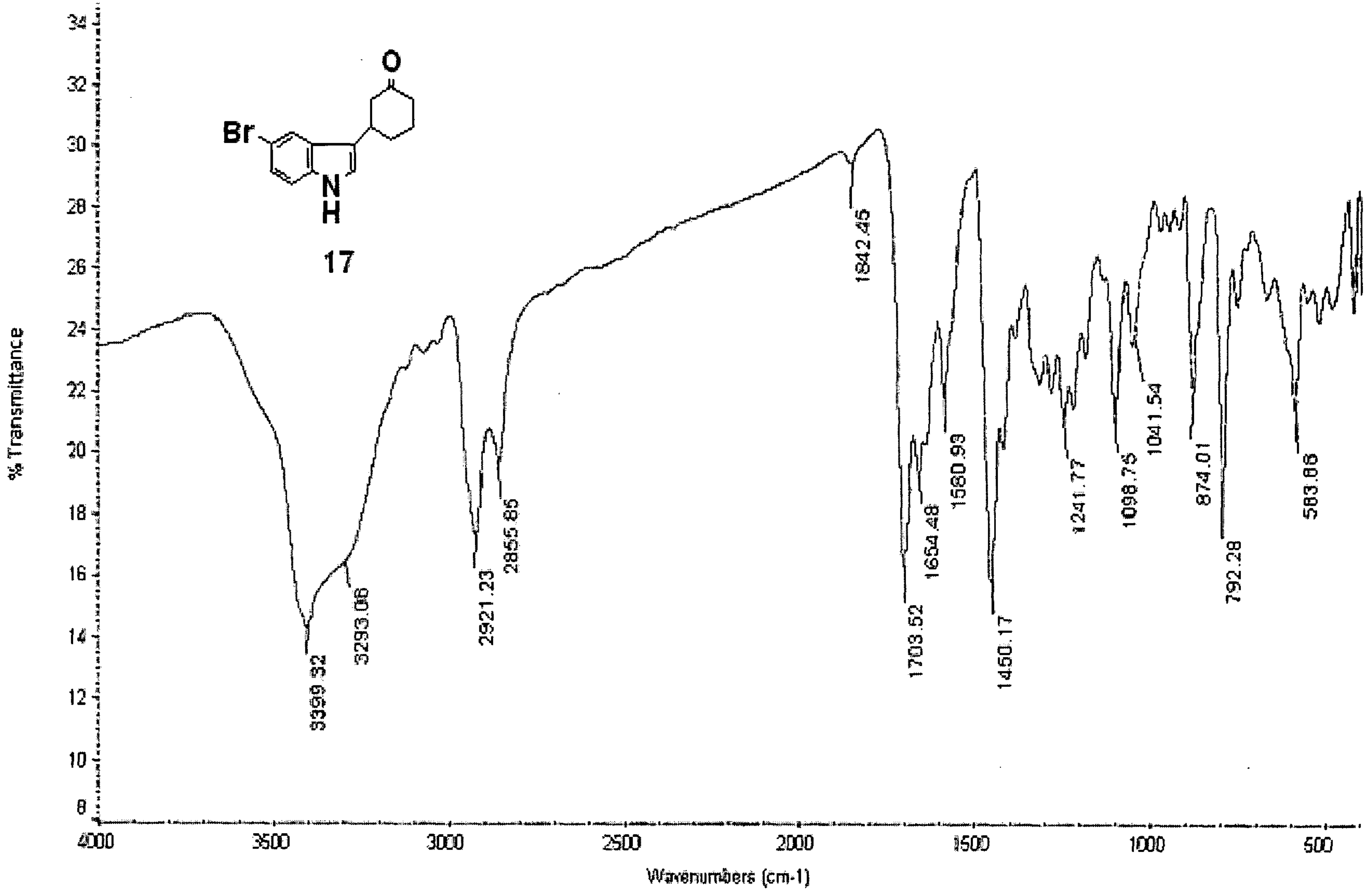


Fig 65. IR spectrum of 3-(5-bromo-3-indolyl)cyclohexan-1-one

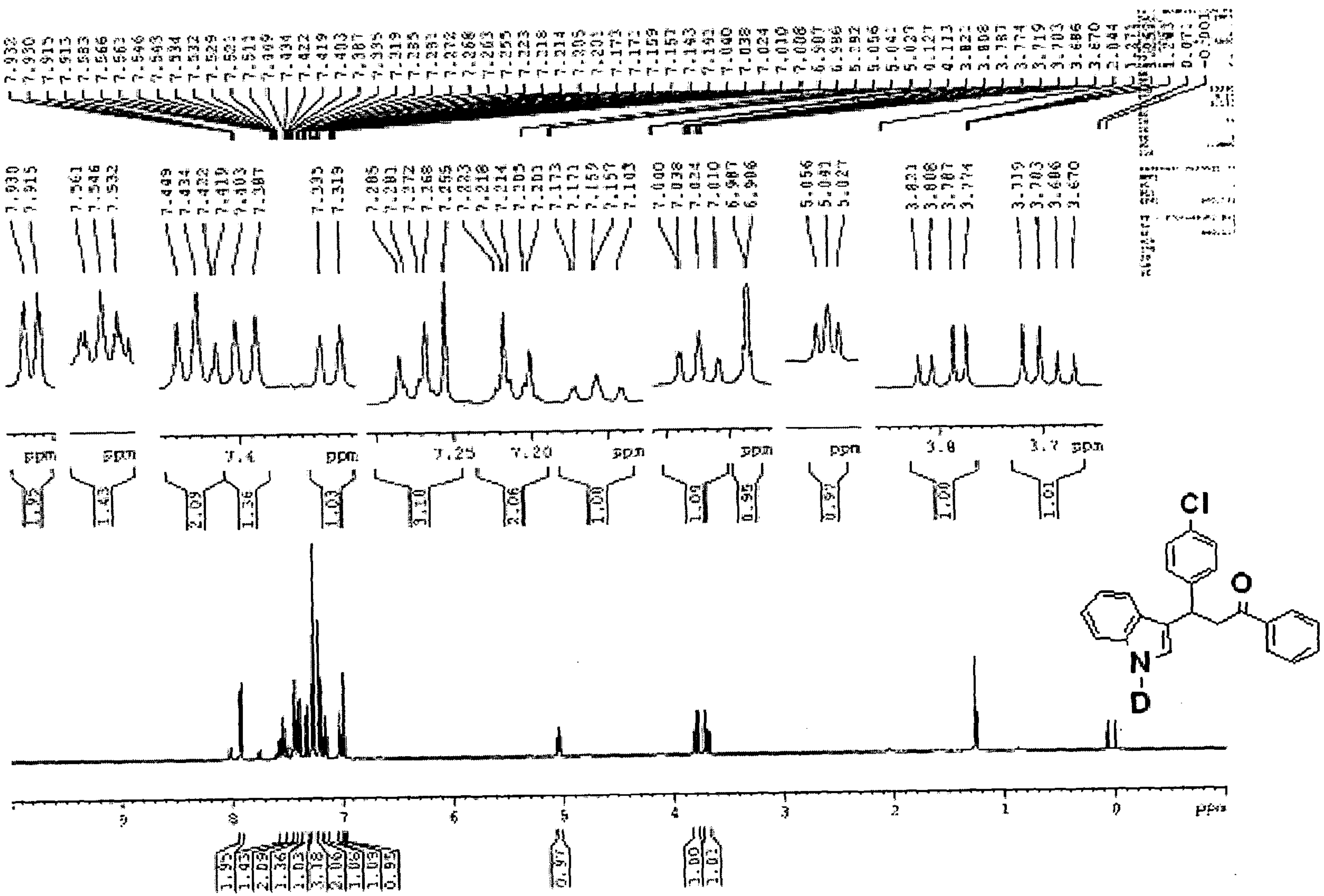


Fig 66. ^{1}H NMR (500 MHz) spectrum of 3-(4-chlorophenyl)-3-(1D-indol-3-yl)-1-phenylpropan-1-one

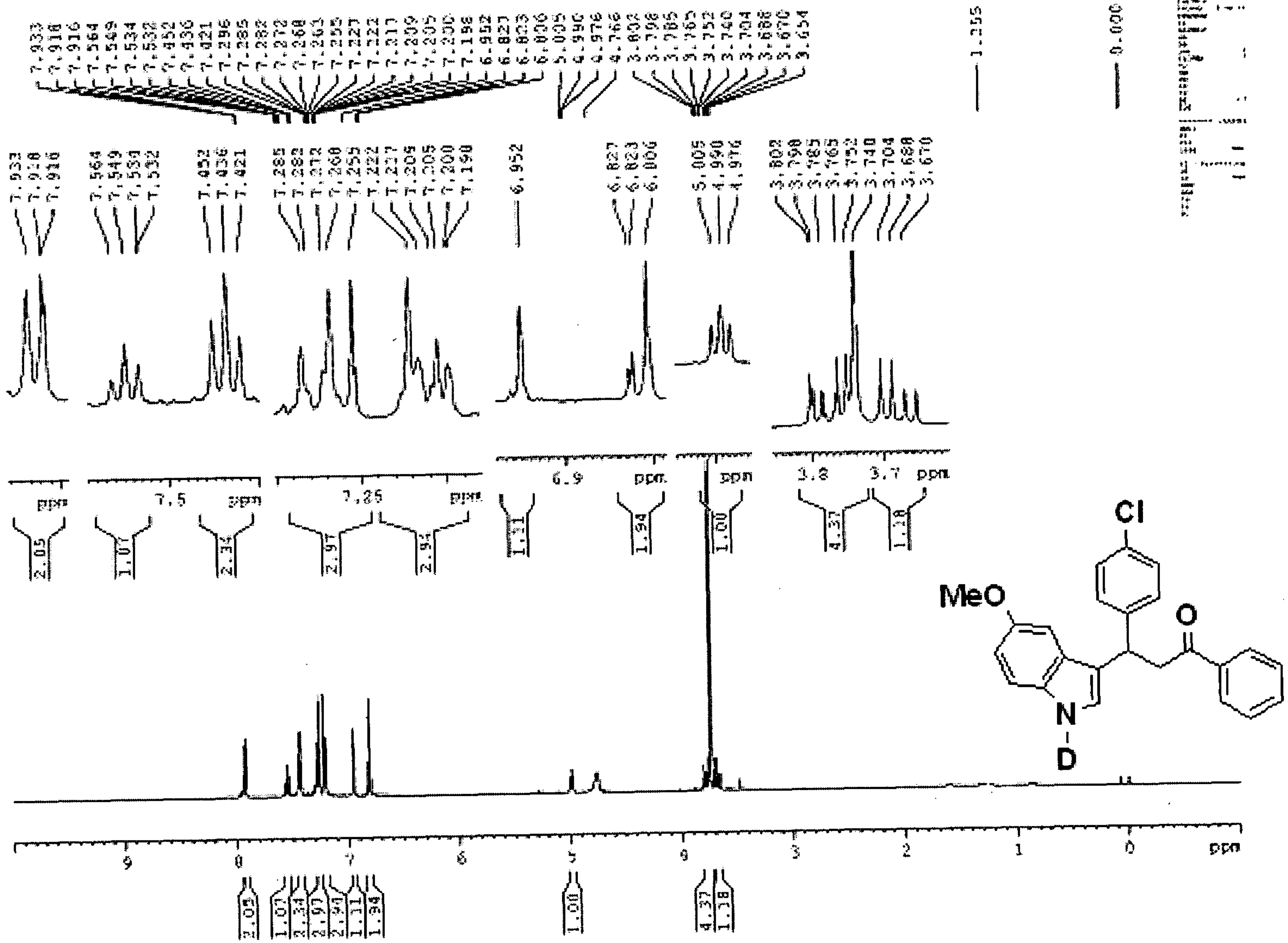


Fig 67. ^{1}H NMR (500 MHz) spectrum of 3-(4-chlorophenyl)-3-(5-methoxy-1D-indol-3-yl)-1-phenylpropan-1-one

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APPENDIX - I

1. Synthesis of 1,3-diphenylprop-2-en-1-one

A solution of 11 g NaOH in 100 ml of water was taken in a flask along with 50 ml of ethanol. Flask was immersed in ice bath and acetophenone (10 mmol, 1.17 ml) was poured into it. The mixture was stirred and benzaldehyde (10 mmol, 1.02 ml) was added to it. The stirring was continued at room temperature till the solution was so thick that stirring is no longer effective (approximately 4 hrs). The reaction mixture was left in refrigerator overnight. The product was filtered on Bückner funnel and washed with cold water till the washings were neutral to litmus. The crude chalcone, after drying in air, was recrystallized from ethanol at 50 °C and 1.25 g of product was obtained (yield : 60%).

2. Synthesis of 3-(4-chlorophenyl)-1-phenylprop-2-en-1-one

A solution of 11 g NaOH in 100 ml of water was taken in a flask along with 50 ml of ethanol. Flask was immersed in ice bath and acetophenone (10 mmol, 1.17 ml) was poured into it. The mixture was stirred and 4-chlorobenzldehyde (10 mmol, 1.44 g) was added to it. The stirring was continued at room temperature till the solution was so thick that stirring is no longer effective (approximately 4 hrs). The reaction mixture was left in refrigerator overnight. The product was filtered on Bückner funnel and washed with cold water till the washings were neutral to litmus. The crude chalcone, after drying in air, was recrystallized from ethanol at 50 °C and 1.17 g of product was obtained (yield : 47%).

3. Synthesis of 4-(3,4-dimethoxyphenyl)but-3-en-2-one

A solution of 11 g NaOH in 100 ml of water was taken in a flask along with 50 ml of ethanol. Flask was immersed in ice bath and acetone (10 mmol, 0.6 ml) was poured into it. The mixture was stirred and 2-methoxybenzaldehyde (10 mmol, 1.4 ml) was added to it. The stirring was continued at room temperature till the solution was so thick that stirring is no longer effective (approximately 4 hrs). The reaction mixture was left in refrigerator overnight. The product was filtered on Bückner funnel and washed with cold water till the washings were neutral to litmus. The crude chalcone, after drying in air, was recrystallized from ethanol at 50 °C and 0.97 g of product was obtained (yield : 55%).