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Experimental and Spectral Analysis Of Fluoxetine Analogues

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ABSTRACT

The SSRIs differ chemically from conventional antidepressants like tricyclic, tetracyclic, and monoamine oxidase inhibitors, but they share the same mechanism of action in that they selectively and potently inhibit serotonin neuronal reuptake while having no or very little impact on norepinephrine, acetylcholine, and histamine neuronal reuptake. Therefore, compared to other antidepressants of the tricyclic and tetracyclic class, these medications have less sedative, anticholinergic, and cardiovascular effects. The SSRI class of medications includes fluoxetine, fluroxamine, sertraline, indalpine, paroxetine, alproclate, femorxetine, and choroxamine.

Keywords: *Fluoxetine, Fluoxetine analogues, sertraline analogues*

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INTRODUCTION

In the absence of a simple mechanistic theory to account for antidepressant action, it is useful to look for pharmacological effects that the various drugs have in common, concentrating more on the slow adaptive changes that follow a similar time course to the therapeutic effect. This approach has led to the discovery that certain monoamine receptors, in particular β_1 and α_2-adrenoceptors, are consistently down-regulated following chronic antidepressant treatment. This can be demonstrated in experimental animals as a reduction in the number of binding sites, as well as by a reduction in the functional response to agonists (e.g. stimulation of cAMP formation by β-adrenoceptor agonists). Receptor down-regulation probably also occurs in humans, because endocrine responses to clonidine, an α_2-adrenoceptor agonist, are reduced by long-term antidepressant treatment. Other receptors have also been studied; α_1-adrenoceptors are not consistently affected, but 5-HT_2-receptors are also down-regulated. Loss of β-adrenoceptors as a factor in alleviating depression does not fit comfortably with theory, because β-adrenoceptor antagonists are not antidepressant, although it is the most consistent change reported. Impaired presynaptic inhibition secondary to down-regulation of α_2-adrenoceptors might, it is argued, facilitate monoamine release and thus facilitate transmission. Consistent with this possibility is the fact that some newer antidepressant drugs, such as mirtazapine, are antagonists at various inhibitory presynaptic receptors, including α_2-adrenoceptors[1]. The excess 5-HT in the synaptic cleft means over activation of the postsynaptic receptors. Over an extended period of time, this causes down regulation of pre- and postsynaptic receptors, a reduction in the amount in the 5-HT produced in the CNS, and a reduction in the number of SERTs expressed. Long-term administration of SSRIs causes down regulation of the SERT, But not the NET[2]. Tricyclic antidepressants so called because of the characteristic three-ring nucleus have been used clinically for four decades. They closely resemble the phenothiazines chemically and, to a lesser extent, pharmacologically[3]. The main immediate effect of TCAs is to block the uptake of amines by nerve terminals, by competition for the binding site of the amine transporter .Synthesis of amines, storage in synaptic vesicles, and release are not directly affected, although some TCAs appear to increase transmitter release indirectly by blocking presynaptic α_2-adrenoceptors. Most TCAs inhibit noradrenaline and 5-HT uptake by brain synaptosomes to a similar degree but have much less effect on dopamine uptake. It has been suggested that improvement of motional symptoms reflects mainly an enhancement of 5-HT-mediated transmission, whereas relief of biological

symptoms results from facilitation of noradrenergic transmission. Interpretation is made difficult by the fact that the major metabolites of TCAs have considerable pharmacological activity (in some cases greater than that of the parent drug) and often differ from the parent drug in respect of their noradrenaline/5-HT selectivity[4].

MATERIALS AND METHOD

Chemicals Used

Acetophenone, F-Acetophenone, Benzyl methyl amine, Dibenzyl amine, Paraformaldehyde, Sodium borohydride, Sodium hydride, Dimethyl acetamide, *p*-Chlorobenztrifluride, α-Napthol, Aluminium chloride, Benzene, Dichlorobenzene, Methyl amine (Alc.), Palladium catalyst, Hydroxyl amine, Sodium metal, Sodium methoxide, Morpholine, N-Phenyl piperazines, Isopropanol, Absolute alcohol, Methanol, n-Propanol, Ammonia solution etc

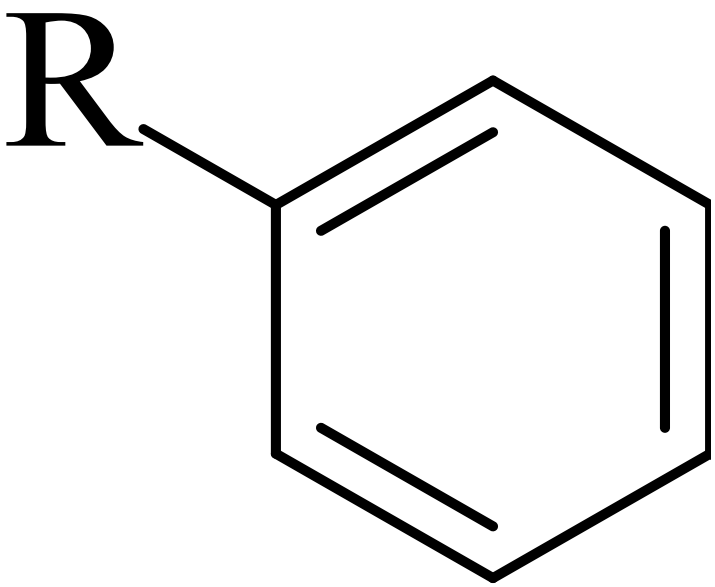
Apparatus Used

Reflux condenser, Magnetic stirrer, Electric oil bath, Dimerstat, Rotavapour, Suction pump, Guard tubes, precoated TLC plates.

Analytical Work

Melting points (M.P.) were determined using melting point apparatus and are uncorrected. Reaction progress was monitored by performing thin layer chromatography on silica gel G plates, using iodine vapours and UV chamber as visualizing agents. After physical characterization, the compounds were subjected to spectral analysis. Proton Nuclear Magnetic resonance spectra were recorded on Bruker WM-300 (at 300 MHz) spectrometer and chemical shifts were reported in parts per million (δ value) from TMS (δ 0 ppm for ^{1}H NMR) as an internal standard.

SYNTHETIC SCHEME



PROCEDURE

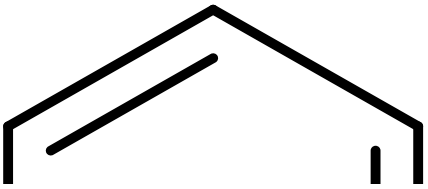
Synthesis of 3-(benzyl(methyl)amino)-1-phenylpropan-1-one [1(a)]

Experimental Procedure

A mixture of benzyl methyl amine hydrochloride (1 mole) and isopropanol (15 ml) was cooled in an ice-bath (0-5°C) for 25 min and conc. HCl (0.07ml) was added drop wise with stirring. After 30 min the mixture was allowed to attain room temperature Acetophenone and paraformaldehyde ($1/5^{th}$ of the required 0.075 mole) was added. The flask was heated at 100-110°C for 30 min.Similarly other three portions of paraformaldehyde were added and finally the reaction mixture was heated for 3hr at 100-110°C. Then it was allowed to cool to room temperature overnight. Solid and Organic layer are separated and dried over suction pump and neutralized by liquid ammonia.

TLC: 5% Methanol: 95% Chloroform
Melting Range: 198-202°C
Yield: 82.5%
Solubility: Chloroform, acetone, methanol

4.3.1.2: Synthesis of 3-(benzyl(methyl)amino)-1-phenylpropan-1-ol [1(b)]

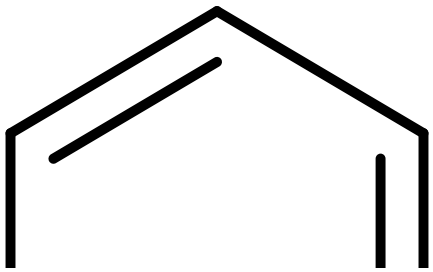


Experimental Procedure

A solution of 3-(benzyl(methyl)amino)-1-phenylpropan-1-one (free base 0.013mol) in methanol was cooled in ice-bath for 30 min and powdered sodium borohydride (0.037 mol) was added in equal portion in 1 hr. The reaction mixture was further stirred in ice-bath for 30 min. The reaction mixture was concentrated under reduced pressure in a rotavapor and the residue was treated with water (5ml) and ethyl acetate (30 ml). The ethyl acetate layer was separated, washed with water till neutral washings and dried (anhyd. $NaSO_4$).

TLC: 3% Methanol: 97% Chloroform
Melting Range: Oily
Yield: 46.8%
Solubility: Chloroform, acetone, methanol

4.3.1.3: Synthesis of N-benzyl-N-methyl-3-phenyl-3-(4-(trifluoromethyl) phenoxy)propan-1-amine [1(c)]

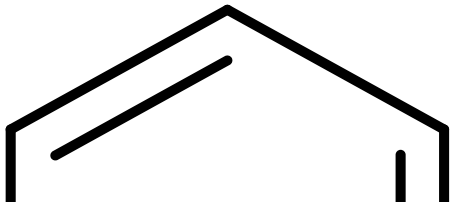


Experimental Procedure

A mixture of sodium hydride (0.0382 mol) and dimethylacetamide (DMAC,15 ml) was cooled in an ice-bath for 15min and a solution of hydroxy compounds (0.024 mol) in DMAC (10 ml) was added drop wise with stirring. After 15 min the reaction mixture was allowed to attain room temperature. The flask was then placed in an oil bath and heated slowly to 80-90°C for another 2 hr. The colour is changed from yellow to brown. This brown solution was cooled to room temperature and *p*-chlorobenzotrifluride (0.0382 mol) was added in 15 min with stirring. The mixture was again heated at 100-110°C for 5-6 hr. The reaction mixture was allowed to attain at room temperature and treated with ethyl

acetate and water successively. The organic layer was separated and aqueous layer was extracted with ethyl acetate. The combined layer was washed with water till neutral pH, dried (anhyd. $NaSO_4$) & purified by column chromatography.
TLC: 7% Ethyl acetate: 93% Hexane
Melting Range: Oily
Yield: 60.3%
Solubility: Chloroform, acetone

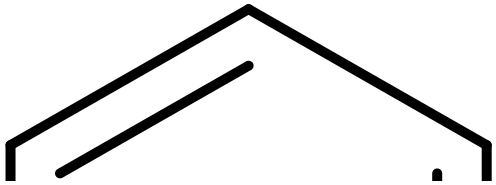
4.3.2.1: Synthesis of 3-(dibenzylamino)-1-phenylpropan-1-one [2(a)]



Experimental Procedure

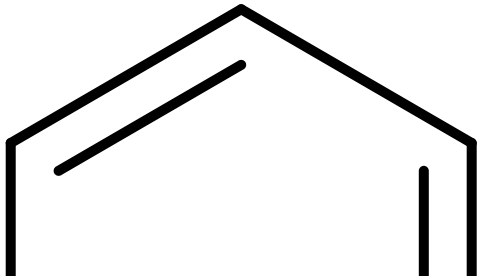
A mixture of dibenzyl amine hydrochloride (1 mole) and isopropanol (15 ml) was cooled in an ice-bath (0-5°C) for 25 min and conc. HCl (0.07ml) was added drop wise with stirring. After 30 min the mixture was allowed to attain room temperature Acetophenone and paraformaldehyde ($1/5^{th}$ of the required 0.075 mole) was added. The flask was heated at 100-110°C for 30 min. Similarly, other three portions of paraformaldehyde were added and finally the reaction mixture was heated for 3hr at 100-110°C. Then it was allowed to cool to room temperature overnight. Solid and Organic layer are separated and dried over suction pump and neutralized by liquid ammonia.
TLC: 5% Methanol: 95% Chloroform
Melting Range: 160-162°C
Yield: 82.6%
Solubility: Chloroform, acetone, methanol

4.3.2.2: Synthesis of 3-(dibenzylamino)-1-phenylpropan-1-ol [2(b)]



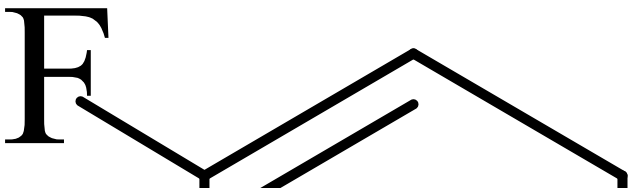
Experimental Procedure

A solution of 3-(dibenzylamino)-1-phenylpropan-1-one (free base 0.013mol) in methanol was cooled in ice-bath for 30 min and powdered sodium borohydride (0.037 mol) was added in equal portion in 1 hr. The reaction mixture was further stirred in ice-bath for 30 min. The reaction mixture was concentrated under reduced pressure in a rotavapor and the residue was treated with water (5ml) and ethyl acetate (30 ml). The ethyl acetate layer was separated, washed with water till neutral washings and dried (anhyd. $NaSO_4$).
TLC: 3% Methanol: 97% Chloroform
Melting Range: Oily
Yield: 71.4%
Solubility: Chloroform, Acetone, Methanol
Synthesis of N,N-dibenzyl-3-phenyl-3-(4-(trifluoromethyl)phenoxy) propan-1-amine [2(c)]

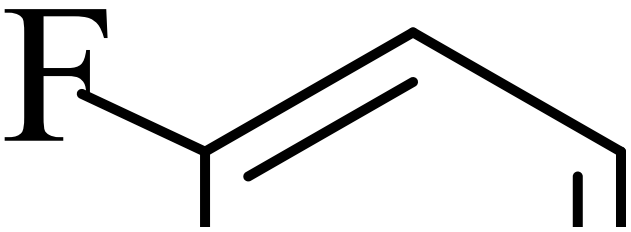


Experimental Procedure

A mixture of sodium hydride (0.0382 mol) and dimethylacetamide (DMAC,15 ml) was cooled in an ice-bath for 15min and a solution of hydroxy compounds (0.024 mol) in DMAC (10 ml) was added drop wise with stirring. After 15 min the reaction mixture was allowed to attain room temperature. The flask was then placed in an oil bath and heated slowly to 80-90°C for another 2 hr. The colour is changed from yellow to brown. This brown solution was cooled to room temperature and *p*-chlorobenzotrifluride (0.0382 mol) was added in 15 min with stirring. The mixture was again heated at 100-110°C for 5-6 hr. The r.m. was allowed to attain at room temperature and treated with ethyl acetate and water successively. The organic layer was separated and aqueous layer was extracted with ethyl acetate. The combined layer was washed with water till neutral pH and dried (anhyd. $NaSO_4$). Compound purified by column chromatography.
TLC: 7% Ethyl acetate: 93% Hexane
Melting Range: Oily
Yield: 55%
Solubility: Chloroform, acetone, methanol
Synthesis of 3-(benzyl(methyl)amino)-1-(4-fluorophenyl)propan-1-one [3(a)]

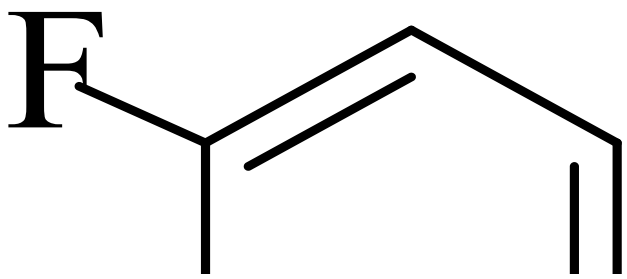


Experimental Procedure
A mixture of Benzyl methyl amine hydrochloride (1 mole) and isopropanol (15 ml) was cooled in an ice-bath (0-5°C) for 25 min and conc. HCl (0.07ml) was added drop wise with stirring. After 30 min the mixture was allowed to attain room temperature Fluoro acetophenone and paraformaldehyde ($1/5^{th}$ of the required 0.075 mole) was added. The flask was heated at 100-110°C for 30 min. Similarly, other three portions of paraformaldehyde were added and finally the reaction mixture was heated for 3hr at 100-110°C. Then it was allowed to cool to room temperature overnight. Solid and Organic layer are separated and dried over suction pump and neutralized by liquid ammonia.
TLC: 5% Methanol: 95% Chloroform
Melting Range: 198-202°C
Yield: 78.4%
Solubility: Chloroform, acetone, methanol
Synthesis of 3-(benzyl(methyl)amino)-1-(4-fluorophenyl)propan-1-ol [3(b)]



Experimental Procedure
A solution of 3-(benzyl(methyl)amino)-1-(4-fluorophenyl)propan-1-one (free base 0.013mol) in methanol was cooled in ice-bath for 30 min and powdered sodium borohydride (0.037 mol) was added in equal portion in 1 hr. The reaction mixture was further stirred in ice-bath for 30 min. The reaction mixture was concentrated under reduced pressure in a rotavapor and the residue was treated with water (5ml) and ethyl acetate (30 ml). The ethyl acetate layer was separated, washed with water till neutral washings and dried (anhyd. $NaSO_4$).
TLC: 3% Methanol: 97% Chloroform
Melting Range: Oily
Yield: 71.8%
Solubility: Chloroform, acetone, methanol

4.3.3.3: Synthesis of N-benzyl-3-(4-fluorophenyl)-N-methyl-3-(2-nitro-4-(trifluorome thyl)-phenoxy)propan-1-amine [3(c)]



Experimental Procedure

A mixture of sodium hydride (0.0382 mol) and dimethylacetamide (DMAC,15 ml) was cooled in an ice-bath for 15min and a solution of hydroxy compounds (0.024 mol) in DMAC (10 ml) was added dropwise with stirring. After 15 min the reaction mixture was allowed to attain room temperature. The flask was then placed in an oil bath and heated slowly to 80-90°C for another 2 hr. The colour is changed from yellow to brown. This brown solution was cooled to room temperature and *o*-Nitro-*p*-chlorobenzotrifluride (0.0382 mol) was added in 15 min with stirring. The mixture was again heated at 100-110°C for 5-6 hr. The r.m. was allowed to attain at room temperature and treated with ethyl acetate and water successively. The organic layer was separated and aqueous layer was extracted with ethyl acetate. The combined layer was washed with water till neutral pH and dried (anhyd. $NaSO_4$). Compound purified by column chromatography.

TLC: 7% Ethyl acetate: 93% Hexane
Melting Range: Oily
Yield: 51.3%
Solubility: Chloroform, acetone, methanol

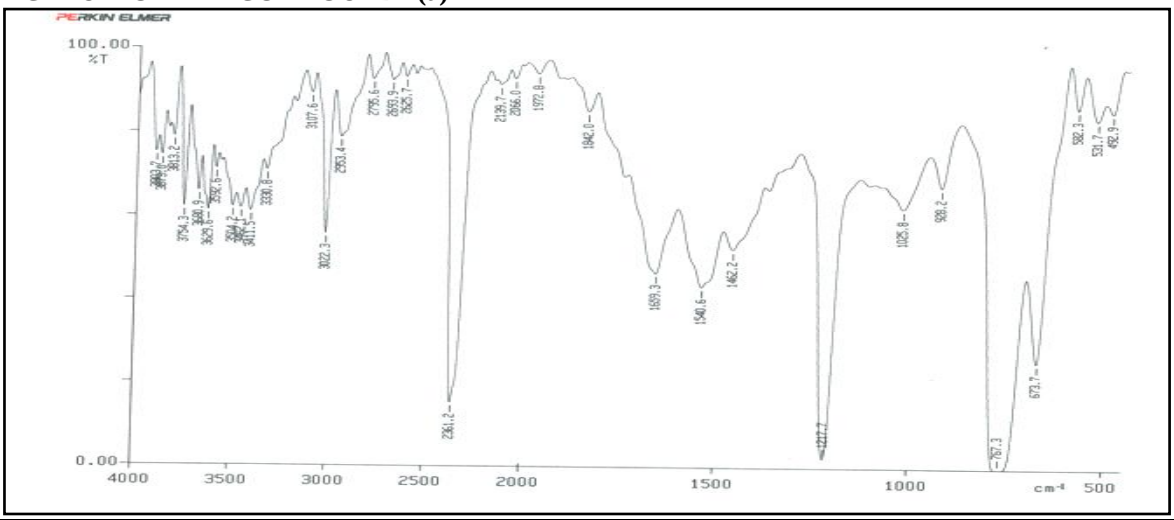
Table 4.1 : The Physicochemical data of compounds

S.N	Compd code	Molecular formula	Solubility	Colour	% yield	M.P. (°C)	R_f value
1	1 (a)	$C_{17}H_{17}NO_2$	$CHCl_3$	White	82.5	198-202	0.86
2	1 (b)	$C_{17}H_{19}NO_2$	$CHCl_3$	Transparent	76.8	Oily	0.61
3	1 (c)	$C_{25}H_{25}F_3NO_3$	$CHCl_3$	Yellow	60.3	Oily	0.54
4	2 (a)	$C_{23}H_{19}NO_3$	$CHCl_3$	White	82.6	160-162	0.84
5	2 (b)	$C_{23}H_{21}NO_3$	$CHCl_3$	Transparent	71.4	Oily	0.49
6	2 (c)	$C_{30}H_{24}F_3NO_3$	$CHCl_3$	Transparent	55	Oily	0.56
7	3 (a)	$C_{17}H_{16}FNO_2$	$CHCl_3$	White	78.4	145-150	0.85
8	3 (b)	$C_{17}H_{18}NO_2$	$CHCl_3$	Transparent	71.8	Oily	0.56
9	3 (c)	$C_{24}H_{20}N_4N_2O_4$	$CHCl_3$	Transparent	51.3	Oily	0.64

SPECTRAL STUDIES OF COMPOUNDS

Spectral Data of Compound 1

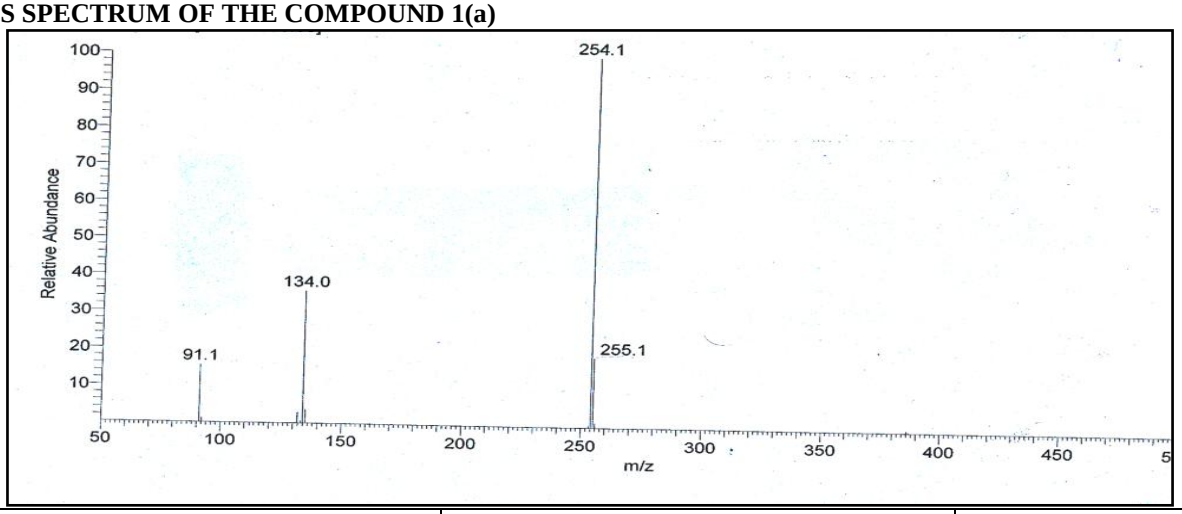
IR SPECTRUM OF THE COMPOUND 1(a)



Functional Group	IR Frequency (cm^{-1})

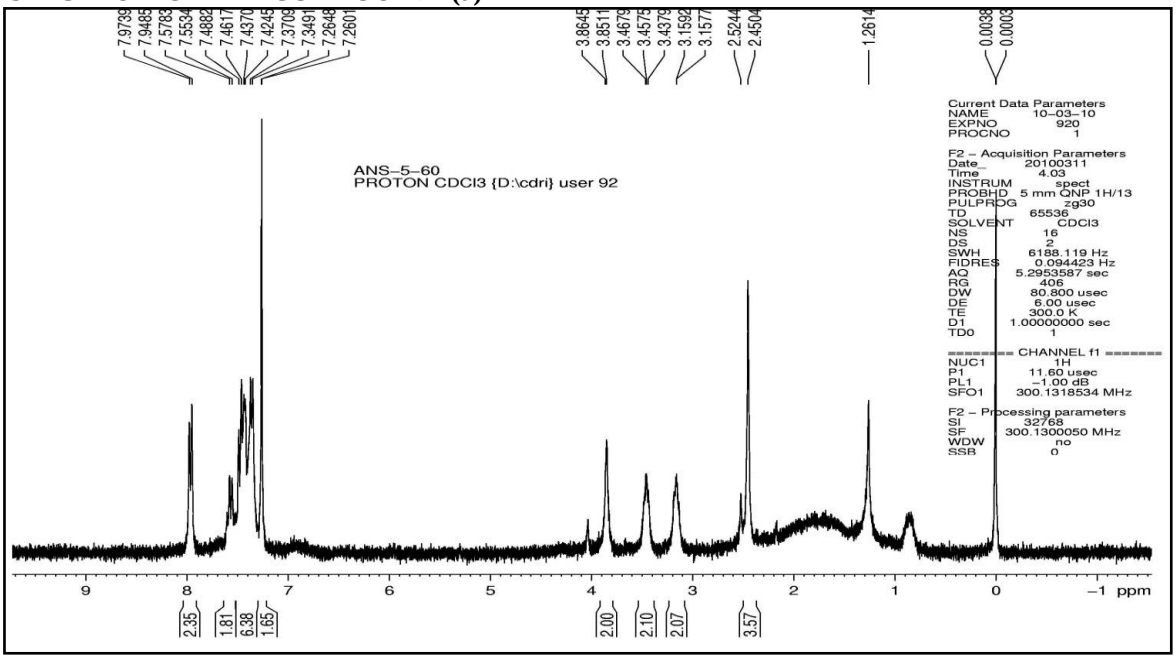
C-H (Ar)	3022.3
C=O	1659.3
C-N	1217.7
C-H (Ar oop)	767.3

MASS SPECTRUM OF THE COMPOUND 1(a)



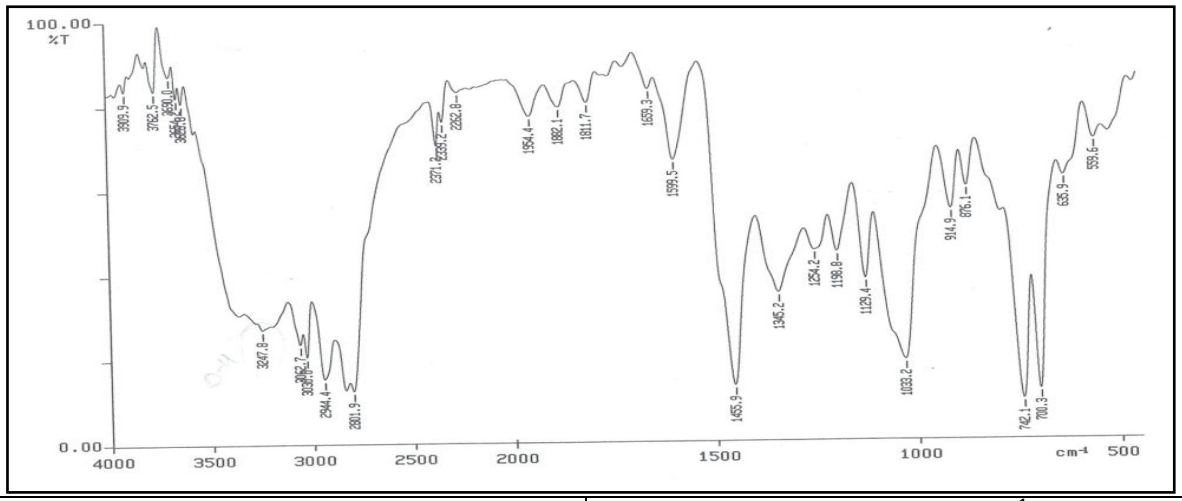
Observed Molecular weight	Molecular ion peak	Interpretation
253	254	M^++1

NMR SPECTRUM OF THE COMPOUND 1(a)



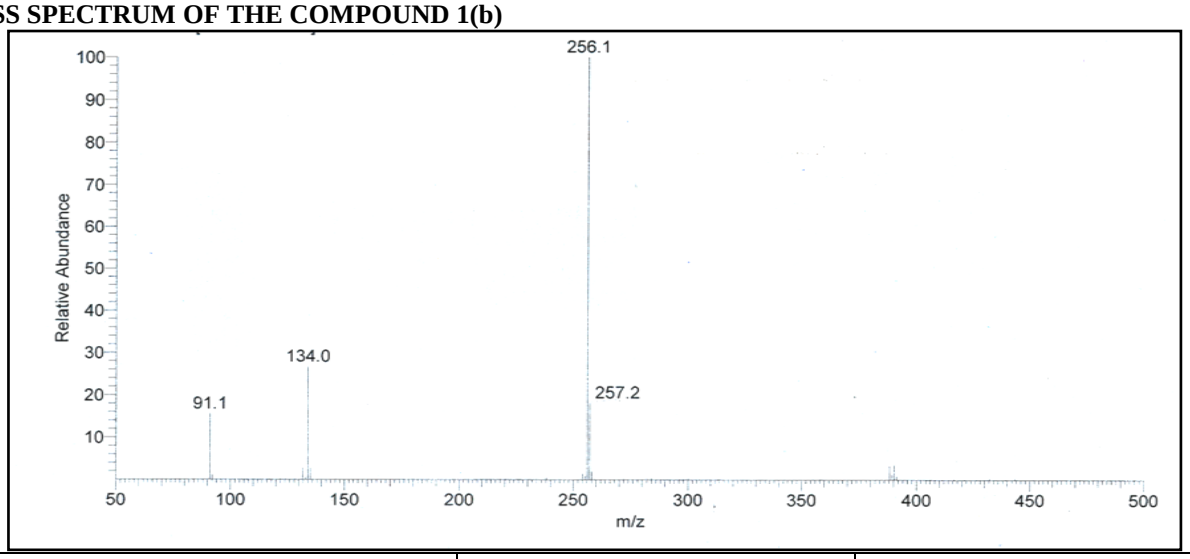
^{1}H-NMR: $CDCl_3$ - δ 2.4504-2.5244 (s, 3H, Ali-H), δ 3.1577-3.1599 (m, 2H, Ali-H), δ 3.4379-3.4679 (m, 2H, Ali-H), δ 3.8511-3.8645 (s, 2H), δ 7.3461-7.9736 (m, 10H, Ar-H)

IR SPECTRUM OF THE COMPOUND 1(b)



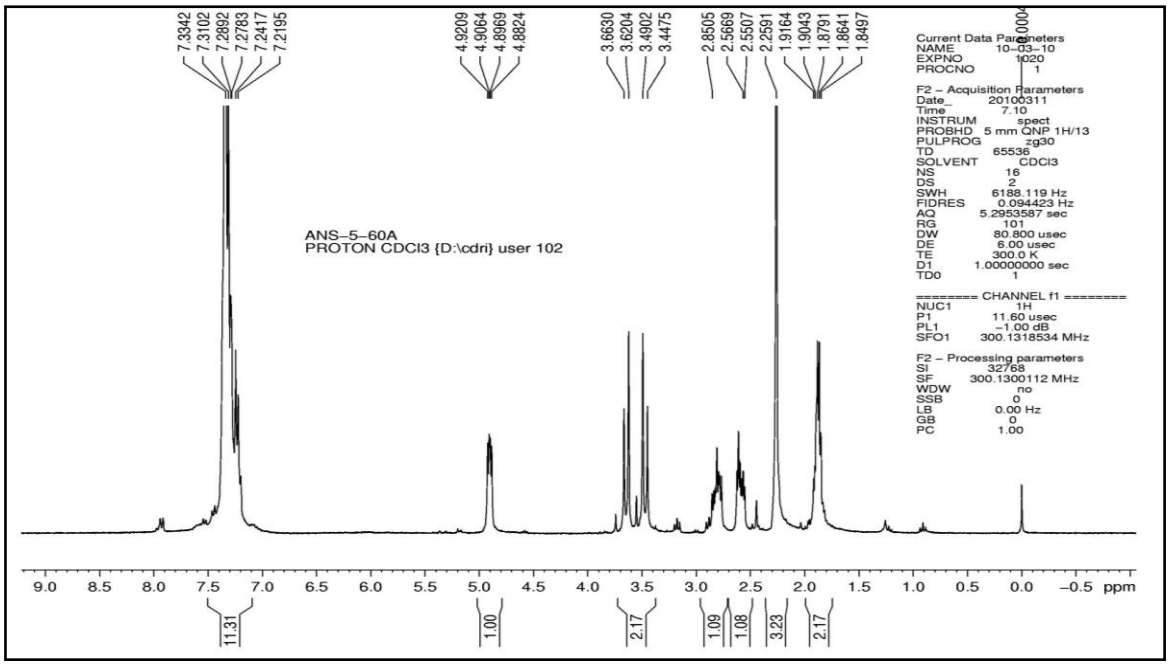
Functional Group	IR Frequency (cm^{-1})
O-H	3247.8
C-H(bend $–CH_2$-)	1455.6
C-N	1345.2
C-O	1033.2
C-H (Ar oop)	742.1

MASS SPECTRUM OF THE COMPOUND 1(b)



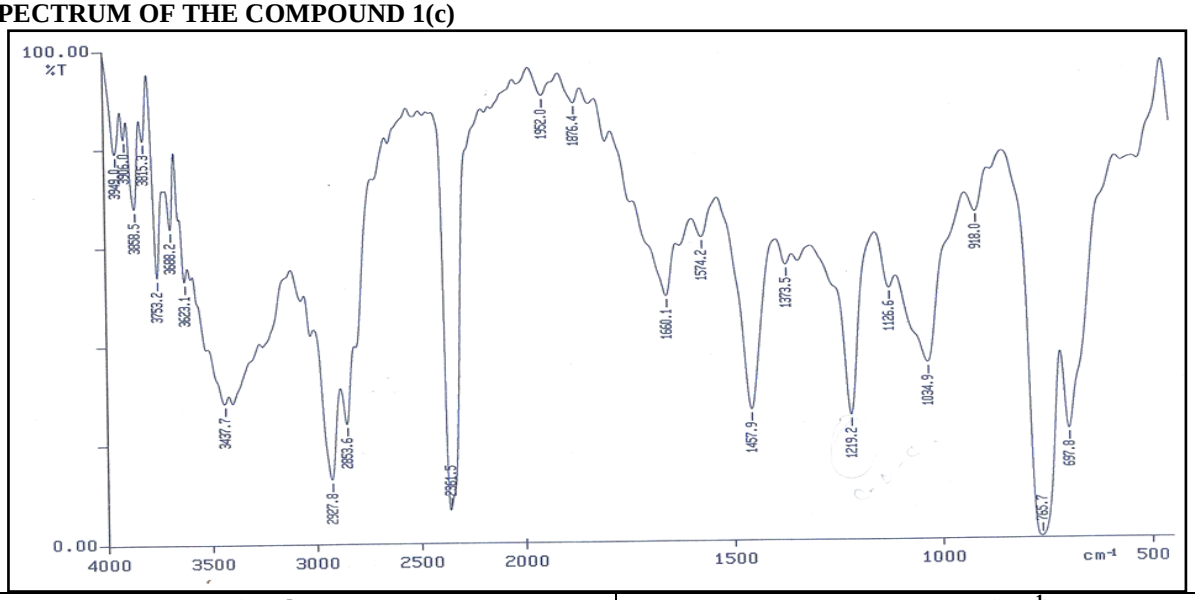
Calculated Molecular weight	Molecular ion peak	Interpretation
255	256	M^++1

NMR SPECTRUM OF THE COMPOUND 1(b)



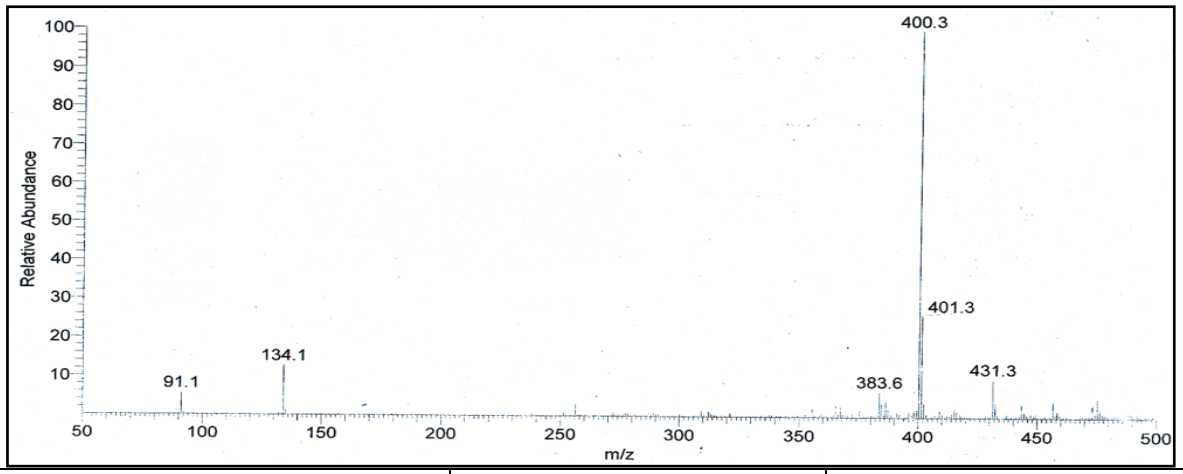
^{1}H-NMR: $CDCl_3$– δ 1.84-1.91 (m, 2H, Ali-H), δ 2.25 (s, 3H, Ali-H), δ 2.55-2.56 (m, 1H, OH), δ 2.85 (m, 1H, Ali-H), δ 3.44-3.66 (dd, 2H, Ali-H), δ 4.8824-4.9209 (m, 1H, Ali-H), δ 7.2195-7.3342 (m, 10H, Ar-H)

IR SPECTRUM OF THE COMPOUND 1(c)



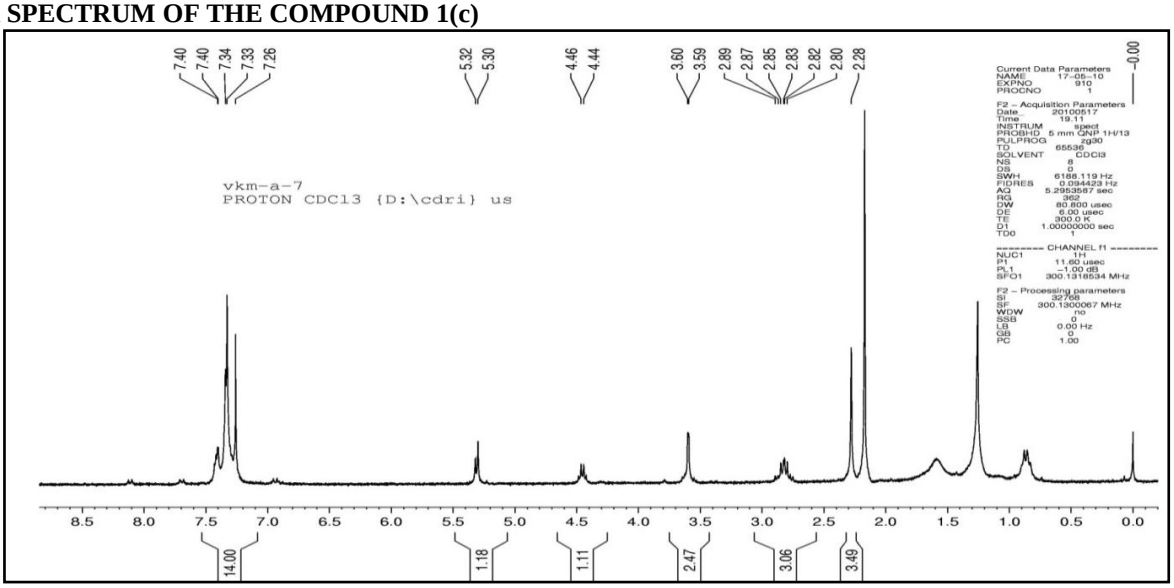
Functional Group	IR Frequency (cm^{-1})
C-H (Ar)	2927.8
C-N	1457.9
C-O-C	1219.2
C-F	1034.9
C-H (Ar oop)	765.7

MASS SPECTRUM OF THE COMPOUND 1(c)



Calculated Molecular weight	Molecular ion peak	Interpretation
399	400	M^{+}+1

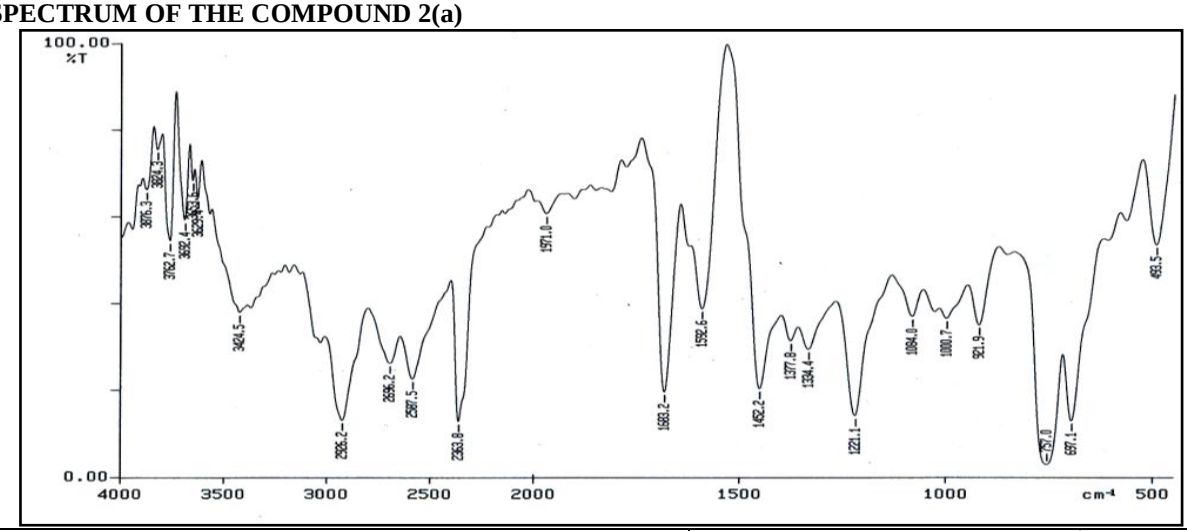
NMR SPECTRUM OF THE COMPOUND 1(c)



^{1}H-NMR : $CDCl_3$– δ 2.28 (s, 3H, Ali-H), δ 2.80-2.89 (m, 3H, Ali-H), δ 3.59-3.60 (m, 2H, Ali-H), δ 4.46-4.44 (m, 1H, Ali-H), 5.30-5.32 (m, 1H, Ali-H), 7.33-7.40 (m, 14H, Ar-H)

Spectral Data of Compound 2

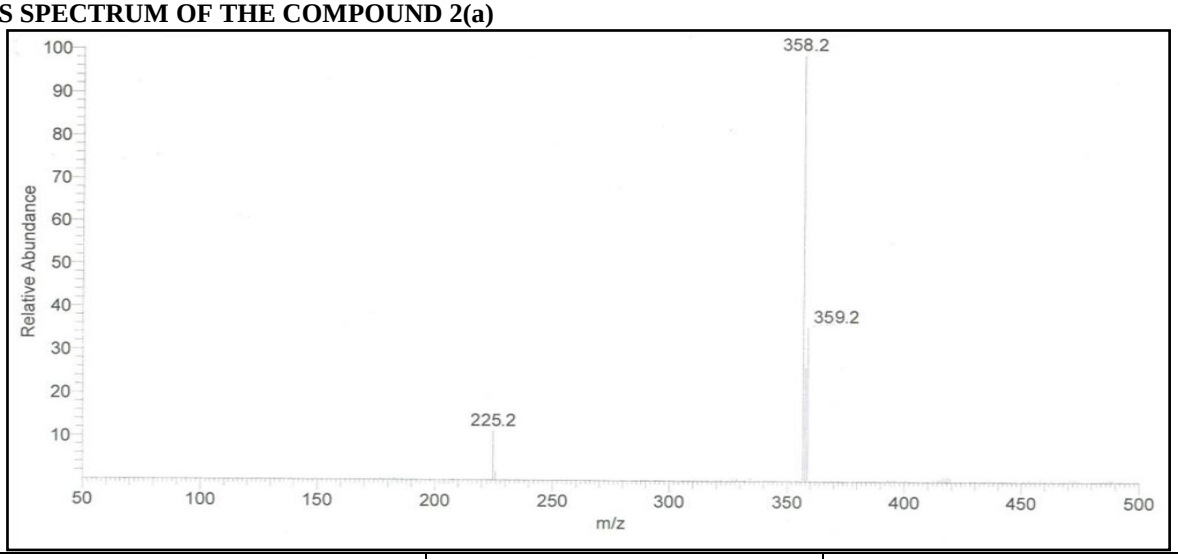
IR SPECTRUM OF THE COMPOUND 2(a)



Functional Group	IR Frequency (cm^{-1})
C-H (Ar)	3424.5

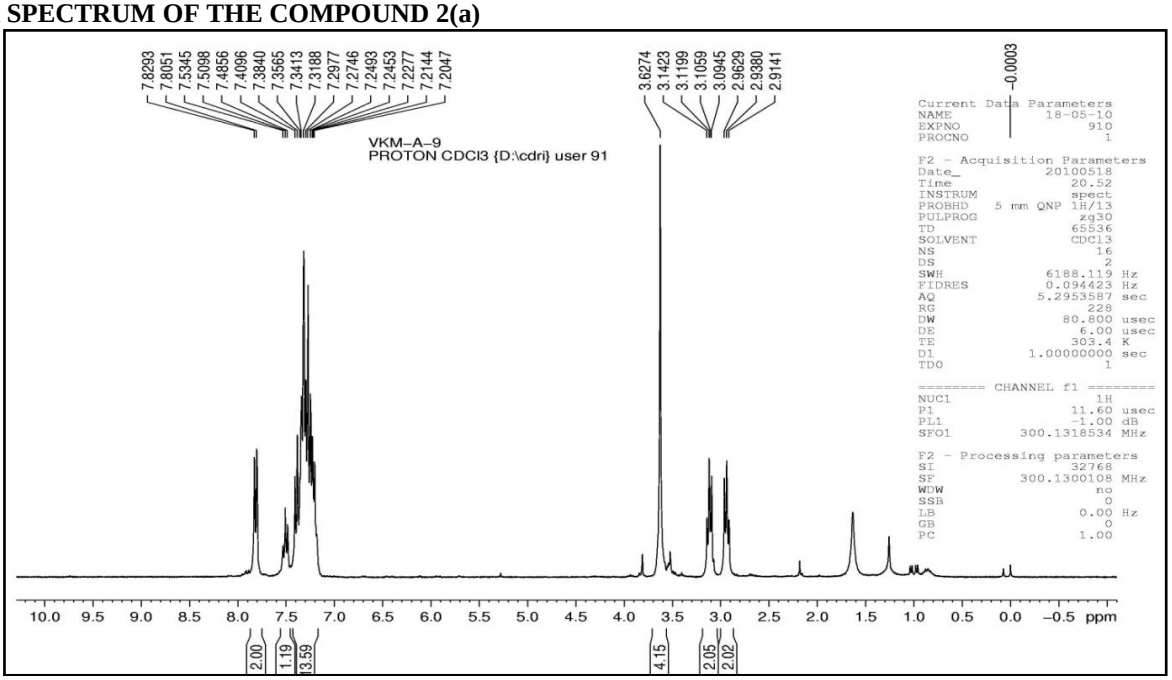
C-H (Ali)	2926.2
C=O	1683.2
C-N	1221.1
C-H(Ar oop)	757.1

MASS SPECTRUM OF THE COMPOUND 2(a)



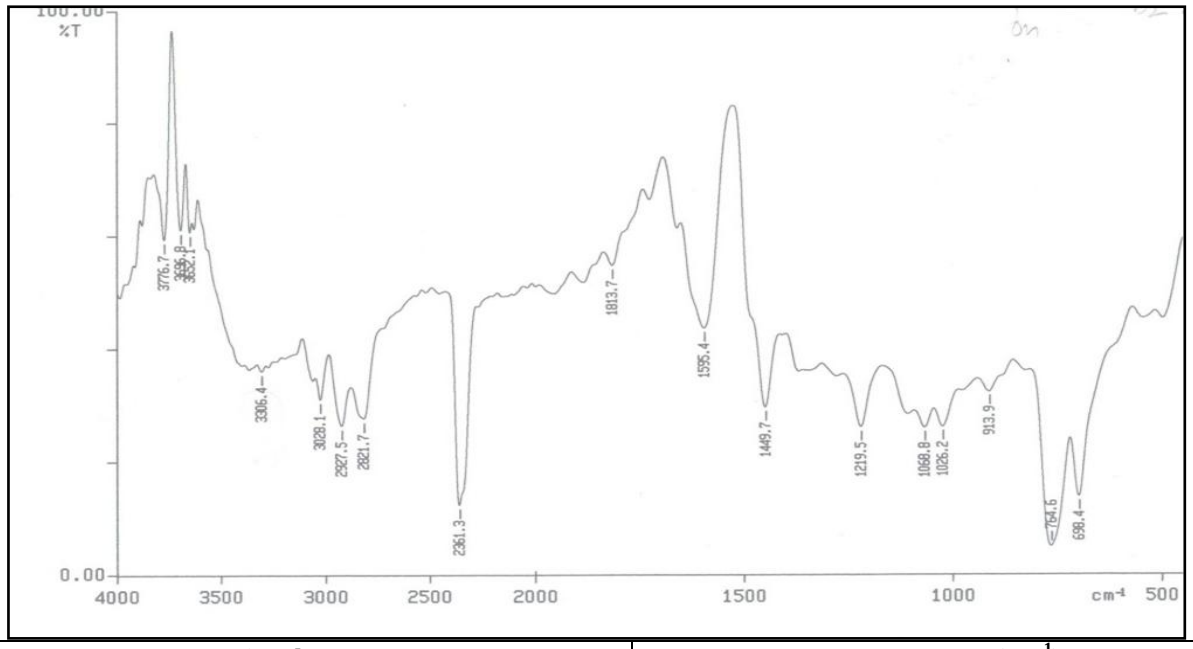
Calculated Molecular weight	Molecular ion peak	Interpretation
357	358	M^{+}+1

NMR SPECTRUM OF THE COMPOUND 2(a)



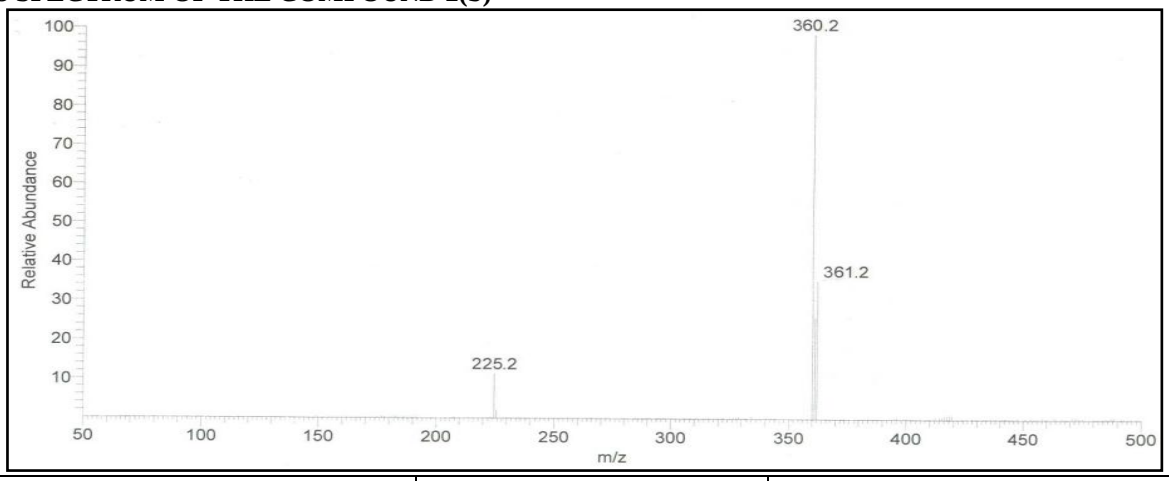
^{1}H-NMR : $CDCl_3$– δ 2.91-2.96 (m ,2H, Ali-H), δ 3.09-3.14 (m, 2H, Ali-H), δ 3.62 (s, 4H, Ali-H), δ 7.20-7.40 (m, 12H, Ar-H), δ 7.48-7.53 (m, 1H, Ar-H), δ 7.80-7.82 (m, 2H, Ar-H)

IR SPECTRUM OF THE COMPOUND 2(b)



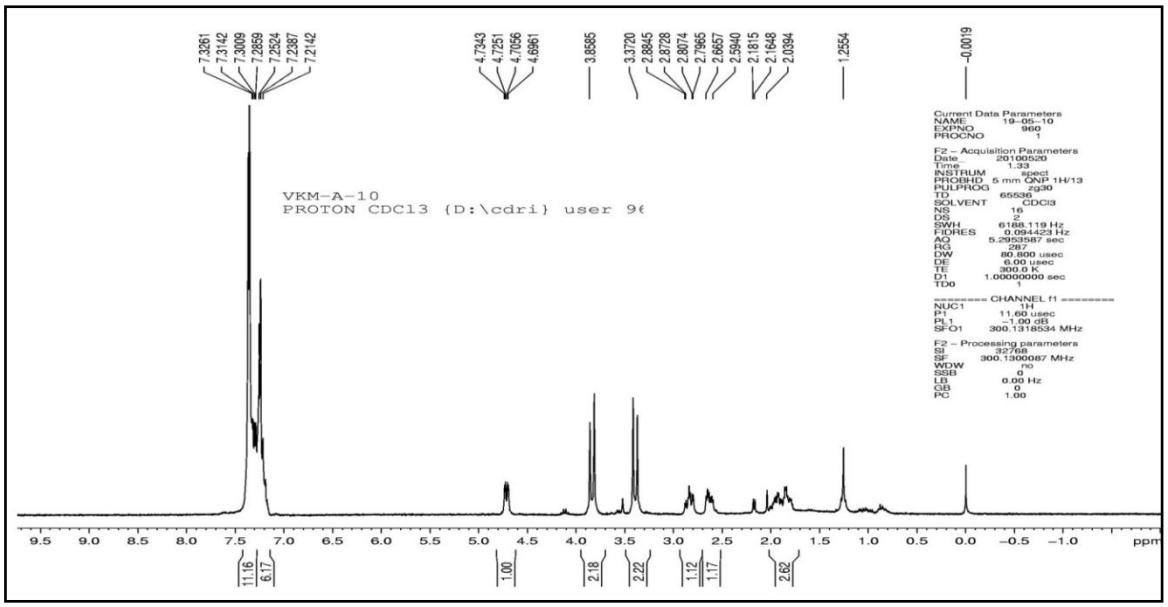
Functional Group	IR Frequency (cm^{-1})
O-H	3306.4
C-H (Ali $–CH_2-$)	1449.7
C-N	1219.5
C-H (Ar oop)	764.6

MASS SPECTRUM OF THE COMPOUND 2(b)



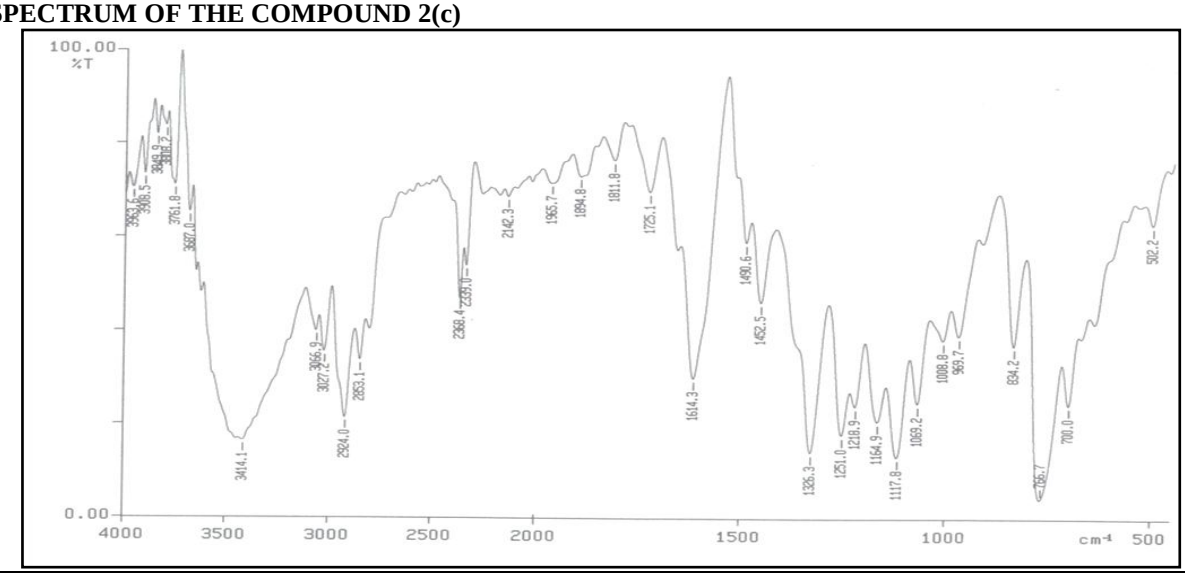
Calculated Molecular weight	Molecular ion peak	Interpretation
359	360	M^++1

NMR SPECTRUM OF THE COMPOUND 2(b)



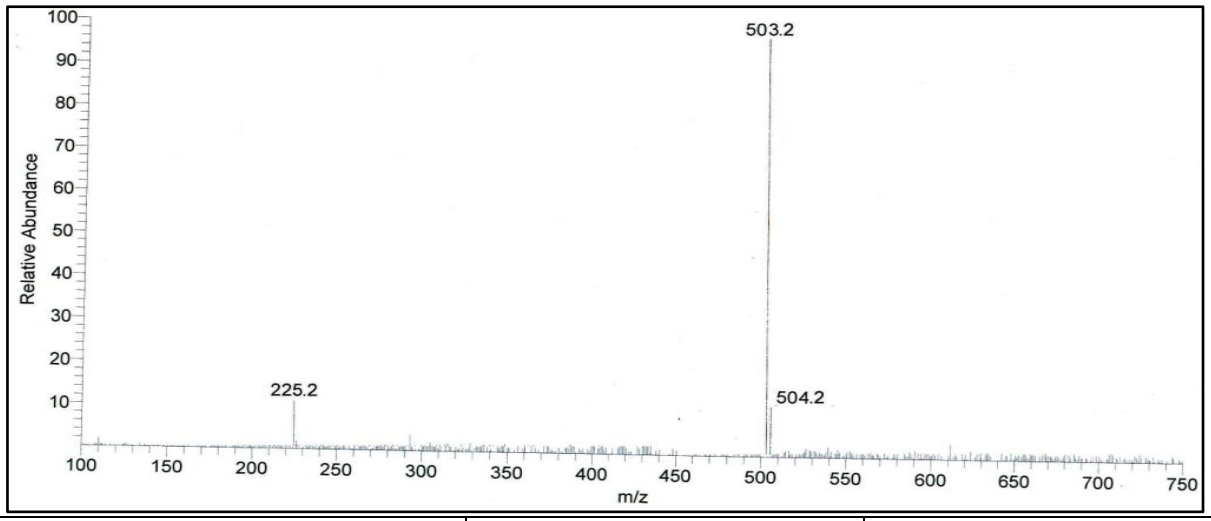
^{1}H-NMR : $CDCl_3$– δ 2.0394- 2.1815 (m, 2H, Ali-H), δ 2.5940-2.6657 (m, 1H, Ali-H), δ 2.7965-2.8845 (m,1H, Ali-H), δ 3.3720 (m, 2H, Ali-H), δ 3.8585 (m, 2H, Ali-H), δ 4.6961-4.7343 (m, 1H, OH), δ 7.2142-7.3261 (m, 15H, Ar-H).

IR SPECTRUM OF THE COMPOUND 2(c)



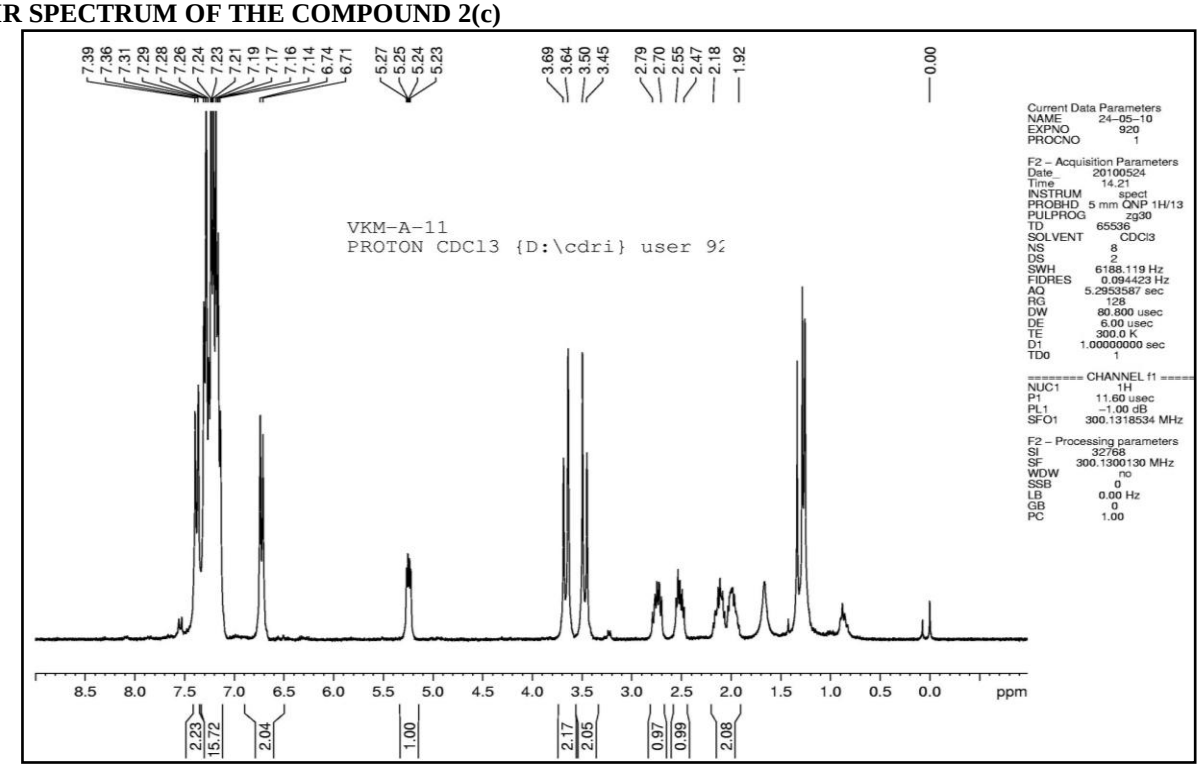
Functional Group	IR Frequency (cm^{-1})
C-H (Ali)	2924.0
C-N	1326.3
C-O-C	1251.0
C-F	1117.8
C-H (Ar oop)	766.7

MASS SPECTRUM OF THE COMPOUND 2(c)



Calculated Molecular weight	Molecular ion peak	Interpretation
503	503	M^+

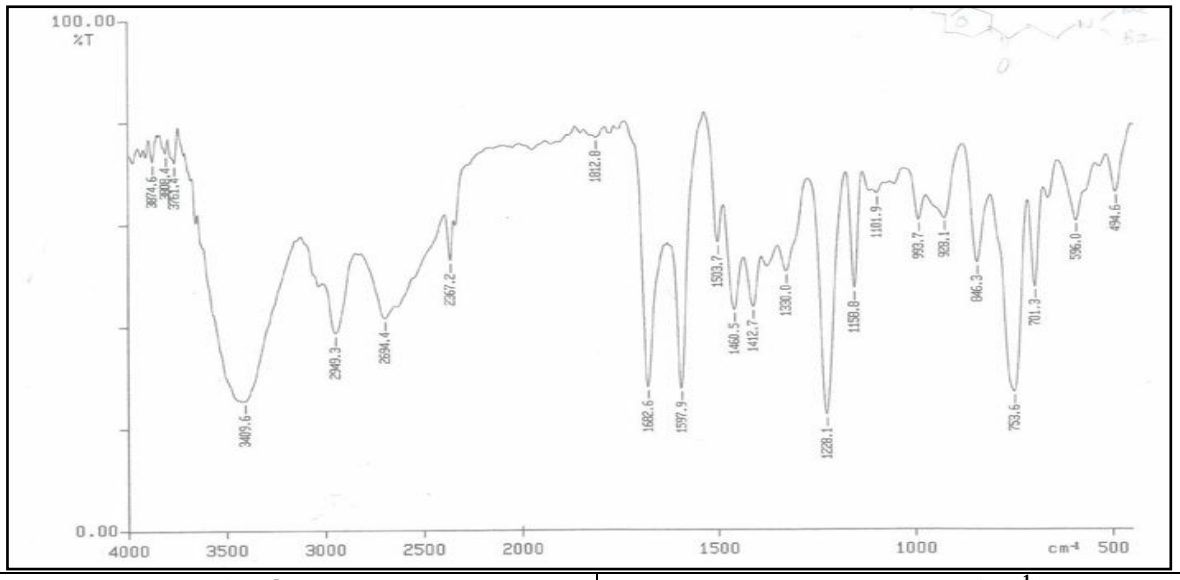
NMR SPECTRUM OF THE COMPOUND 2(c)



^{1}H-NMR : $CDCl_3$ – δ 1.92-2.18 (m, 2H, Ali-H), δ 2.47-2.55 (m, 1H, Ali-H), δ 2.70-2.79 (m, 1H, Ali-H), δ 3.45-3.50 (m, 2H, Ali-H), δ 3.64-3.69 (m, 2H, Ali-H), δ 5.23-5.27 (m, 1H, Ali-H), δ 6.71-6.74 (m, 2H, Ar-H), δ 7.14-7.36 (m, 17H, Ar-H)

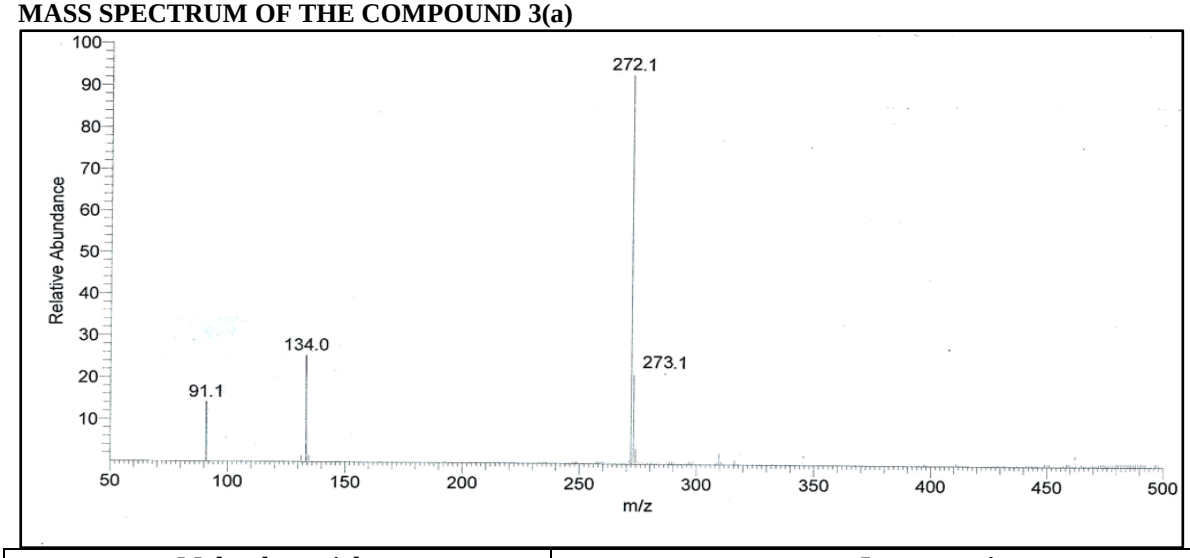
3.5.3 Spectral Data of Compound 3

IR SPECTRUM OF THE COMPOUND 3(a)



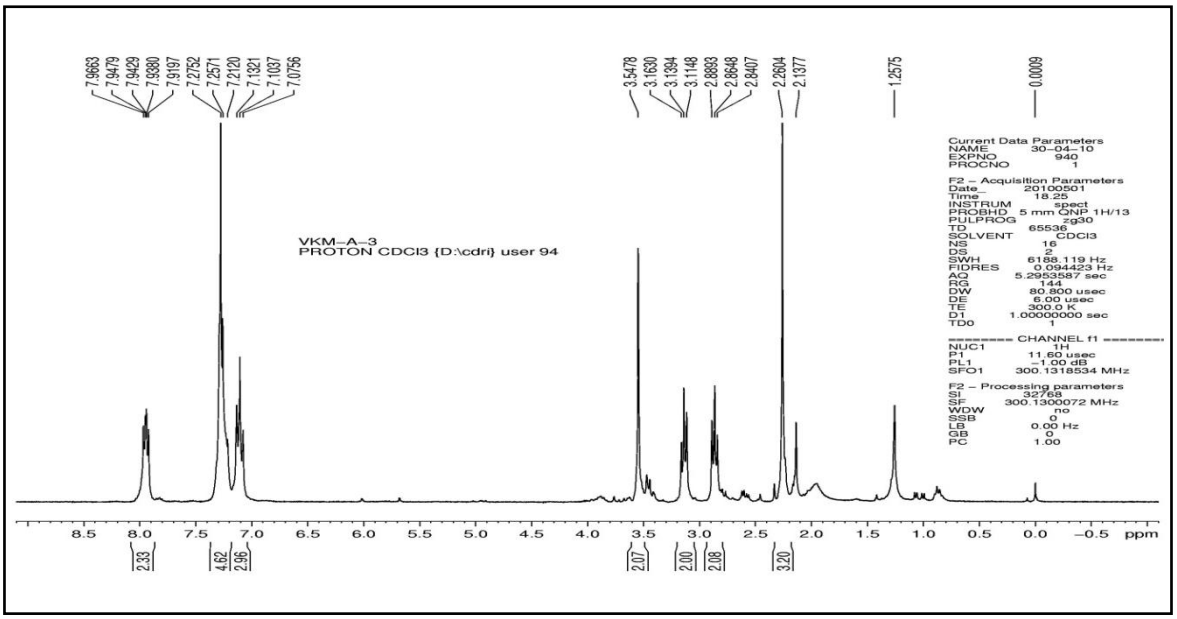
Functional Group	IR Frequency (cm^{-1})
C-H (Ali)	2949.3
C=O	1682.6
C-N	1228.1
C-F	1158.8
C-H (Ar oop)	753.6

MASS SPECTRUM OF THE COMPOUND 3(a)



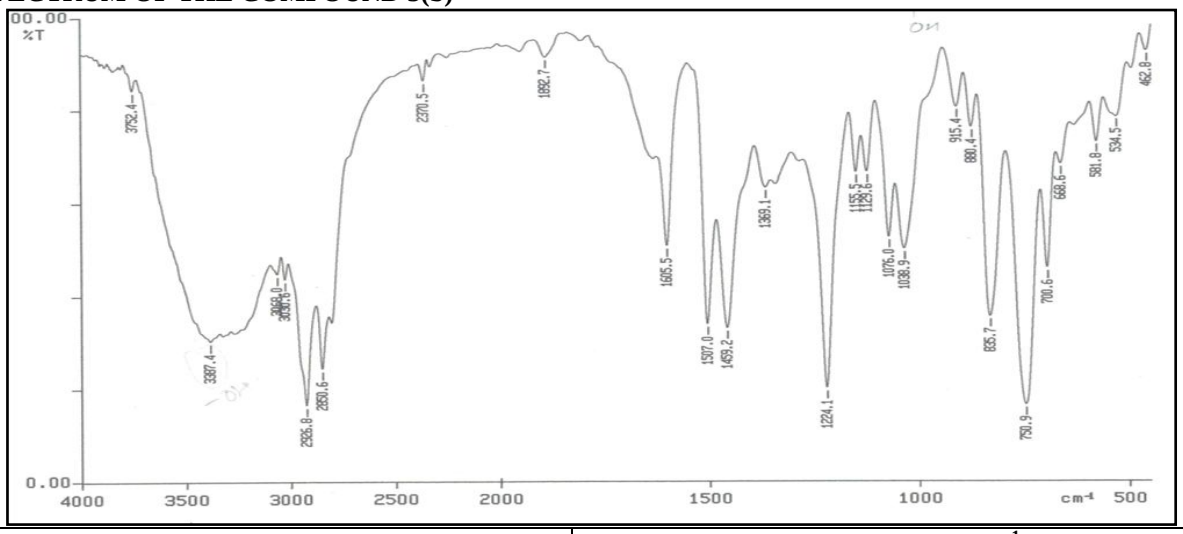
Molecular weight	Interpretation
271	M^{+}+1

NMR SPECTRUM OF THE COMPOUND 3(a)



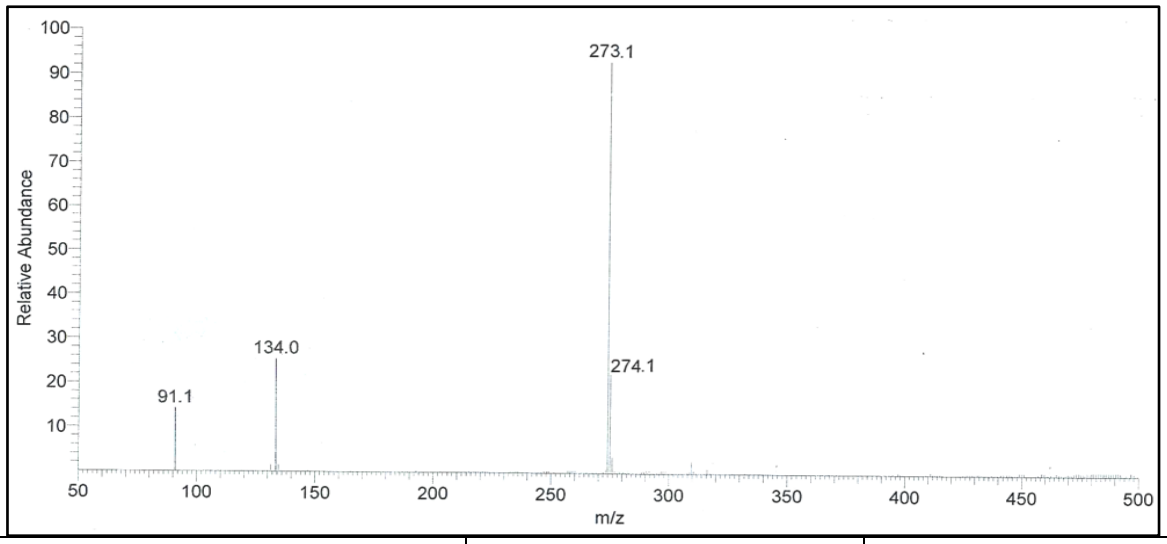
[1]H-NMR : $CDCl_3$– δ 2.2604 (s, 3H, Ali-H), δ 2.8407-2.8893 (m, 2H, Ali-H), δ 3.1148-3.1630 (m, 2H, Ali-H), δ 3.5478 (s, 2H, Ali-H), δ 7.0756-7.2752 (m, 7H, Ar-H), δ 7.9197-7.9663 (m, 2H, Ar-H).

IR SPECTRUM OF THE COMPOUND 3(b)



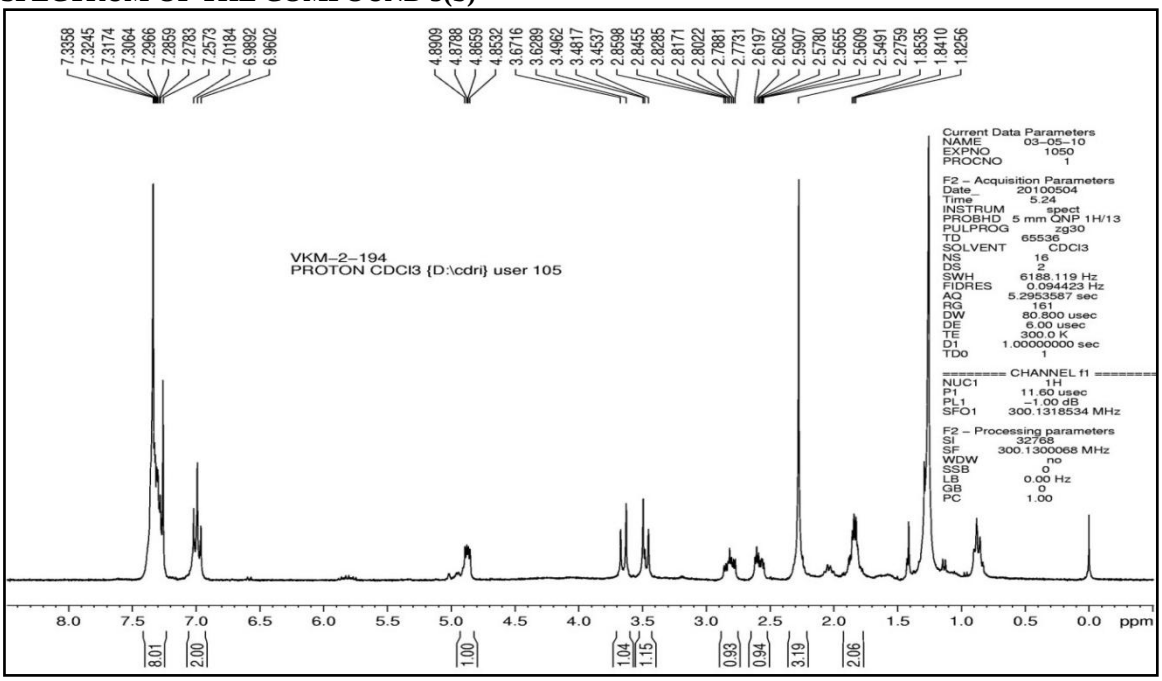
Functional Group	IR Frequency (cm^{-1})
-OH	3387.4
C-H (Ali)	2926.8
C-N	1224.1
C-F	1038.9
C-H (Ar oop)	750.9

MASS SPECTRUM OF THE COMPOUND 3(b)



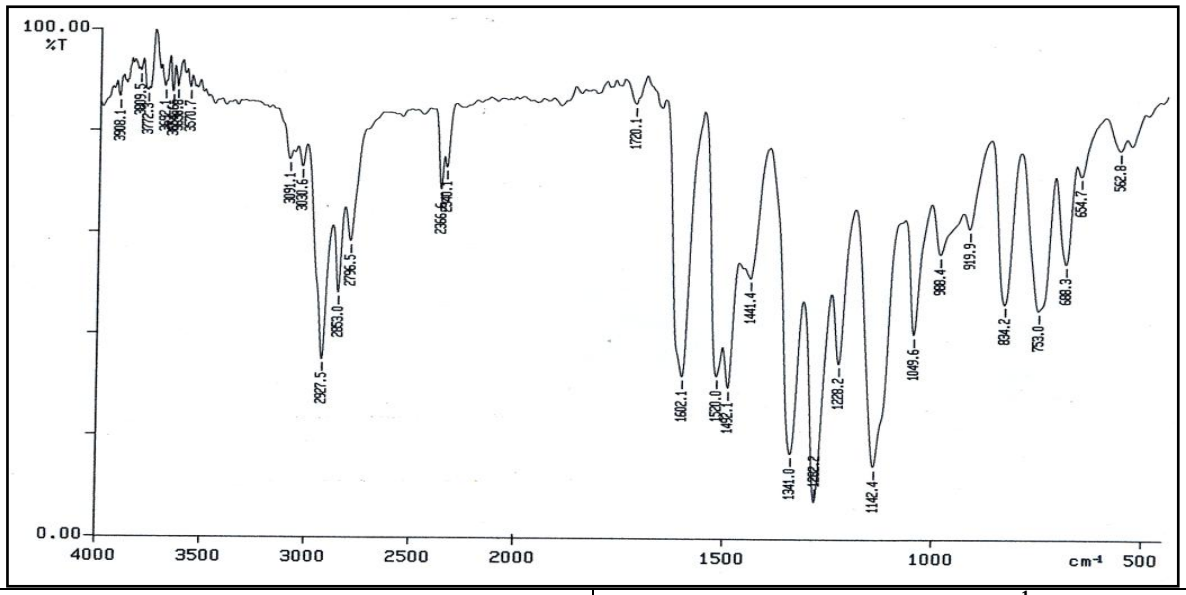
Calculated Molecular weight	Molecular ion peak	Interpretation
273	273	M^+

NMR SPECTRUM OF THE COMPOUND 3(b)



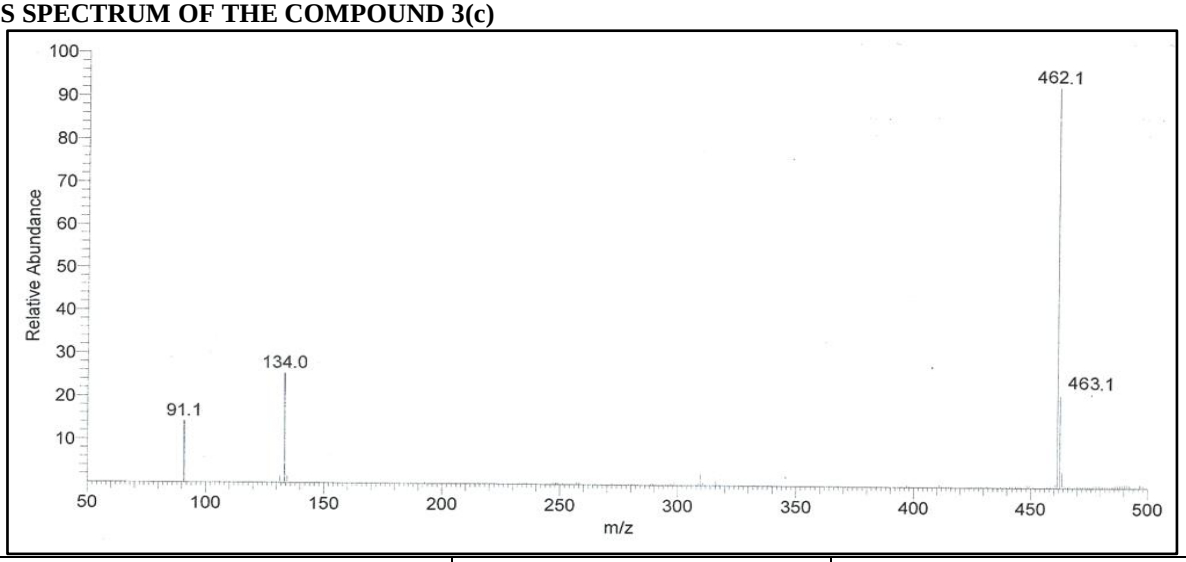
^{1}H-NMR : $CDCl_3$ – δ 1.8256-1.8535 (m, 2H, Ali-H), δ 2.2789 (s, 3H, Ali-H), δ 2.5491-2.6197 (m, 2H, Ali-H), δ 3.4597-3.6716 (m, 2H, Ali-H), δ 4.8532-4.8909 (m, 1H, Ali-H), δ 6.9602-7.0184 (m, 2H, Ar-H, OH), δ 7.2783-7.3358 (m, 8H, Ar-H)

IR SPECTRUM OF THE COMPOUND 3(c)



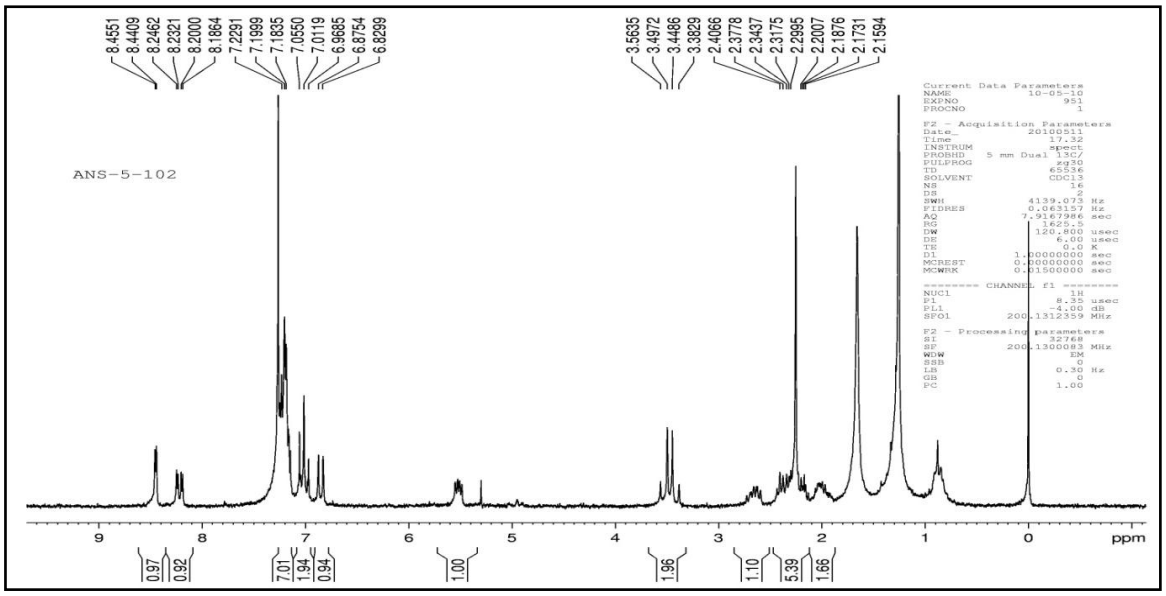
Functional Group	IR Frequency (cm^{-1})
C-H	2927.5
C-F	1341.0
C-N	1282.2
C-O-C	1142.4
C-H (Ar oop)	753.0

MASS SPECTRUM OF THE COMPOUND 3(c)



Calculated Molecular weight	Molecular ion peak	Interpretation
462	462	M^+

NMR SPECTRUM OF THE COMPOUND 3(c)



[1]H-NMR (δ ppm) – δ 2.16-2.20 (m, 1H, Ali-H), δ 2.30 (m, 5H, Ali-H), δ 2.32-2.41(m, 1H, Ali-H), δ 3.38-3.56 (m, 2H, Ali-H), δ (m, 1H, Ali-H), δ 6.83-7.25 (m, 9H, Ar-H), δ 8.19-8.25 (m, 1H, Ar-H), δ 8.44-8.46 (m, 1H, Ar-H).

CONCLUSION

The SSRIs are chemically distinct from traditional antidepressants like tricyclic, tetracyclic and monoamine oxidase inhibitors, but share the common route of selective and potent inhibition of neuronal reuptake of serotonin, and have none or very little effect on neuronal reuptake of norepinephrine, acetylcholine and histamine. Thus, these drugs have less sedative, anticholinergic and cardiovascular effects than other antidepressants of tricyclic and tetracyclic class. Fluoxetine, fluroxamine, sertraline, indalpine, paroxetine, alproclate, femorxetine and choroxamine belong to SSRI group of drugs.

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4. Rang, H.P.; Dale, M.M.; Ritter, J.M.; Moore, P.K(2006). *Pharmacology*, 5th ed.; Reed Elsevier: New Delhi, pp 535-549.